Tissue oxygenation as a target for goal-directed therapy in high-risk surgery

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MEETING ABSTRACTS

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P1

Minimising prescribing errors in the ICU

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Critical Care 2014, **18(Suppl 1):**P1 (doi: 10.1186/cc13191)

Introduction We aimed to audit the prescribing practice on a busy 14-bedd general ICU, and develop standardised practices and tools to improve safety. Prescribing errors occur as commonly as in 10% of UK hospital admissions, costing 8.5 extra bed days per admission, and costing the National Health Service an estimated £1 billion per annum [1]. The majority of these mistakes are avoidable [2].
Methods We audited the daily infusion charts of all patients in three separate spot checks, over 1 week. We assessed all aspects of prescriptions that make them legal and valid, in accordance with national guidance [3]. New procedures were introduced, which included a standardised prescription sticker, with common, pre-printed, infusion prescriptions on (noradrenaline, propofol, and so forth), and education on using the new prescription stickers. A month later the audit process was repeated.
Results We assessed 129 prescriptions in the first round, and 111 after intervention, demonstrating a 70% improvement in safe prescribing. Only 24% of prescriptions initially fulfilled best practice criteria, improving to 94% afterwards. We also reduced the number of infusions running without prescription, 7 (6%) versus 24 (19%). See Figures 1 and 2.
Conclusion Our audit supports the need for standardised prescribing practices within critical care, especially when dealing with potentially harmful vasoactive/sedative drugs. With a small, cost-effective intervention (£20 for 6,200 stickers), we improved prescribing accuracy, and thus patient safety in intensive care.

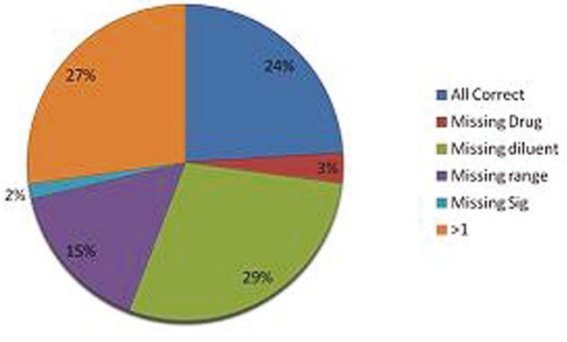

Figure 1 (abstract P1). Accuracy of prescriptions before intervention.

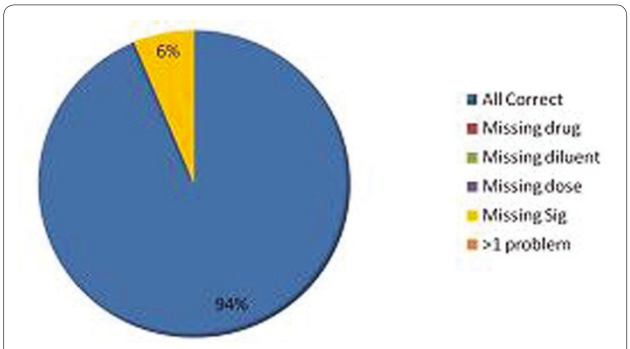

Figure 2 (abstract P1). Accuracy of prescriptions after intervention.

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P2

The Limpet controlled drug cabinet alarm and camera

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Critical Care 2014, **18(Suppl 1):**P2 (doi: 10.1186/cc13192)

Introduction The theft and tampering of controlled drugs (CDs) remains a prevalent patient safety issue. Sadly there are numerous reports of critical care staff stealing CDs for personal use or financial gain and notably there have been some cases where CDs have been substituted for other medications in order to delay detection of the theft. This creates both the hazard of medication errors and potentially exposes patients to opioid intoxicated healthcare workers. As most critical care staff have access to CDs, when drugs are found to be missing it can be difficult to identify the perpetrators. Therefore the implementation of a deterrent which also improves the methods of detection is warranted.
Methods The Limpet, a device which incorporates a proximity sensor and a camera unit, was installed within the CD cupboard of the critical care unit. Whenever the cupboard was accessed the date and time were recorded and a photograph was taken to identify the staff member. Mock thefts were subsequently undertaken by a designated staff member at random times. This allowed testing of the product to determine the number of times the 'thief' was correctly identified.

Results Mock thefts were successfully accomplished on six occasions over a 4-week period. On each occasion the Limpet photographed the 'thief' and recorded the date and time of access. Therefore, in the event of a real theft it would be possible to quickly and easily indentify the culprit.
Conclusion When CDs are missing it can be extremely stressful for the staff involved. Those who have access to CDs may feel unfairly scrutinised and the potential for false accusation exists. Investigating the theft of CDs is costly and usually involves pharmacists, managers and the police. Until the issue is resolved, potential suspects are usually suspended from work, leading to disruptions in patient care. The utility of the Limpet in modifying staff behaviour by reducing the number of occasions and the duration of time that open drug cupboards are left unattended, has previously been demonstrated [1]. By providing the facility to determine exactly who accessed each CD cupboard at which time, this initial study has shown the benefits of the Limpet as a tool for detecting theft. Therefore the installation of the Limpet mitigates the difficulties of investigating CD theft and is likely to prove an effective deterrent.
Reference
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P3
Role of pharmacist in multidisciplinary pediatric intensive care rounds: a retrospective descriptive study
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Critical Care 2014, **18(Suppl 1):**P3 (doi: 10.1186/cc13193)

Introduction Multidisciplinary rounding practices in the ICU have now become the standard of care in most institutions. Few objective data are available, however, on the value each individual member of the team brings to the patient care. In our institution, pediatric pharmacists have been an integral part of the PICU rounds since 2002, although their role has evolved over the course of years. This study was undertaken with the primary aim of identifying the impact of pharmacist involvement in PICU rounds, with respect to changes in therapy.
Methods Since January 2003, pharmacists have recorded their clinical interventions and outcomes of those interventions in an institutionally developed Pharmaceutical Care database (P-Care). An intervention is defined as any recommendation the pharmacist makes to the patient care team regarding a change in the patient management or medication therapy. P-Care is designed to assist the pharmacist to optimize medication therapy, identify medication-related problems, decrease medication costs, improve pharmacist efficiency and document pharmacist workload. Data concerning pharmacists' interventions were extracted from the P-Care database in yearly increments via a reporting functionality that is available in the P-Care system. This study was exempted for review by the Mayo Clinic IRB.
Results From 1 January 2003 through 31 December 2012 pharmacists made 24,207 clinical interventions in the PICU and 19,252 of those interventions resulted in changes in medication therapy or therapy monitoring. Interventions that were accepted by the team involved 10,361 (53.8%) drug dosing regimen changes, 292 (1.5%) drug interactions or incompatibility, 969 (5%) drug monitoring suggestions, 1,665 (8.7%) drug routes/methods of administration, 3,895 (20.2%) drug selections, and 2,070 (10.8%) medication profile/order clarifications. As the pharmacist role on the PICU multidisciplinary rounds has evolved, the number of interventions has increased from 1,643 in 2003 to 3,799 in 2012. Of the 19,252 interventions that were implemented, 304 were deemed to be of potentially life-threatening consequences, 10,767 had a moderate impact, and 8,181 had minimal impact on patient outcome.
Conclusion To our knowledge this is the largest reported data on pharmacist's involvement in pediatric intensive care. This can serve as background knowledge on implementing measures on novel methodologies to integrate pharmacists in intensive care practice.

P4
Improvement in the identification and management of inadvertent hypothermia in the critically ill: an audit cycle
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Critical Care 2014, **18(Suppl 1):**P4 (doi: 10.1186/cc13194)

Introduction The purpose of this study was to assess our practice in identifying and managing inadvertent hypothermia and whether this could be improved by education and introduction of a protocol. Hypothermia is associated with multiple physiological abnormalities including reduced myocardial contractility, peripheral vasoconstriction, increased infection risk and impaired coagulation [1]. Inadvertent hypothermia may therefore be an avoidable risk factor in the critically ill. The UK National Institute of Clinical Excellence has issued guidance for avoidance of inadvertent hypothermia (temperature <36°C) during the perioperative period. We audited our practice against three standards from these guidelines: all patients should have at least 4-hourly temperature observations; no patient should become inadvertently hypothermic; and all inadvertently hypothermic patients should be rewarmed.
Methods Data were collected prospectively. Body temperature was recorded routinely by nursing staff using a tympanic thermometer. We noted any occasion where the body temperature dropped below 36°C along with any associated interventions – such as the use of additional bed sheets or a forced air warming device. After the first audit period a simple education programme was delivered. We also introduced a departmental protocol for the prevention and management of inadvertent hypothermia. Six months later we re-audited our practice.
Results Data were collected from 130 patients (2,931 patient-hours) in the first audit period and from 87 patients (2,070 patient-hours) in the second audit period. In the first period 29% of patients had at least 4-hourly temperature measurements compared with 40% in the second period (P <0.01). The average number of overdue temperature observations per day was 1.4 in the first period and 0.9 in the second (P <0.01). Twenty-four per cent of patients became hypothermic in the first period compared with 22% in the second (P = 0.07); however, the time these patients remained hypothermic reduced from an average of 7.9 hours to 6.1 hours (P <0.01). An intervention was made and documented in 15% of cases in the first period and 46% in the second (P <0.001).
Conclusion We saw some improvement following an education programme and introduction of a clinical protocol although there remains room for further improvement.
Reference
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P5
Incidence of adverse events in a Brazilian coronary ICU
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Critical Care 2014, **18(Suppl 1):**P5 (doi: 10.1186/cc13195)

Introduction Security policies for the patient are an interest to any health professional. The rates of adverse events in hospitals reach values ranging between 3.7 and 16.6%, being the highest range (40 to 70%) considered preventable or avoidable [1]. The objective of this study is to analyze the incidence of adverse events and their severity in a Brazilian coronary ICU (CICU).
Methods Research conducted from database analysis regarding hospitalizations from 1 May 2012 until 31 October 2013 in a coronary care unit of the city of Presidente Prudente, Brazil. Statistical analysis was performed using EPI INFO, version 3.5.2 software, which was considered significant at P <0.05 two-tailed and CIs at 95% (CI) were used for the odds ratios (OR) estimated in the sample. Demographics (gender and average age) and aspects related to adverse events were analyzed, the latter being under the impact and probability of death.

Results A total of 1,067 admissions were analyzed in the period, with 57.38% male and 42.63% female. The average age was 67.7 ± 13.2 years. The average CICU length of stay was 3.74 ± 5.51 days. A total of 211 adverse events occurring in 140 different admissions were recorded. The most frequent were drug administration errors (24.3%), pressure ulcer (24.3%), phlebitis (22.1%), loss of enteric tube (13.6%) and central venous cannulation accident (7.1%). The statistical analysis shows that hospitalization time longer than 2 days are related to the occurrence of the events (OR: 8.08 CI: 4.95 to 13.2) and that the presence of the first occurrence is significant to increase the probability of death in the unit (OR = 5.33, CI: 3.49 to 8.12). Pressure ulcer (OR = 16.73, CI: 8.04 to 34.81), enteral tube loss (OR 3.64, CI: 1.36 to 9.75) and drug administration errors (OR = 2.87, CI: 1.31 to 6.31) were also related to higher mortality.
Conclusion The research draws attention to a significant incidence of adverse events and shows that their occurrence implies an increase of death in the unit. Therefore, security measures should be employed for the reduction, and thus enhance the quality of service provided by health professionals to patients admitted to a coronary care unit.
Reference

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P6

Compliance of a ventilator-associated pneumonia care bundle in an adult intensive care setting

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Critical Care 2014, **18(Suppl 1):**P6 (doi: 10.1186/cc13196)

Introduction Ventilator-associated pneumonia (VAP) is the leading cause of death amongst hospital-acquired infections and is also linked to an increased length of stay and cost of care. The Institute for Healthcare Improvement ventilator bundle is comprised of a series of interventions, which, when implemented together, have been shown to decrease the incidence of VAP. The aim of this study was to determine the compliance of the bundle and if <95% [1] devise strategies to improve compliance.
Methods A retrospective review of the compliance of an existing VAP bundle was conducted for all adult patients ventilated in the ICU of a large district general hospital in 2011. The bundle comprised four elements: head up 30°, peptic ulcer prophylaxis, deep vein thrombosis (DVT) prophylaxis and sedation hold. The bundle was considered compliant if all four were performed. The findings of the audit were presented to the department and, through subsequent discussions, barriers to noncompliance were identified. Following a period of education, a revised and updated bundle was implemented. A repeat audit covering 3 months was subsequently conducted.
Results Pre-intervention, overall compliance of the bundle stood at 32% and subsequently increased to 63% post intervention (P <0.05). Compliance at the level of individual elements varied: head up 30°, 94%; ulcer prophylaxis, 91%; DVT prophylaxis, 85%; sedation hold, 37%. Post intervention, a statistically significant increase in compliance with regard to sedation hold was observed; 72% (P <0.05). The other individual elements did not show a statistical change. However, the new elements that were introduced demonstrated high levels of compliance; cuff pressure 20 to 30 cm H_2O 83% and oral hygiene with chlorhexidine 90%.
Conclusion Post intervention, a statistically significant improvement in overall bundle compliance was found. Thereby highlighting that through engaging all members of the multidisciplinary team in identifying barriers to noncompliance and delivering education, it is possible to improve compliance. While total compliance was suboptimal as the target was 95%, the bundle redesign has given a tool that records compliance with greater clarity due to the presence of clearly defined exclusion criteria. It has also been a significant step in the right direction to improving the reliability of care delivered to patient and reinforces the concept that quality improvement is a continuous cycle.
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P7

Referrals to a critical care unit: compliance with the NCEPOD recommendations

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Introduction The report of the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) 2005 [1] provides recommendations to reduce morbidity and mortality among acutely ill patients. It highlights the importance for involvement of consultants in the referral process, clear physiological monitoring plans for each patient, and review by a consultant intensivist within 12 hours of admission to critical care. The objective of the audit was to assess compliance with these recommendations, ensuring safe management of acutely unwell patients and appropriate utilisation of scarce critical care resources.
Methods Prospective data on referrals to adult critical care in a 20-bed unit in a teaching hospital were collected over 8 weeks. Collected data included: source, time, seniority of doctor referring and receiving referral, outcome of referral, involvement of team consultant prior to referral, documented management plan and review by a critical care consultant within 12 hours of referral.
Results Seventy-three referrals were analysed, the majority of which were medical. One-half of referrals came out of hours; 24% of referrals were made by a consultant; 51% were seen by a consultant prior to referral; 73% of referrals were admitted; likelihood of admission increased from 63% to 83% if the patient was reviewed by home consultant prior to referral. In 56% of cases the referral was received by a foundation doctor (all referrals were discussed with a consultant intensivist). Among the rejected referrals (maximal ward therapy not reached), 54% were from a trainee below registrar grade. Twenty-five per cent of patients were not seen by a consultant intensivist within 12 hours of referral.
Conclusion Acutely unwell patients require the expertise of the most senior clinicians regarding further management, including planning for end-of-life care. Our audit demonstrated poor adherence to NCEPOD [1] and Department of Health [2] recommendations. The majority of referrals to critical care were made by nonconsultants and for patients who had not been reviewed by a team consultant, prior to referral. The workload in critical care demonstrated that almost one-half of the referrals happen out of hours. These findings have resulted in significant changes to working practice, including the presence of an onsite consultant intensivist for a minimum of 13 hours daily.
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P8

Organisational changes in service provision outside critical care impact on referral patterns

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Critical Care 2014, **18(Suppl 1):**P8 (doi: 10.1186/cc13198)

Introduction Demand for critical care (CC) resources is constantly increasing in the face of limited availability. Guidance for triage exists but may no longer reflect current practice [1,2]. We previously identified nonmedical and medical factors (comorbidities, physiological derangement and functional status) as predicting likelihood of admission of referred patients to CC [3-5]. Reduction in UK doctors' working hours and numbers has resulted in new ways of multidisciplinary teams working the hospital at night (H@N), which may have an impact on CC referral. We aimed to establish any effect of

hospital changes in service provision outside CC on the referral pattern and admissions.

Methods Data from prospectively enrolled urgent patient referrals were analysed comparing two periods: before (period 1: 2011/12) and after (period 2: 2013) the introduction of H@N. We collected data on acute physiological parameters, hospital length of stay, demographic and functional status, dependency and comorbidities. STATA was used for these preliminary analyses.

Results Comparing the two periods we found no significant differences in age, gender distribution, degree of acute physiological derangement, comorbidities, specialty of origin, time spent in hospital prior to referral and grade of referrer. By contrast, the proportion of out-of-hours referrals greatly increased (from 49.3% to 69.7%) along with the proportion of referrals deemed inappropriate for CC (from 37.3% to 54.8%); the proportion of patients accepted increased only marginally (from 46.7 to 50%) in the second period, compared with the first. Neither the number of beds available within the critical care department ($P = 0.59$) nor receiving the referral out of hours ($P = 0.8$) influenced the likelihood of admission. The factors predicting admission to CC (functional status, acute physiological derangement) did not differ significantly between the two periods examined. Housebound status was consistently found to be an independent predictor of admission refusal (OR 0.11, 95% CI 0.05 to 0.23, $P < 0.001$).

Conclusion Decision-making about admission to CC is based mainly on the assessment of patients' functional status. Organisational changes in the provision of healthcare services outside CC, such as H@N, have had a significant influence on CC workload and patterns of referrals.

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P9

Demand versus supply in intensive care: an ever-growing problem

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Critical Care 2014, **18(Suppl 1):**P9 (doi: 10.1186/cc13199)

Introduction The demand for intensive care has reached new heights, where medical advancement and aging populations have increased the proportion of patients with multi comorbidities. Ideally, bed occupancy on the ICU should be around 70% whereas beyond 80% has been associated with increased mortality. William Harvey Hospital is a district general hospital with nine ICU beds where the ICNARC national database suggested a consistently high occupancy. The purpose of this study was to assess bed occupancy and its impact on service delivery.

Methods Data were collected between 2005 and 2013 to analyse trends in ICU bed occupancy, overnight discharges, surgical cancellations, and nonclinical transfers. Data were gathered from April 2012 to March 2013 using quality indicators (Intensive Care Society): readmissions; premature discharges; discharges at night; cancelled planned surgery; and nonclinical transfers. Regression analysis was conducted to assess: correlation between mortality and effects of excess occupancy; and causality of increasing demand for ICU beds.

Results Bed occupancy remained high between 2005 and 2013 with a 15% increase. This was associated with increased overnight discharges (29%), surgical cancellations (90%), and nonclinical transfers (88%). Between 2012 and 2013, the calculated demand for beds was 174. There were 1.8 ICU to 100 hospital beds and 4.5 ICU beds per 100,000 population, which dropped significantly when including regional specialty services. A persistent gap between ICU bed supply and demand was associated with increased unfavourable outcomes in all quality indicators.

Conclusion A steady increase in occupancy over the last 8 years was due to multiple factors, including an increase in clinical services such as in the coronary care centre, head and neck unit, and trauma centre. Presentation of our results to managerial level facilitated increased bed capacity by 22%.

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P10

Demands on a continuing education online-study program for physicians

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Critical Care 2014, **18(Suppl 1):**P10 (doi: 10.1186/cc13200)

Introduction Physicians have an intense and irregular workday life. Thus, they need to use their time for continuing education in the most efficient way. This presents a major challenge to suppliers of continuing study programs. Our online master program Physico-Technical Medicine (PTM) addresses working physicians who want to acquire knowledge in the fields of biomedical engineering and medical physics [1]. We attach great importance to the special needs of our participants. Therefore, we investigated which general conditions are most important for the working physician regarding qualifying continuing education.

Methods The general conditions of our continuing education program (PTM) were examined on the basis of evaluation questionnaires. Additionally, students were asked in interviews about their demands, and they could give anonymous feedback on feedback cards.

Results *Flexibility*: students appreciated flexibility regarding time and environment of their learning activities. This flexibility enables the students to use even small time frames or traveling times for learning. Students can choose their preferred time and place for their learning activities. *Security in planning*: students have to organize their time frames for learning besides their daily work, their family life, and possibly their academic career. Especially phases of attendance should be planned and communicated as early as possible. *Transparency of structure*: participants ask for transparency in terms of the expected workload and expenditure of time to plan their studies and get focused. *Relation to previous knowledge*: learning success is supported by relating new contents to previous knowledge from the student's first medical degree. Mainly clinical examples illustrate abstract topics, which also helps students to recognize the relevance of the content. *Individual support*: students need contact persons in terms of learning organization, technical support, and for questions regarding the course material.

Conclusion We could show that an extra-occupational continuing study program for physicians should be adjusted to their special situation and therefore has to comply with particular requirements. As such we could identify five main requirements which are continuously fulfilled by the online master program PTM and regularly surveyed by evaluations.

Reference

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P11

Do generic measures fully capture health-related quality of life in adult, general critical care survivors?

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Critical Care 2014, **18(Suppl 1):**P11 (doi: 10.1186/cc13201)

Introduction We examined the extent to which the two generic health-related quality of life (HRQL) measures recommended for use in adult, general critical care [1] – the SF-36 and EQ-5D – captured survivors' HRQL, which is important in assessing the effectiveness of critical care. Unlike other fields of healthcare that employ both generic and specific HRQL measures, most recent studies in critical care have used only generic measures, despite uncertainty as to their appropriateness.
Methods A patient-based conceptual framework for survivors' HRQL was built using: a systematic review of the literature; secondary analysis of 40 in-depth interviews with adult critical care survivors; and primary analysis of in-depth interviews with a maximum variation sample of 25 white critical care survivors in England. Two methods were then used to assess the extent to which the SF-36 and EQ-5D captured their HRQL, as detailed in the framework: the content of both instruments was examined, alongside data collected from the in-depth interviews; and the opinions that survivors expressed about how accurately the SF-36 and EQ-5D reflected their ideas on health and HRQL were analysed and taken into account.
Results The patient-based framework was in two parts: the first covered survivors' personal status which consisted of their physical status, emotional/psychological status and cognitive status; and the second comprised nine subdomains affected by their personal status. The latter were: activities and behaviours; physical zone of comfort and/or activity; interactions and relationships with others; perception of, interpretation of, and responses to life; personality; external appearance; suitability and availability of clothes; place of residence; and finances. The current generic measures recommended on the basis of expert consensus for use with survivors of adult, general critical care have substantial gaps in their coverage of this conceptual framework for survivors' HRQL, particularly in relation to their cognitive status and its subsequent impact.
Conclusion The two most commonly used generic HRQL measures in adult, general critical care have significant gaps in their coverage of survivors' HRQL. Any (new) critical care-specific HRQL measure should be designed specifically to capture the impact of critical illness on survivors' cognitive status and its subsequent effects.

Reference

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P12

Surgical HDU admissions: utilisation, organ support and finance

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Critical Care 2014, **18(Suppl 1):**P12 (doi: 10.1186/cc13202)

Introduction The aim was to explore the HDU booking process, organ support requirements and financial implications as the current approach to booking surgical cases for HDU has somewhat been based on a 'just in case' principle.
Methods The booking and admission details from October 2012 to July 2013 were gathered from the HDU log-book and Ward Watcher software. The cost of HDU beds and staff were provided by the finance department. Data were analysed using MS Excel and SPSS software.
Results There were 105 handwritten bookings over 10 months, several missing essential data. Only 89 admissions actually took place; 61 were elective, 66 colorectal, six urgent, 19 scheduled and three unspecified (Figure 1). Most patients required basic cardiovascular and respiratory support (Figure 2). Data revealed 16 cancellations. Each booking requires allocated nursing staff which bears a basic cost of £23/hour (estimated annual loss >£10.000). If we add the daily cost of basic HDU care (approximately £1,000 for single organ support), the losses rise rapidly. We also registered 38 days in delayed discharges. This was predominantly due to ward bed shortages. In financial terms there is at least £500/day difference between surgical and HDU (potential annual loss >£22,000). In addition there were 13 patients who spent a total of 37 days on the HDU but did not require an HDU level of care.
Conclusion The currently limited resource is not being utilised effectively with implications on both staff deployment and finances. A more holistic approach is needed where all requests are reviewed by a consultant anaesthetist in conjunction with preadmission data. This could better identify patients for HDU care and potentially decrease cancellations. We have developed an improved booking form for this purpose.

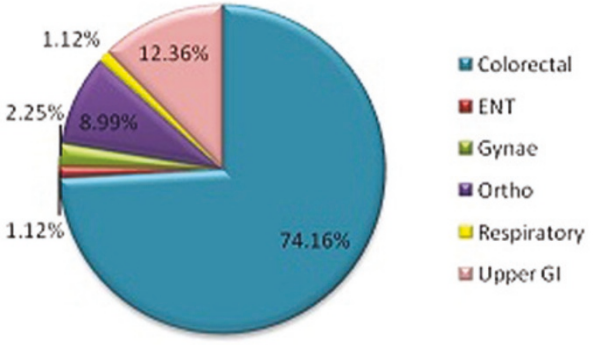

Figure 1 (abstract P12). Admissions per speciality.

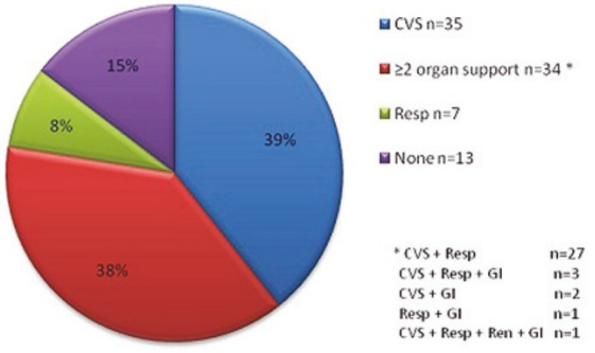

Figure 2 (abstract P12). Organ support requirements.

P13

Convalescence via critical care collaboration

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Critical Care 2014, **18(Suppl 1):**P13 (doi: 10.1186/cc13203)

Introduction A collaborative approach to patient management has been shown to improve patient outcomes. In a resource-limited NHS, critical care beds are at a premium, therefore preventing unnecessary admissions by optimising ward-based management is essential. The objective of this service quality improvement project was to improve collaboration between the critical care directorate and neurosurgical high care unit at a tertiary university teaching hospital. We proposed that the use of a simple ward round tool on collaborative rounds would facilitate systematic patient review, prompt early recognition of those critically unwell and improve patient outcomes.
Methods An initial observation period of behaviours and practice on the neurosurgical unit was conducted with qualitative and quantitative data collection. Following analysis of these outcome measures a simple ward round tool was constructed, with the mnemonic 'DON'T FORGET', and we devised a programme for collaborative ward rounds to take place three times per week over a 1-month period. During this

time further data were collected to assess whether our interventions resulted in modified behaviours and to document the number of changes made to patient management as a consequence of the collaborative approach to care.
Results Our results showed that improvements were made in all assessed domains. Consultant-led ward rounds increased, attendance by members of the multidisciplinary team (MDT) dramatically improved and as a result MDT discussion was enhanced. In addition, documentation of structured plans improved and review of prescription charts significantly increased. As a consequence of collaborative rounds, a total of 343 changes were made to patient management under the domains of the ward round tool. This was an average of 21.4 changes per collaborative round, with most changes being made to medication charts or decisions regarding thromboprophylaxis.
Conclusion The use of a simple ward round tool combined with a collaborative approach to ward rounds improved MDT involvement and discussion, promoted structured patient review and resulted in positive changes to multiple areas of patient management. In conclusion, structured collaborative rounds result in significant changes to patient management that may prevent admission, or readmission, to critical care which has the potential to reduce healthcare costs and morbidity.

P14

Can dynamic light improve melatonin production and quality of sleep?

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Introduction Hospital lighting may cause disruption in the circadian rhythm, partly due to suppression of melatonin production. This may create sleep difficulties and delirium for ICU patients and health issues such as fatigue, poor sleep quality and chronic diseases for ICU staff. Dynamic RGB coloured light which changes colour and intensity in correlation with the time of day has been installed in a Danish ICU, aiming to create lighting conditions being close to daylight variations and supporting patient and staff rhythms. As the effect of dynamic light on patients may be biased by illness, organ failure, and so forth, the aim was to examine the influence of dynamic light on ICU nurses' melatonin production, quality of sleep, and well-being.
Methods An intervention study examining the impact of dynamic light regarding the impact on the circadian rhythm (measured by melatonin profiles from saliva samples), quality of sleep (sleep efficiency, number of awakenings and subjective assessment of sleep; measured by sleep monitors and sleep diary), and subjective experiences of well-being, health, and sleep quality (measured by a questionnaire survey). Results from the intervention group were compared with a control group of nurses from a similar ICU without dynamic light. Light conditions were documented by measurements. Data collection was from February to May 2013.
Results A total of 55 nurses (89%) from the intervention ICU (ICU1) and 58 nurses (88%) from the control ICU (ICU2) participated. No significant differences were found between the two groups regarding personal characteristics. The nurses from ICU1 described their work light as comfortable, relaxing and natural compared with artificial, institutional and gloomy in ICU2. Preliminary analyses did not shown any significant differences in melatonin level. During a 10-day period, the nurses from ICU2 assessed their actual sleep as less effective (OR 2.17; $P = 0.03$) and felt less rested (OR 1.89; $P = 0.006$) compared with nurses from ICU1. The nurses in ICU2 had 16% more awakenings ($P = 0.05$) during sleep, but there were no significant differences in duration of awakenings or in total sleep efficiency between the two groups.
Conclusion Most participants from the intervention ICU found the dynamic light agreeable and assessed their sleep more positively than participants from the control ICU. No significant differences were found between monitored sleep efficiency and melatonin level.

P15

Targeting blood tests in the ICU may lead to a significant cost reduction

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Introduction Daily blood tests are an essential diagnostic tool and routine practice in the management of ICU patients, but are associated with cost and a risk of anaemia. There is no evidence for the frequency or breadth of blood testing but there is evidence that by rationalising blood tests, significant cost saving can be made without a negative effect on mortality or length of ICU stay [1]. Blood tests in our ICU are requested by nurses, this is a unique practice to the ICU compared with other hospital departments.
Methods We had previously carried out a survey to assess blood requesting practise in UK ICUs. This demonstrated that routine tests were, as in our ICU, nurse led and the majority of staff underestimated the costs of tests. Using the results of this survey and a literature review we developed routine blood test guidelines for our general mixed 26-bed ICU/HDU. Following a period of staff education, we audited our blood requesting practice over 28 days.
Results Our blood testing did not comply with our guidelines. Over the 28-day period, €12,849.96 was spent on all blood tests. According to our guidelines, €2,914.96 was spent on inappropriate tests (€37,998.63 per year) (Table 1). Over 40% of this cost was spent on the coagulation screen.

Table 1 (abstract P15)

Test	Number of inappropriate requests	28-day cost (€)	Annual cost (€)
Full blood count	4	21.82	284.44
Urea and electrolytes	6	29.44	383.77
Liver function tests	95	583.18	7,602.1
Coagulation screen	117	1,276.86	16,644.78
C-reactive protein	45	245.55	3,200.91
Bone profile	112	274.75	3,581.56
Magnesium	88	483.35	6,300.81

Conclusion In our ICU, unnecessary blood tests have a significant cost burden of approximately €38,000 per year. To limit unnecessary costs, consultants now lead requesting by completing a blood test *pro forma* on the evening ICU ward round indicating which blood tests are clinically needed the following day.
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P16

Analysis of the acoustic environment in an ICU using patient information as a covariate

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Introduction Noise levels in ICUs are often very high, potentially affecting patient health outcome, which are also considered to be among the risk factors contributing to ICU delirium [1]. In the current study, multivariate linear regression models were established to relate the acoustic data to the indicators of patient status.
Methods Acoustic measurements were taken in eight single-bed patient rooms in a level 3 ICU, while patient information was also collected, including APACHE IV score and mortality rate together with other potentially relevant variables; for example, the usage of mechanical ventilators, and so on. The hourly and daily trends of the acoustic data were obtained, and an analysis of variance was carried

out to investigate the effect of relevant factors (for example, the time of day). Furthermore, multiple linear regression models were established to relate the different types of patient-related data (as independent variables) to each type of the acoustic data (as dependent variable), where independent variables were selected based on an exhaustive search method.

Results Data were collected for 3 months for 106 patients. The 24-hour trends of acoustic parameters corresponded well to the daily routine events in the ICU. The analyses for the first 4 days of the patients' ICU stay showed that the average SPL varied depending on the day ($P = 0.023$) and on the time of the day (day/night) ($P < 0.001$). The average noise level decreased from day 1 to day 2 with a significant reduction at night ($P = 0.008$), but it was found to rebound from day 2 where the increase of the daytime noise level from day 2 to day 4 was significant ($P = 0.005$). The results of the multiple linear regression showed that various patient conditions influenced different types of noise-level parameters. For example, the location of the patient room, the usage of mechanical ventilators and the mortality rate were found to correlate to the 10th-percentile SPL (L90) in the first 48 hours (adjusted $R^2 = 0.58$; $P < 0.001$). Also, the room location, gender and the usage of mechanical ventilators were found to be related to the 50th-percentile SPL (L50) in the same period (adjusted $R^2 = 0.54$; $P < 0.001$).

Conclusion Noise-level parameters were found to vary depending on the day of ICU stay, the time of day, and other indicators of the patient's status. For a rigorous analysis of the influence of noise on patients' outcome, the effects of these factors must first be controlled or corrected.

Reference

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P17

Results of the Telemedicine Program for implementation of the Surviving Sepsis Campaign Protocol in a community Brazilian hospital

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Introduction Sepsis has high incidence around the world, approximately 400,000 new cases occur annually in Brazil. In developing countries, it is still an important cause of death due to poor adherence to best-practice medicine protocols. The Brazilian mortality rate of septic shock is around 60%. The aim of this study is to describe the initial results for the implementation of the Brazilian initiative of a Telemedicine (TM) Project for therapeutic support of septic patients in a community hospital in São Paulo, Brazil.

Methods Since May 2012, a TM Program has been implemented at two hospitals in São Paulo – Hospital Municipal Dr. Moysés Deutsch (HMMD), a public, secondary hospital, and Hospital Israelita Albert Einstein (HIAE), a tertiary private philanthropic entity – due to a partnership with Brazilian Health Ministry. A TM Central Command was located at HIAE with Endpoint 97 MXP Cisco® Solution and Medigraf Gowireless® technology. Mobile Intern MXP ISDN/IP Cisco® and Medigraf Gowireless® for the remote hospital (HMMD) via a dedicated connection. At HMMD, the sepsis protocol, based on the Surviving Sepsis Campaign, has been started for every recruited patient admitted to the emergency department (ED) or the ICU, and assessed by the Central Command through TM with an experienced consultant of HIAE. We compared the results of this group of patients with the group of patients with diagnosis of severe sepsis and septic shock, admitted to HMMD during 2011, who were not assisted with TM resources.

Results From January to December 2011, 283 septic patients were treated at HMMD, 161 (56.8%) patients were male, mean age was 53.7 years and the hospital mortality was 65.3%. After the implementation of the TM Program, 189 septic patients were admitted to the hospital and evaluated by skilled doctors of HIAE via TM, with the institution of the Surviving Sepsis Campaign protocol. In total, 68.9% of the consultations originated from the ICU and 31.1% from the ED; 111 patients were male (58.4%), mean age was 54.1 years and the hospital mortality was 32.9% ($P < 0.05$).

Conclusion Use of the TM Program for the implementation of the Surviving Sepsis Campaign Protocol at a community Brazilian hospital improved compliance with recommended care bundles and significantly decreased the hospital mortality of septic patients.

P18

ICU nursing connectivity and the quality of care in an academic medical center: a network analysis

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Introduction A collaborative nurse work environment is associated with ICU quality, yet collaborative interaction is difficult to measure. Network analysis may be an innovative tool to measure interactions. We sought to determine the feasibility of network analysis to measure ICU nurse connectivity and test whether key network measures were associated with the ICU quality of care.

Methods We performed a network analysis in eight ICUs within an urban academic medical center in the United States during 2011. Using scheduling data, we defined network ties as instances when two ICU nurses worked together in the same ICU for 4 hours or more. We examined each ICU's network by visualizing sociograms and by measuring two network properties: density and clustering. Density measures the cohesion within a network on a scale from 0 to 100, with a higher score indicating more cohesion. Clustering assesses the local neighborhoods on a scale from 0 to 100, with a higher score indicating a more decentralized network. We examined variation in network measures across ICUs and tested the correlation between network measures and the proportion of patients receiving daily interruption of sedation (DIS).

Results There was wide variation in the networks, with density ranging from 79 to 96 and clustering ranging from 88 to 97. Two sample sociograms are shown in Figure 1: ICU A had a very high density (96) and clustering coefficient (97) suggesting a cohesive and decentralized network, contrasting with ICU H that had the lowest density (79) and clustering coefficient (88). Greater density and clustering was positively associated with DIS (B = 0.02 (–0.10, 0.14); B = 0.003 (–0.07, 0.07)) but did not achieve statistical significance in our small sample.

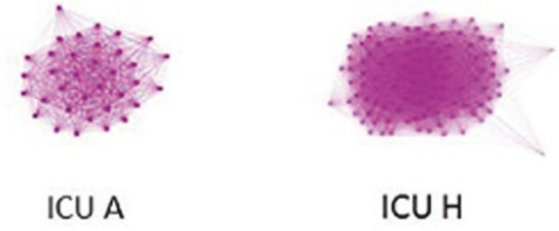

Figure 1 (abstract P18). Sociograms of ICU A and ICU H.

Conclusion We found substantial variation in ICU nursing networks across eight ICUs in one academic medical center. These patterns may have implications for evidence-based practice implementation. More work is needed to understand the role of network analysis as a reliable tool for improving and understanding ICU organization.

P19

Compassion fatigue and burnout among healthcare professionals in the ICU

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Introduction This study comprises a systematic review of studies focusing on the prevalence of compassion fatigue (CF) and burnout

(BO) among professionals in the ICU, to indicate the size of this problem. Both CF and BO have an important impact on daily quality of life of professionals and may threaten patient care. A growing body of research suggests that BO appears to be common among ICU nurses [1] and physicians [2] due to a highly stressful work environment. However, BO might be overestimated and seen as a fashionable diagnosis [3]. The overlap of BO with CF, secondary traumatic stress (STS) and vicarious traumatisation has recently been explored [4]; CF seems to apply more to ICU staff and might be a lead in future preventive strategies.

Methods A review of the literature between 1998 and December 2013 was conducted using eight databases, and included the keywords CF, STS, BO, ICU, nurses and physicians. The references were screened for relevancy at title/abstract using predefined inclusion and exclusion criteria. Studies were limited to original and review articles in the English language. Two independent researchers assessed the methodological soundness of each article.

Results All references, retrieved from electronically database search (n = 1,432) and manual search (n = 3), resulted in 100 relevant publications for full-text screening. Subsequently, articles with only an abstract available (n = 28), a language barrier (n = 27), or prevalence not shown in percentages (n = 23) were removed. Finally, a sample of 22 eligible articles were appraised as methodologically sound and systematically analysed for this review. The prevalence of BO in the ICU varied from 1.2 to 49% and differed in defining a severe BO. Two studies reported the prevalence of CF, 7.3% and 40%, and five studies described the prevalence of STS in a range from 21 to 44%.

Conclusion The emotional price of working at the ICU can become a burden in personal life, but the size of the problem in ICU staff remains unclear. Because the decreased well-being of the professionals might negatively influence the quality of care, preventive strategies should be developed in order to alleviate the distressed. Further exploration of CF might provide sufficient starting points.

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P20

Effect of divergences about patient's care plan on the outcome of critically ill patients

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Introduction There is an actual discussion about the best way to provide medical care for critically ill patients, particularly between the classical opened versus closed ICU models [1,2]. In Brazil, all ICUs have to have a full-time and dedicated physician at the unit but the primary physician also can visit his patient every day and, most of the time, participates in the patient's care plan. This hybrid model creates opportunity for patient's care plan divergences between the ICU staff and the primary physician. The objective of this study is to evaluate the effect of divergences about patient's care plan on the outcome of critically ill patients.

Methods A prospective court study was conducted (from January to May 2013) to point out the patient's care divergences (blood transfusion, diuretics, antibiotics, vasopressors, mechanical ventilation, and so forth) that happened in the first 72 hours of ICU admission in a 30-bed adult Brazilian ICU. We enrolled only patients that stayed more than 48 hours in the ICU.

Results In a court of 357 patients at least one divergence between the ICU medical staff and the primary(s) physician(s) were identified in 31 cases (8.6% – divergence group (DG)). The age (67.9 years), gender (55.2% of male), SAPS3 score (45.7) and reasons for ICU admission (emergency surgery 7.6%, nonemergency surgery 30%, clinical 62.4%) were similar in DG and nondivergence (NDG); however, the ICU length of stay (6.2 vs. 3.9 days, P = 0.023), use of mechanical ventilation (48.4% vs. 27%, P = 0.012), vasopressors (77.4% vs. 46%, P = 0.001) and blood transfusion (41.9% vs. 27.6%, P = 0.073) were higher in the DG compared with NDG. Discordance was associated with higher ICU and hospital mortality (35.5 vs. 11%; OR = 4.09; P <0.001 and 45.2 vs. 20.1%; OR = 2.77; P = 0.02 respectively).

Conclusion The occurrence of divergences, even during the first days of ICU admission, about medical plans of care for critically ill patients is frequent and is associated with higher ICU and hospital mortality and more use of medical resources.

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P21

Prevalence, risk factors and consequences of intra-team conflicts in the ICU

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Introduction The ICU is a stressful place with several sources of conflicts. Among ICU workers, conflicts lead to burnout, loss of psychological well-being, and deterioration of the work performance. Intra-team conflicts (conflicts that occur among members of the intensive care team) are one of the most frequent types of conflicts in the ICU. The objectives of this study were to determine the prevalence, risk factors and consequences associated with intra-team conflicts in the ICU.

Methods A survey was conducted in 12 Uruguayan adult ICUs in 2009. ICUs and clinician's characteristics were assessed for their association with the prevalence of conflicts. All factors associated with conflicts were introduced into a multivariable model.

Results A total of 384 questionnaires were collected, 74.5% (n = 286) were nurses and 23.2% (n = 89) were intensivists. From the 384 forms, 45.8% perceived at least one conflict in the past year. Conflicts were perceived more frequently by intensivists (61.8%) than nurses (40.9%) (P = 0.001). A worse relationship with intensivists (OR 1.3; 95% CI 1.09 to 1.59; P = 0.004) is independently associated with conflicts. However, lower grade of irritability (OR 0.8, 95% CI 0.73 to 0.97; P = 0.01) and a higher position in the ICU (OR 0.57 95% CI 0.36 to 0.92; P = 0.02) are factors independently associated with a lower incidence of intra-team conflicts. Interestingly, this study confirms that workers with at least one conflict had more frequently: libido disturbances (56% vs. 40%; P = 0.002), eating problems (52% vs. 40%; P = 0.02), as well as the wish to leave the ICU (53% vs. 39%; P = 0.005).

Conclusion The prevalence of conflicts is very high among ICU workers in Uruguay. We have identified different risk factors associated with the development of conflicts. These results confirm previous findings and highlights that strategies to decrease intra-team conflicts in the ICU are urgently warranted.

P22

Do we spend less on older critically ill patients? Relationship among intensity of care, severity of illness and mortality

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Introduction The Therapeutic Intervention Scoring System (TISS-28) quantifies the type and number of intensive care treatments; therefore, it indicates the workload of ICU and may be used for calculating costs [1]. A previous cohort study [2] demonstrated that seriously ill older patients receive fewer invasive procedures and less resource-intensive hospital care, showing a preferential allocation of hospital services to younger patients regardless of severity of illness. The objective of this study is also to compare resource utilization across different ages of critically ill patients in an open model, mixed ICU.

Methods During 7 years (2007 to 2013), TISS-28 was prospectively applied to all consecutive adult critically ill patients at 24 and 72 hours of ICU admission in a private hospital in Brazil. Demographic data, diagnoses on admission, comorbidities, ICU length of stay and mortality were recorded. Patients were stratified according to their ages.
Results TISS-28 scores at 24 and 72 hours of ICU admission were analyzed for 4,128 patients. Mean patient age was 68.3 (SD ± 17.6), 46.8% were female and 37% were surgically ill. The mean APACHE II score was 16 (SD ± 8) and 40% were submitted to mechanical ventilation at any time of the stay. Overall mortality was 14.4%. Neither APACHE II score adjusted for age nor TISS-28 in 24 and 72 hours of admission differs among age groups. However, mortality was significantly higher in patients aged 70 years or older (P <0.001).
Conclusion Mortality remained higher in older patients despite an absence of age-related differences in resource use at ICU. Comparing our results to a previous prospective cohort study [2], we emphasize the lower overall mortality of our population (14.4% vs. 50%). Limitations of our analysis include our unicenter design and lack of data for a closed model ICU.
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P23

New policy for ICU visits: prospective study

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Introduction ICU visits are generally limited to 2 hours per day selected at any time during the 24 hours. At our institution we abide to the international regulations which were recently modified allowing family members and significant others to be present throughout the day accompanying their ICU-admitted relatives, participating in an uninterrupted timely fashion and no time limits with their daily activities.
Methods From January 2012 through April 2012, 200 questionnaires were filled by families of ICU-admitted patients; each questionnaire includes 13 questions concerning their overall degree of satisfaction at our unit and evaluating the quality. Accommodating spaces were offered for families of ICU patients, offering them a state of freedom within the ICU premises surrounding their beloved sick relatives; additionally they were constantly advised by a designated secretary to share their experience and any possible insight to improve the overall polity of our service.
Results Two hundred patients were included in the study, the average age of patients was 68.55 years and the average length of ICU stay was 5.2 days. Most family (85%) desired their presence accompanying their related patients within the ICU premises when meals were served. Those families expressed satisfaction while offering psychological support to their beloved ill ones. Fifteen per cent of the families argued about the permitted number of visitors (one person) per visit and 12% addressed lack of communication between the medical staff and patient's families.
Conclusion Compared with the limited visit status within the ICU ward in the past, the majority of families expressed general acceptance and satisfaction toward the newly adopted policy. Additionally and by this new policy, patients displayed marked improvement at the psychological level, being more cooperative and experiencing less episodes of agitation. Even the medical team elaborated their interest towards this policy as being a more profound and comprehensive way of supporting the ICU patients. Further investigations are currently being employed to strengthen the outcome of the study.
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P24

Dealing with cultural diversity during the process of communication and decision-making in the ICU: a literature review

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Introduction Studies have shown that communication in the ICU is related to the cultural background of all involved actors. As a consequence, hospitals in multiethnic areas in western countries are currently forced to rethink their models of communication as they are increasingly transformed into spaces of cultural encounter. During this process one needs to be aware of the cultural differences in attitudes and experiences towards communication in critical medical situations. However, the growing academic interest in intercultural relations in the critical care has not yet led to the construction of cumulative knowledge. The aim of this study is to review the experiences of the involved actors, namely the care providers, the patients and their family members, with cultural diversity during the process of communication and decision-making in the ICU.
Methods A literature review was conducted. PubMed was searched. The following combinations of Mesh terms were used: [(decision-making) OR (communication)] AND (intensive care) OR (intensive care units)] AND [(cultural diversity) OR (multiculturalism) OR (migrants) OR (culture) OR (ethnicity)]. A total of 111 studies were retrieved. We excluded nonempirical studies, studies not written in English and articles published before 2003. After screening the titles and abstracts 12 articles were selected. The full text of these articles was analyzed and synthesized with a thematic-synthesis approach. During the process we performed additional searches based on the bibliographies of all the relevant articles.
Results Culturally specific expectations about communication and decision-making, different views on gender roles, organization of the care and expression and resolving emotional and social crises may cause extra stress. The communication becomes more complex when the language of the care providers differs from the language of the patient and family. Intercultural communication can be improved by specific actions such as ethnic matching, using an interpreter and the formation of cultural-competent healthcare professionals.
Conclusion There is a lack of knowledge regarding the specific experiences of patients, families and care providers with communication and especially decision-making in multicultural ICUs in Western Europe.

P25

Symptoms of anxiety, depression and post-traumatic stress in pairs of patients and their family members during and following ICU stay: who suffers most?

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Introduction To compare the incidence of anxiety, depression and post-traumatic stress symptoms in pairs of patients and respective family members during the ICU stay and at 30 and 90 days post ICU discharge. According to the literature, both patients and family members suffer from psychological distress during and following an ICU stay [1]. Although these issues have been discussed, to date few studies have addressed the pairs at three times.
Methods A prospective study conducted in a 22-bed adult general ICU including patients staying >48 hours. The Hospital Anxiety and Depression Scale (HADS) was completed by pairs (patients/respective family members). They were interviewed by telephone at 30 and 90 days after ICU discharge with the Impact of Event Scale (IES) and the HADS. We separated them into three different groups (patients – group A, family member of patient who survived – group B and family member of patient who deceased – group C).
Results A total of 184 pairs were interviewed at the ICU. Mean patient age was 59.33 ± 15.5 years. The admission SAPS III was 47.6 ± 15.7 points. Median ICU LOS was 4 days (2 to 47). Family's age

was 51.79 ± 13.47 and 64% were spouses. Patients had symptoms of anxiety (26.1%), depression (12%) or both (8.7%) during the ICU stay. Regarding family members, the incidence of anxiety, depression or both during the ICU was 33.2%, 9.8% and 8.2% respectively. Symptoms of PTSD within patients were found in 6.9% at 30 days and disappeared at 90 days. Differently, these symptoms in family members were found in 6.2% at 30 days and 9.0% at 90 days. There was a positive correlation between HADS at ICU and IES at 30 days for family members ($r = 0.527$, $P < 0.001$). The HADS score over time between patients, family members of patients who deceased and who survived were different ($P = 0.002$). In *post-hoc* analysis, group A presented less symptoms than group C at 30 days ($P = 0.001$) and less than groups B and C at 90 days ($P < 0.001$ for both). At 90 days, group B showed less symptoms than group C ($P = 0.039$).

Conclusion Family members of ICU patients suffer more than the patients principally when their loved one died. Patients' symptoms of anxiety, depression and PTSD decrease with time but in family members these symptoms continue along the 90 days.

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P26

Heart-focused anxiety in critically ill patients' relatives

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Introduction A series of studies have shown an association between the ICU environment and symptoms of psychological distress in critically ill patients' relatives [1-3]. The aim of this study was to investigate the risk of cardiophobia and panic attack crisis on ICU patients' family members.

Methods In the period from March 2012 to July 2013, we studied 223 family members (81 men and 142 women, mean age 41.5 ± 11.0 years) of critically ill patients. These patients were admitted to the intensive care department with various medical and surgical conditions (147 patients, 103 men and 44 women, mean age 58.3 ± 18.6 years). We used a questionnaire in which were included: social–demographic characteristics of the patients' family environment, and the Cardiac Anxiety Questionnaire (CAQ). The results from the CAQ [4] were compared with those of the general population of Greece (GGP).

Results In comparison with the general Greek population, the relatives of critically ill patients demonstrate statistically significant higher scores ($P < 0.001$) on the scales of fear and anxiety in regards of thoracic and heart sensations (1.1 ± 0.9 vs. 0.9 ± 0.9 in GGP), avoidance of activities considered to reproduce cardiac symptoms (1.3 ± 1.0 vs. 1.1 ± 0.9 in GGP), heart-focused attention and self-monitoring of cardiac activity (0.9 ± 0.7 vs. 0.7 ± 0.6 in GGP), and at total CAQ score (1.1 ± 0.6 vs. 0.9 ± 0.6 in GGP). Analysis of variance among family members on heart-focused attention and self-monitoring of cardiac activity showed that hospitalization provoked heart-focused attention (that is, the main factor of perceived panic crisis risk). In accordance with the Bonferroni criterion, we found that patients' siblings demonstrated statistically significant difference compared with patients' children ($P = 0.015$), with the latter showing lower levels of heart-focused attention and self-monitoring of cardiac activity. Further MANCOVA analysis showed a statistically significant correlation between age and cardiophobia, and also between education level and heart-focused anxiety ($P = 0.041$ and $P = 0.044$ respectively).

Conclusion The hospitalization of a patient in the ICU is considered to be a factor that is affecting the mental health of patients' relatives. Our results highlight a risk for psychologically induced symptoms on ICU relatives and underline the need for a psychosocial support system for them. The cardiophobia and self-monitoring of heart activity which inflicts the patients' relatives appears to be more intense in the siblings, parents and partners of patients.

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P27

Family satisfaction in the ICU: a 6-month experience

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Introduction The aim of the study was to prospectively assess family satisfaction in the intensive care setting and identify fields of possible improvement.

Methods The study was performed over a 6-month period in a 10-bed ICU. A properly translated and validated Family Satisfaction in the ICU (FS-ICU 24) questionnaire was used. A total of 126 questionnaires were handed out to family members upon patient discharge. The number of questionnaires returned for evaluation was 120 (91.5% participation). Five-point Likert scale responses were transformed to percentage scores, higher values representing better satisfaction.

Results Overall satisfaction with care was reported as very good or excellent by 81% of family members (32% and 49% respectively) both for ICU staff concern and caring as well as symptom management. Favorable scores were also noted in terms of decision-making, 89% of relatives reporting very good and excellent rates as regards information needs. On the other hand, most of the family members (73%) felt neither included nor excluded from the decision-making process. Moreover, a small number of them (6%) answered that they received poor emotional support. Finally, the frequency of communication with ICU nurses and the atmosphere in the waiting room were noted as fair by 28% and 47% of subjects respectively.

Conclusion Most family members were highly satisfied with ICU care their patients received. Nevertheless, our study showed that the fields of communication with the nurses as well as the waiting room atmosphere definitely need further improvement. Concerning emotional support and decision-making, the study revealed that currently used measures in our ICU still do not apply to all families and probably require a few changes.

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P28

Qualitative analysis of a family satisfaction in an adult ICU

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Introduction Patient satisfaction is a key determinant of the quality of care within the hospital environment. Critically ill patients often lack capacity. Under such circumstances, family members are often main decision-makers and their satisfaction about the ICU experience resembles an important surrogate in evaluating the quality of care. We aimed to measure family satisfaction with different aspects of medical care.

Methods In February 2013, surveys, including 24 qualitative questions, were sent out to relatives of 50 patients 1 month after their discharge from ICU St George's, UK. Responses were graded 1 to 5, with higher values representing a greater degree of satisfaction.

Results Most respondents were satisfied with the overall performance and the respect received (mean ± SD score 4.7 ± 0.68). Skills and competency of doctors (4.38 ± 0.67) and nurses (4.57 ± 0.68) was also perceived very positive. However, family satisfaction with communication with doctors (3.52 ± 1.47) and nurses (3.71 ± 0.96), as well as inclusion in decision-making (3.39 ± 1.24), resulted in somewhat lower scores. In particular, ease, clarity, consistency, honesty, and completeness of information given by doctors resulted in inhomogeneous perceptions between relatives (Figure 1). Additionally, the majority of responders felt only moderately satisfied with time and support to make a decision.

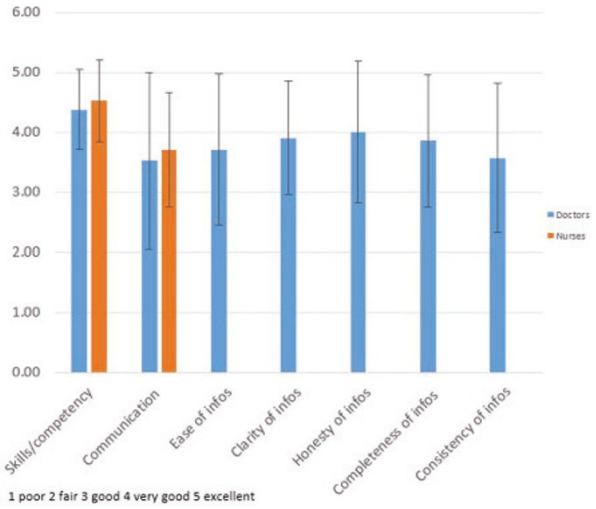

Figure 1 (abstract P28). Team performance.

Conclusion In general, relatives felt very satisfied with the ICU, especially with the care of the patients and the professional workforce. The complete decision-making process was rated moderately good, which highlights some areas of improvement in involving relatives in the care of their beloved by providing regular, clear, easy to understand and consistent information.

P29

Outcomes of ventilated surgical and medical ICU patients: do patients die from ARDS or with ARDS?

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Introduction Patients with acute respiratory distress syndrome (ARDS) have a high mortality rate. Whether this excess mortality is contributed by ARDS or is a consequence of prolonged mechanical ventilation is unclear.
Methods A longitudinal retrospective study focusing on noncardiac ICU patients who required mechanical ventilation. Patients were classified as having ARDS on admission, late-onset ARDS or no ARDS. The analysis included patients ventilated for longer than 48 hours. Primary outcomes were mortality at 28 days, 1 year and 2 years from ICU admission.
Results A total of 1,396 patients were enrolled between 2001 and 2008: 485 (34.7%) had ARDS on admission (early-onset ARDS), 219 (15.6%) developed ARDS during their ICU stay (late-onset ARDS) and 692 (49.5%) did not meet ARDS criteria prior to ICU discharge or death. Twenty-eight-day mortality rates were 23.7%, 25.6% and 25.7% for early, late and non-ARDS respectively. After adjusting for age, weight on admission, unit of admission (MICU vs. SICU), severity of disease score, comorbidity score, and primary diagnosis on admission, and mortality risk at 28 days, 1 year and 2 years were not significantly different between the three study groups. Neither severity of ARDS or timing of ARDS (early versus late) was associated with mortality. Sensitivity analysis, analyzing all ventilated patients, including those who were ventilated less than 48 hours, showed the same results.
Conclusion Neither the presence of ARDS or the severity or timing contribute independently to the short and long mortality risk after adjustment for age, severity of disease, comorbidity score and diagnosis on presentation in patients hospitalized in a noncardiac ICU with acute respiratory failure.

P30

Advance care planning in critically ill haematology patients

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Introduction Significant improvements in chemotherapy, haematopoietic stem cell transplantation and general intensive care mean that more patients are now living longer and often present to the ICU at various stages of their disease [1,2]. Encouraging patients with haematological malignancy (HM) to express their wishes and values on end of life (EoL) prior to ICU admission would ensure that their autonomy is respected. The aim of our study was to determine whether patients with HM that were admitted and died in the ICU had any form of advance care planning (ACP) documented prior to their admission.
Methods Data were collected on all adult patients with HM that were admitted and died in the ICU of a tertiary haematology referral centre in London during the period of 1 year.
Results Information was collected for 34 patients and their characteristics are shown in Table 1. In 62% of the patients EoL decisions were made, and do-not-attempt-resuscitation documentation was found in 65% of the cases. Documentation on information exchange, and participation in the deliberation or the decision-making process was found in only 30% of the patients, even though more than 75% of the haematology physicians estimated the prognosis of these patients as moderate (17%) or poor (59%). In the vast majority of cases (31/34) the deaths occurred after withholding or withdrawal of treatment in ICU.

Table 1 (abstract P30). Patient characteristics

Mean age	30
Median APACHE II score	26
>3 organ support	60%
Leukaemias	>50%

Conclusion Only a small number of patients with HM that die in the ICU have documented ACP prior to admission. Since the majority of ICU patients lack personal decision-making capacity, ACP would ensure that care is consistent with patients' wishes, EoL actions are congruent with their values, the burden on family and healthcare providers is alleviated and cost is decreased.
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P31

A new questionnaire to determine the effect of team interaction in the ICU on perceived futility and intention to quit: results of a pilot study in two German hospitals

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Introduction Perceived futility of care may jeopardize patient quality of care and increase ICU staff turnover. It is related to workload and interdisciplinary collaboration. Our aim was to evaluate concepts from team science, namely inclusive leadership (a style that invites and appreciates others' contributions) and psychological safety (a key antecedent of speaking up and learning behavior), and to determine their effect on perceived futility and intention to quit.
Methods A staff survey in four interdisciplinary ICUs and two intermediate care units of two tertiary care hospitals. The questionnaire contained validated scales to assess inclusive leadership of head nurses and attending physicians, nurse–physician collaboration, collaborative

decision-making, psychological safety, workload, intention to quit and a newly developed scale for perceived futile care. English questions were translated into German by state-of-the art forward and backward translations. Reliability – that is, internal consistency and inter-rater reliability of scales – was evaluated. Predictors of perceived futile care and intention to quit were identified by multiple regressions.

Results A total of 220 nurses and 55 physicians participated. Scales showed good reliability with all Cronbach's alpha ≥0.8 and significant between unit variability (all $P \leq 0.011$). On a scale from 0 ('never') to 5 ('very often'), ICU staff rated frequency of futile care as median 3.6 (IQR: 3 to 4). On a seven-point Likert scale with 7 denoting maximal values, intention to quit was rated as 2.3 (1 to 4). Nurses gave significantly lower ratings of job satisfaction than physicians (4 (3 to 5) vs. 5 (4 to 6), $P \leq 0.001$), perceived futility more often than physicians ($P \leq 0.001$), and rated all aspects of nurse–physician collaboration worse than physicians, including attendings' inclusive leadership, collaboration, decision-making and psychological safety (all $P \leq 0.001$). Futility and intention to quit were each predicted by high workload and low psychological safety (all $P \leq 0.009$). Among nurses, inclusive leadership by the head nurse prevented intention to quit ($P = 0.001$) and a composite score of good nurse–physician interactions predicted less perception of futile care ($P \leq 0.001$).

Conclusion The scales of the new questionnaire showed good reliability and differentiated between nurses and physicians. Psychological safety and inclusive leadership proved to be important concepts.

P32

ASA helps prediction of the death rate in surgical ICU patients

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Introduction Many scoring systems have been designed to predict mortality in surgical patients; however, these systems require the collection of several parameters that may not be available at ICU admission. As a result, these classification systems are not used as a routine part of clinical practice. The aim of this study was to evaluate the prognostic value of ASA classification predicting ICU and hospital mortality.

Methods We analyzed the records of 11,230 ICU admissions. ASA and elective/nonelective nature of the admission were combined into eight categories. We used the chi-square test and accepted the null hypothesis if $P > 0.05$. Areas under the ROC curve using ASA and ASA/admission categories were constructed.

Results We included 5,998 patients admitted to the ICU immediately after surgery. Forty-one percent were older than 65 years and 51% were female. Length of stay previous to ICU admission was 2.5 ± 6.1 days and duration of ICU stay was 1.9 ± 2.4 days. Elective hospital admission occurred in 65% of the patients. Neurosurgery with 21% of the procedures was followed by abdominal surgery (20%), and orthopedic surgery (15%). The death rate at the hospital was 6.9% (2.8% in ASA I patients and 31% in ASA IV/E). Higher ASA classification was significantly associated with the death rate both in the ICU and at the hospital ($P < 0.00001$). The nonelective nature of the hospital admission was also associated with higher risk of death at the ICU ($P < 0.0001$) and in the hospital ($P < 0.0001$). Gender and hour of admission was not associated with the death rate. The combination of ASA classification with the nonelective nature of the hospital admission produced an eight-category index significantly associated with mortality ($P < 0.00001$). Analyzing hospital mortality, the area under the ROC curve was 0.77 (95% CI 0.74 to 0.79) for this index and was 0.72 (95% CI 0.69 to 0.75) for ASA. When analyzed for death at the ICU the AUROC was 0.71 (95% CI 0.69 to 0.75, $P < 0.0001$) for ASA and 0.75 (95% CI 0.71 to 0.78, $P < 0.0001$) for ASA nonelective admission index.

Conclusion These results show that the ASA index can be used, preferably in combination with other data from electronic records, to predict mortality for surgical ICU patients.

P33

Till death do us part: amyotrophic lateral sclerosis in the ICU

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Introduction The aim of the ICU is to give the best life care to the admitted patients in order to preserve and restore the patients' quality of life. In some critical patients, life-supporting therapies become actions to support the end stage of their life [1]. This is the paradox of the ICU. Patients affected by amyotrophic lateral sclerosis (ALS) belong to this category: for these patients, all medical actions do not improve the quality of life but just prolong it. ALS or Charcot's disease is the most common motor neuron disease which causes severe motor disability and evolves in a few years to death [2]. We want to present our experience in patients affected by ALS in the ICU.

Methods We collected data about patients affected by ALS admitted to the ICU from 1 January 2010 to 31 October 2013. We considered entry diagnosis, mean age, need to perform tracheostomy and/or percutaneous endoscopic gastrostomy (PEG), and mortality in the ICU.

Results Sixty patients were admitted for neuromuscular respiratory failure complicated by aspiration pneumonia. Mean age was 43 years. The male to female ratio was 3:1. All patients underwent percutaneous tracheostomy and PEG. One of them died in the ICU because of septic shock. In every case we honestly communicated the worsening of the disease and we perceived the awareness of it by the patients and/or their family. In no case did patients ask us to withdraw the necessary cures such as percutaneous tracheostomy and PEG. In no case did they ask us to die. In Europe the 'end of life care' law is very dyshomogeneous because of different cultures, traditions, religions, and beliefs. In Italy euthanasia is not allowed by law. It is the physician often by himself that has to make the final decision according to the patient's mind.

Conclusion Our experience shows that patients affected by severe motor disability are not always willing to die. It is essential that decisions should be patient-centered and taken multidisciplinarily, based on open and emphatic communication, involving family and caregivers.

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P34

Death rate of patients admitted to a Brazilian ICU on weekends and holidays

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Introduction Several studies conducted in a number of different populations indicate that patients admitted to hospitals on weekends have a higher mortality rate. Many factors have been proposed to explain these observations and in most studies, however, this effect disappeared after controlling for illness severity. We undertook the present study to explore the effect that day of ICU admission may have on death rate.

Methods We analyzed 11,230 electronic records from patients admitted from 1 January 2006 to 30 June 2013. The ICU admission dates were categorized as normal weekdays and as weekends and holidays. The dependent variables were ICU mortality and hospital mortality. The chi-square test and Student *t* test were used as appropriate and significant association was accepted when $P < 0.05$. Multiple logistic regression (backward conditional) was used accepting a variable when $P < 0.05$ and rejecting a variable with $P > 0.1$. SPSS version 19.0 was used.

Results Forty-nine percent of these patients were female, 53% was admitted immediately after surgery, 56% had <2 days of previous hospital admission, and 19.2% were admitted during weekends and holidays. Mortality in the ICU for admissions on weekends and holidays was 24% and was 13% for those admitted on weekdays (OR = 2.23, 95% CI 2.02 to 2.47; $P < 0.0001$). The hospital mortality was respectively 35% and 20% (OR = 2.23, 95% CI 2.02 to 2.47; $P < 0.0001$). Differences between

patients admitted on weekends and on weekdays were found in the group admitted after surgery (respectively 10% and 30%, P <0.0001), originating from the emergency unit (respectively 30% and 16%; P <0.0001), originating from step-down units (respectively 31% and 17%; P <0.0001), patients from clinical teams compared with surgical teams (respectively 28% and 13%; P <0.0001), previous hospital length of stay lower versus higher than 2 days (respectively 15% and 25%; P <0.0001) and age ≥65 years (respectively 21% and 18%; P <0.0001). The mortality ratios were significantly different between these groups. Multiple logistic regression showed that the inclusion of other variables reduces the odds ratio associated with admission on weekends and holidays to 1.22 (95% CI 1.08 to 1.39, P <0.002) for ICU mortality and to 1.23 (95% CI 1.09 to 1.38, P <0.001).

Conclusion The higher death rate on weekends and holidays may be related to case mix. The interplay of other variables possibly related either to admission on weekends or higher death rate should be sought.

P35

How many ways are there to die? Identification of ICU death typologies using cluster analysis

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Introduction Although avoidance of death is a key goal of critical care, so too is provision of high-quality end-of-life care when life-prolonging therapy is not desired. One often-used measure of ICU performance is risk-adjusted mortality, yet this measure treats all deaths equally and thus is flawed. In this work, we identify different death typologies using cluster analysis, with the ultimate goal of more narrowly targeted ICU quality improvement measures and efforts.

Methods We performed k-means cluster analysis in 2,047 ICU decedents admitted to a university medical center in 2011/12. Variables for the analysis included ICU length of stay (LOS), mechanical ventilation, tracheostomy, gastrostomy tube insertion, dialysis, enteral or parenteral nutrition, and cardiopulmonary resuscitation (CPR).

Results Four clusters were identified. Short ICU LOS and low life-sustaining therapy utilization but relatively frequent CPR characterized Cluster 1. Intermediate ICU LOS and moderate life-sustaining therapy utilization characterized Clusters 2 and 3. Prolonged ICU LOS and high life-sustaining therapy utilization (except CPR) characterized Cluster 4. Age and severity of illness decreased across clusters with the oldest, sickest patients in Cluster 1 and the youngest, least sick patients in Cluster 4. See Table 1.

Table 1 (abstract P35).

	Cluster 1 (n = 353)	Cluster 2 (n = 755)	Cluster 3 (n = 667)	Cluster 4 (n = 272)
ICU LOS, mean ± SD (days)	0.5 ± 0.2	2.0 ± 0.8	7.2 ± 2.8	25.6 ± 15.2
Mechanical ventilation	282 (79.9%)	631 (83.6%)	604 (90.6%)	269 (98.9%)
Tracheostomy	3 (0.9%)	13 (1.7%)	14 (2.1%)	127 (46.7%)
CPR	20 (5.7%)	19 (2.5%)	16 (2.4%)	8 (2.9%)

Conclusion Cluster analysis can identify unique typologies of death within ICUs. This approach may be a novel method to more specifically target ICU efforts to reduce mortality and improve the quality of death.

P36

Independent risk factors associated with the decision to withhold therapeutic intervention in patients admitted to the emergency room

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Critical Care 2014, **18(Suppl 1):**P36 (doi: 10.1186/cc13226)

Introduction The decision to withhold therapeutic intervention in a patient is a complex decision, wrapped in profound ethical debates. The role of the physician is to cure, treat and alleviate suffering. When the first two goals are not possible the medical role should be dedicated to end-of-life treatments adjusted to the patient's benefit [1,2].

Methods A retrospective cohort study including all adult patients with sepsis admitted to the emergency room (ER) at a tertiary care, university hospital between 1 July 2011 and 30 June 2012.

Results During the study period 162 patients with sepsis were admitted to the ER, of which 40 (25%) had withheld therapeutic decisions. Comparing this group with the group without therapeutic limitations, patients in the first group were older (81 ± 13 vs. 68 ± 14, P <0.001), with more comorbidities (90% vs. 66%, P = 0.004) and a higher proportion needing help in daily activities (Karnofsky performance status (KPS) <70% = 55% vs. 8%, P <0.001). The hospital mortality in patients with a decision to limit the therapeutic intervention was significantly higher (83% vs. 43%, P <0.001). Variables independently associated with the withholding therapy decision were age (adjusted OR per year = 1.078, P <0.001), presence of comorbidities (adjusted OR = 4.632, P = 0.030), chronic wounds (adjusted OR = 5.965, P = 0.005) and patient's needed of help in daily activities (KPS <70%, adjusted OR = 5.391, P = 0.012). In the first group a lower proportion received antibiotics (70% vs. 99%, P <0.001) and when those were considered inadequate for the agent responsible for the sepsis episode it was less frequently changed (15% vs. 50%, P = 0.028). However, no differences were found regarding the elapsed time from admission to the ER until the first medical contact or the time since the recognition of sepsis and antibiotic administration, although the group with withholding decisions had less specimens collected for microbiology: blood cultures (68% vs. 91%, P <0.001) or other specimens (58% vs. 96%, P <0.001).

Conclusion In this study the decision to withhold therapy was independently associated with increasing age, the presence of comorbidities and loss of functional autonomy. For the same level of intervention such as antibiotic administration, the decision to withhold therapy did not influence the efficacy of therapeutic attitudes.

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P37

Autopsy-detected diagnostic errors in critically ill patients with cirrhosis

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Introduction Even with the availability of new and more effective diagnostic procedures over the past decades, autopsy remains one of the most reliable methods to validate clinical diagnoses. The aim of this review was to determine whether autopsy plays a role in extending knowledge about the cause of death in patients with cirrhosis who died in the ICU.

Methods We conducted a retrospective review of medical records and postmortem findings in critically ill patients with cirrhosis who were admitted to a major university teaching medical ICU (MICU) between August 2007 and August 2013. Agreement between diagnoses before death and postmortem findings were compared using the Goldman system [1]. Review was independently performed by a fellow in critical care medicine and a board-certified attending. Autopsy diagnoses included histologic and microbiological findings. The records were also reviewed for demographics, APACHE II score and all performed diagnostic procedures.

Results Of 641 patients admitted with diagnosis of cirrhosis, 86 (13%) died in the MICU. Forty-five (52%) patients underwent an autopsy. Forty-two autopsy reports were available for review, three histologic and microbiological reports were missing. Major missed diagnoses (principal underlying disease related to death and primary cause of death itself) were present in seven patients (17%), four in class I (10%) and three in class II (7%) (Table 1). Minor missed diagnoses were present in 13 patients (31%) (class III and IV). Postmortem findings were in complete agreement (class V) with clinical cause of death in almost one-half of the patients (n = 19, 45%).

Table 1 (abstract P37). Major missed diagnosis

Class I (n = 11)	Class II (n = 3)
1. Metastatic linitis plastica	1. Acute pancreatitis
2. Oesophageal variceal bleeding	2. Necrotizing mucor mycosis pneumonia
3. Disseminated mucor mycosis	3. Focal aspergillosis (myocardial)
4,5,6. Invasive aspergillosis (n = 3)	
7. Invasive candidiasis	
8. Herpes simplex pneumonia	
9. Pneumocystis pneumonia	
10. Gastric rupture	
11. Disseminated HCC, vs. porta thrombosis	

Class I = missed major diagnosis that would have changed management and might have resulted in cure or prolonged survival. Class II = missed major diagnosis that would not have modified ongoing patient care.

Conclusion Despite declining rates worldwide, autopsy remains an important tool for quality and safety assurance. In this retrospective study, autopsy showed that knowledge of the correct premortem diagnosis would have altered therapy in 10% of critically ill cirrhotic patients.

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P38

Profile, outcomes, and predictors of mortality of abdomino-pelvic trauma patients in a tertiary ICU in Saudi Arabia

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Introduction Saudi Arabia (KSA) has the world's highest number of deaths from motor vehicle accidents (MVAs). Numerous trauma victims sustain abdomino-pelvic injuries which are associated with considerable morbidity and mortality. The purpose of this study is to describe the profile, outcomes and predictors of mortality of patients with abdomino-pelvic trauma admitted to the ICU in a tertiary care trauma center in Riyadh, KSA.

Methods This is a retrospective analysis of a prospectively collected ICU database. All consecutive patients older than 14 years with abdomino-pelvic trauma from March 1999 to June 2013 were included. The followings were extracted: demographics, injury severity, mechanism and type of injury, associated injuries, use of vasopressors and mechanical ventilation, and worse laboratory results in the first 24 hours. The primary outcome was hospital mortality. Secondary outcomes were ICU mortality, mechanical ventilation duration, need for tracheotomy, and ICU and hospital length of stay. We compared the profile, outcomes, and the predictors of mortality between survivors and nonsurvivors.

Results Of 9,974 trauma patients during the study period, 702 patients with abdomino-pelvic trauma were admitted to the ICU. The average age was 30.7 ± 14.4 years and the majority was male (89.5%). MVA was the most common cause of abdomino-pelvic trauma (86%). Pelvis (46.2%), liver (25.8%), and spleen (23.1%) were the most frequent injuries; and chest (55.6%), head (41.9%), and lower extremities (27.5%) were the most commonly associated injuries. Mechanical ventilation was required in 89.6%, emergency surgery was performed in 45% and vasopressors were used in 46.6% of patients. The most commonly performed interventions during the ICU stay were surgery (39.5%) and chest tube insertion (33.3%). Of the 702 patients with abdomino-pelvic trauma, 115 (16.4%) patients did not survive. Associated head trauma and retroperitoneal hematoma, higher level of lactic acid on admission and ISS, and advanced age were independent risk factors for fatality. Compared with survivors, nonsurvivors were older in age; had higher ISS, APACHE II, BMI, lactic acid, INR and creatinine, and lower GCS, PaO_2/FiO_2 and platelet count; were more likely to be mechanically ventilated and on vasopressors; and were associated with more head injuries.

Conclusion In KSA, abdomino-pelvic traumas are serious injuries affecting mainly young male victims; however, with a lower mortality than predicted.

P39

Radiation exposure in trauma patients is affected by age

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Introduction Trauma patients are subjected to higher radiation exposure (RE) as a function of Injury Severity Score (ISS) [1]. Analysis of this dataset was done to ascertain if RE varied with patient age.

Methods Data collection was as previously described [1]. RE was measured in milliSieverts (mSv). RE as a function of the ISS and age was explored for 7,661 trauma patients. The ISS groupings were as follows: ISS 1 to 8, ISS 9 to 15, ISS 16 to 25, and ISS >25. Age groupings were 19 to 39, 40 to 59, 60 to 79, and >80 years.

Results The data were analyzed in a hierarchical fashion: the mean exposure by age group was compared by one-sided, two-sample t tests. Differences were set up to test if mean exposure decreased with increasing age. Bonferroni adjustment was used for all multiple comparisons to maintain the overall error rate at 0.05. Of the six independent difference tests conducted, five were significant: 19 to 39 versus 60 to 79; 19 to 39 versus >79; 40 to 59 versus 60 to 79; 40 to 59 versus >79; and 60 to 79 versus >79 (P <0.01). Analysis was done for ISS categories: ISS 1 to 8, ISS 9 to 15, ISS 16 to 25, and ISS >25. For ISS 1 to 8, five differences were significant: 19 to 39 versus 60 to 79; 19 to 39 versus >79; 40 to 59 versus 60 to 79; 40 to 59 versus >79; and 60 to 79 versus >79 (P <0.01). For ISS 9 to 15, all differences were significant: 19 to 39 versus 40 to 59; 19 to 39 versus 60 to 79; 19 to 39 versus >79; 40 to 59 versus 60 to 79; 40 to 59 versus >79; and 60 to 79 versus >79 (P <0.01). For ISS 16 to 25, four differences were significant: 19 to 39 versus 60 to 79; 19 to 39 versus >79; 40 to 59 versus 60 to 79; and 40 to 59 versus >79 (P <0.01). For ISS > 25, none of the differences were significant.

Conclusion Previous studies show significant RE in trauma patients [1]. We demonstrated the significance of RE to trauma patients, that the amount of RE has gone up chronologically over time, and that patients with an increasing ISS have a higher RE. We sought to determine whether age played a factor in RE. Based on our statistical analyses, older patients receive less RE for a given ISS. Although this is a large assessment of RE and trauma patients broken down by ISS and patient age, data analysis by year was limited by the small number of patients in high ISS groups at higher ages.

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P40

Survival rate and predictors of outcome in intubated patients with haematological malignancies in a Greek ICU

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Introduction The admission of patients with haematological malignancies to the ICU is associated with high mortality, especially when mechanical ventilation is required [1,2]. The purpose of the present study was to explore survival rates and the predictors of survival in this group of patients.

Methods A retrospective study of intubated patients with haematological malignancies, admitted to a general ICU in central Greece, due to any cause.

Results During a 10-year period (2003 to 2013), 16 patients with haematological malignancies (nine with acute myelogenous leukaemia, four with non-Hodgkin lymphoma, one with Hodgkin lymphoma and two with multiple myeloma, mean age 50.75 ± 16.59) (male/female 3/13, mean APACHE II score 23.18 ± 6.67, mean SOFA score 12.50 ± 2.82, CRP 16.00 ± 10.13, WBC 2.055 ± 30.053) were admitted to the ICU. The majority of patients were admitted due to ARDS (PO_2/FiO_2 164 ± 109), one patient was admitted due to intestinal rupture and peritonitis and the other one due to intracerebral haemorrhage. In the majority of the patients (13/16) diagnosis of the malignancy was made during the present admission and only three had the malignancy for a longer period (5 months to 3 years). The mean ICU length of stay was 10.56 ± 16.19 days. A total 68.75% (11/16) of the patients were intubated upon admission, whereas the mean time to intubation for the rest of the patients was 6.37 ± 4.16 hours. Neither intubation upon admission nor time to intubation was correlated with survival. Type of haematological malignancy, duration of immunosuppression and preceding length of stay in the general ward did not correlate with survival either. The survival rate was 18.7% and in linear regression analysis, duration of treatment with NIV in the general ward, increased SOFA score and the number of platelets (<50.000) upon admission to the ICU were independent predictors of survival ($R^2 = 0.77$, $P = 0.017$).
Conclusion The present retrospective study indicates that patients with haematological malignancies have poor survival when they are admitted to the ICU. Longstanding treatment with NIV before ICU admission, high SOFA scores and low platelet levels upon admission negatively affect survival.
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P41

Predictors of outcome in patients with haematological malignancies admitted to critical care

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Introduction Critical care (CC) admission has traditionally been viewed as likely to result in a poor outcome for immune-compromised haemato-oncological (HO) patients [1,2]. Recent studies have challenged such views [3,4]. We recently reported results from a cohort of HO patients admitted to CC, showing the pAO_2/FiO_2 (P/F) ratio to be the only independent predictor of mortality [5]. We report analyses of a larger cohort of HO patients admitted to CC.
Methods We assessed outcome for HO patients at CC (primary outcome) and hospital discharge, and at 6-month and 1-year follow-up. Single variable logistic regression analyses, adjusted by age, gender and haematological diagnosis, and multivariate analyses were performed to identify independent predictors of outcome using STATA.
Results A total of 225 HO patients were admitted to CC. Median age was 59 (interquartile range (IQR) 46 to 66) years. The most common haematological diagnoses on admission were acute myeloid leukaemia in 57 (25.3%) cases, non-Hodgkin lymphoma in 54 (24%) cases and multiple myeloma in 42 (18.7%) patients. Median APACHE II score was 21 (IQR 17 to 26). A total of 164 patients (72.9%) had at least one organ supported. Unit and hospital mortality rates were 34.7% (78 patients) and 49.3% (111 patients), respectively. At 6-month and 1-year follow-up, mortality increased to 63.1% (142 patients) and 70.5% (153 patients), respectively. The APACHE II score (OR = 0.93, 95% CI = 0.89 to 0.97, P <0.001), number of organs supported (OR = 0.34, 95% CI = 0.23 to 0.48, P <0.001), P/F ratio (OR = 1.06, 95% CI = 1.03 to 1.09, P <0.001), inotropic requirement (OR = 0.27, 95% CI = 0.15 to 0.49, P <0.001), and IMV status (OR = 0.06, 95% CI = 0.03 to 0.14, P <0.001) influenced unit survival at single variable analyses. At multivariate analysis, the P/F ratio (OR = 1.05, 95% CI = 1.02 to 1.09, P = 0.002) and IMV status (OR = 0.12, 95% CI = 0.04 to 0.35, P <0.001) independently predicted outcome.
Conclusion Organ failures and need for organ support correlated with outcome. P/F ratio and need for IMV were independent predictors of mortality, in agreement with previously published data [6]. The CC mortality rate was 34.7%; at 1 year, mortality had risen to 70.5%.
Acknowledgement AT and KB are joint first authors.
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P42

Early risk stratification in patients with oncological and hematological malignancies in the emergency department

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Introduction There are no well-validated risk scores for patients with oncological and hematological malignancies presenting to the emergency department (ED). Previous research found the prognostic blood biomarker pro-adrenomedullin (proADM) to be associated with infection-related complications and mortality and thus may be helpful in managing febrile patients with malignancies. Yet the prognostic value of proADM in general oncological patients presenting to the ED remains unclear. Herein, the objective of this study is to evaluate the prognostic potential of proADM and clinical parameters in a consecutive cohort of patients with oncological and hematological malignancies with regard to ICU admission and 30-day mortality.
Methods We enrolled all consecutive patients with oncological and hematological malignancies seeking ED care at a tertiary care hospital from February 2013 to October 2013. We prospectively collected various clinical features, and measured blood parameters including proADM upon admission. To assess outcomes, data from electronic medical records – that is, ICU admission, length of stay (LOS), and post-acute care location – were used and we contacted all patients 30 days after hospital admission. Logistic regression models with area under the receiver operating curve (AUC) were used to assess association of baseline parameters and outcomes.
Results We included a total of 469 patients with oncological and hematological malignancies, of whom 8.9% (n = 42) were admitted to the ICU and 18.7% (n = 88) did not survive until the 30-day follow-up. There was a strong association of initial proADM levels and 30-day mortality risk (odds ratio (OR) per 10-fold increase 9.9, 95% CI 4.3, 22.9) with an AUC of 0.67 (95% CI 0.60, 0.74). This association remained significant after multivariate adjustment for initial vital signs (blood pressure, pulse, temperature) and comorbidities (chronic heart failure, chronic obstructive pulmonary disease, diabetes, coronary heart disease) with an adjusted OR of 9.0 (95% CI 3.1, 26.4). There was also a significant association of proADM and LOS (adjusted regression coefficient per 10-fold increase: 6.6, 95% CI 2.0, 11.2).
Conclusion This study including consecutive patients with oncological and hematological malignancies found a moderate association of proADM with 30-day mortality and LOS. proADM in combination with clinical parameters may help to improve site-of-care decisions for these patients in the future.

P43

Calculated radiation exposure for trauma patients is lower when using the New Injury Severity Score versus the Injury Severity Score to calculate injury severity

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Introduction We studied radiation exposure (RE) in trauma patients [1]. To adjust for injury severity the New Injury Severity Score (NISS) or the Injury Severity Score (ISS) can be used to group patients. We sought to

determine whether there is a difference in the calculated RE per group when the patients are grouped using either the NISS or ISS.
Methods Data collection was as previously described [1]. RE was measured in milliSieverts (mSv). Group analysis was done for both ISS and NISS using the following severity score ranges (SSR) 1 to 8, 9 to 15, 16 to 25, and >25.
Results The analysis conducted in previous research [1] was repeated for the data recategorized by NISS. The conclusions were identical; increased NISS is associated with increased radiation exposure. A total of 465 patients fell into different SSR when classified by NISS. The distribution of exposure for each SSR, NISS versus ISS, was compared using Wilcoxon's test. For the range 1 to 8, there was no detectable difference. There was a significant shift in the distribution of exposures for the remaining three ranges (P <0.02). The exposure shift was downward for NISS compared with ISS.
Conclusion In this analysis, with the exception of patients in groups 1 to 8 there was a significant decrease in RE in the NISS groups when compared with the compared ISS group. Further analysis is needed to determine the cause for this change and whether this difference will be clinically significant.
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P44

Early warning scores: breaking or building barriers to critical care

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Introduction A prospective multicentre observational study was carried out to assess the extent to which critical care teams manage patients in hospital who are cared for outside the critical care unit. The Health Service Executive (HSE) in Ireland is in the process of implementing a national Early Warning Score (EWS) and, at an EWS of 7 or above, a referral to critical care is recommended. This study recorded the EWS of patients referred to the critical care team and describes the subsequent interventions made by the critical care team and patient outcomes.
Methods Six critical care departments in university-affiliated hospitals across Ireland collected data on all referrals to the critical care team over a 6-week period. Data were anonymised, coded and analysed centrally.
Results A cumulative total of 399 calls were made to the critical care teams in the six hospitals. The most common reason for referral was to request a critical care review of a patient (n = 319, 79.9%). Other reasons for referral included cardiac arrest, request to transfer patients from other hospitals and requests for vascular access. The average duration spent by the critical care team reviewing patients on the wards was 57 minutes. This increased up to 67 minutes for cardiac arrest calls. Of the 319 critical care reviews, 160 (50.2%) patients were subsequently admitted to critical care. A total 118 of this 160 had EWS of 7 or above, while 42 scored less than 7 but were still deemed to require admission to critical care.
Conclusion Regardless of the EWS, critical care teams are heavily involved in the management of patients outside critical care units. Fifty per cent of patients reviewed by the critical care team subsequently required admission to a critical care unit. The trigger threshold (7 and above) for referral to a critical care team currently recommended by the EWS escalation protocol is more likely to predict need for critical care admission. However, one in four patients referred below the threshold also required admission to a critical care environment. This study questions the safety of introducing such a protocol into acute hospitals. Will noncritical care staff be forced to wait until patients deteriorate further and reach the trigger threshold for referral or will the role of the critical care team expand further to look after all patients with abnormal EWS in hospital?

P45

Factors affecting the clinical response to National Early Warning score triggers

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Introduction We aimed to assess actions taken in response to variations in the National Early Warning (NEW) score and to identify factors associated with a poor response. The NEW score is a physiological score, which prescribes an appropriate response for the deteriorating patient in need of urgent medical care. This allows enhanced observation and clinical review of patients, identifying patients at risk of acute mortality.
Methods We performed a prospective observational study of adult patients admitted to an acute medical ward in a London district general hospital over a 2-week period. Patient characteristics, NEW score, time of day, day of week and clinical response data were collected for the first 24 hours of admission. Patients with less than a 12-hour hospital stay were excluded. The primary outcome measure was the quality of clinical response. Data were analysed with univariate and multivariate logistic regression.
Results During the study period 200 patients were included with a median age of 70 (20 to 102) years. NEW scores were evenly distributed between day and night (52% vs. 48%) with a greater proportion on weekdays compared with weekend days (82% vs. 18%). The majority of patients scored <5 (93% vs. 7%). Forty-seven (27%) patients received an inadequate clinical response. Univariate analysis showed no association with time of day (night 34% vs. day 38%, OR 0.83 (0.47 to 1.49), P = 0.556). However, day of the week (weekend 56% vs. weekday 32%, OR 2.8 (1.30 to 5.84), P = 0.01) and increasing score (NEWS ≥5 100% vs. NEWS <5 31%, OR 65 (3.8 to 1100), P < 0.0001) were significantly associated with an inadequate response. Day of the week was independently associated with an inadequate response after adjusting for confounders (OR 3.08 (1.27 to 7.46), P = 0.013).
Conclusion Clinical response to NEW score triggers is significantly worse at weekends, highlighting an important patient safety concern.
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P46

Impact of obesity on outcomes in patients with sepsis

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Introduction The purpose of this study was to evaluate the impact of obesity on outcomes in patients with severe sepsis. Since obesity is considered an inflammatory disease and is associated with elevations in several inflammatory mediators important in the outcome of sepsis, the relationship between obesity and outcome in septic patients was studied.
Methods This retrospective cohort study included all patients over the age of 40 with a confirmed diagnosis of severe sepsis and an ICU stay at our academic medical center from 1 January 2005 to 31 March 2011. Obesity was defined as a body mass index of 30 or greater. Data on other patient demographics and APACHE II score at the time of sepsis were collected from patient charts. Outcomes measured included in-hospital mortality, development of acute respiratory distress syndrome (ARDS), days on mechanical ventilation, hospital cost, and length of stay.
Results We identified 824 patients who met the inclusion criteria for this study. Of these patients, 257 (31.2%) were classified as obese. The mean APACHE II score was similar between obese and nonobese patients (23.3 vs. 22.4; P = 0.068). Obese patients had a similar rate of in-hospital mortality (31.9% vs. 33.7%; P = 0.810) compared with nonobese patients, but a significantly higher rate of development of ARDS (49.4% vs. 34.4%; P <0.001). Obese patients also had significantly

more days on mechanical ventilation (6.2 days vs. 5.0 days; $P = 0.005$). There was no relationship between mortality in obese patients on mechanical ventilation (34.4% vs. 39.5%; $P = 0.26$) or ARDS (33.9% vs. 42.6%; $P = 0.13$) compared with nonobese patients. Hospital costs and length of stay did not differ between the groups.

Conclusion Obesity significantly increased the incidence of ARDS and days on mechanical ventilation in patients with sepsis. Previous work has reported that obesity is associated with elevations in inflammatory cytokines and adipokines, particularly IL-6, which is a known risk factor for ARDS. The higher rate of ARDS in obese patients with sepsis identifies a high-risk group where new therapies may be most beneficial and where new methods of preventing ARDS can be targeted.

P47

Obesity is not associated with poor outcomes in older patients with sepsis

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Introduction Studies suggest that obesity may influence mortality in patients who develop sepsis. However, the mechanisms linked to improved outcomes are unclear. Our aim was to assess the impact of obesity on mortality at 30 and 180 days and cytokine expression.

Methods We used a platform of a negative randomized control trial in subjects ($n = 51$) with a diagnosis of severe sepsis with ≥1 organ failure. The cohort of severe septic subjects was stratified by obesity status based on the body mass index (BMI >30). Primary outcomes: 30-day and 180-day mortality; secondary outcome: difference in median (IQR) of five inflammatory cytokines including tumor necrosis factor alpha (TNFα), TNFα-receptor 2, interleukin (IL)-6, IL-1-receptor-antagonist (IL-1ra) and IL-10. The measurement of median baseline cytokine levels was done in serum by Luminex technology. Statistical significance was defined as $P < 0.05$.

Results Fifty-one subjects with severe sepsis were included in the study; 37% of the patients were obese (BMI >30). Paradoxically, obese severe septic patients had lower 30-day mortality ($n = 1$ (5%) vs. $n = 9$ (28%), $P = 0.069$) and 180-day mortality ($n = 1$ (5%) vs. $n = 13$ (41%), $P = 0.008$), when compared with nonobese. The expression of TNFα, TNFα-receptor 2, IL-6, IL-1ra and IL-10 was not statistically significant different among obese versus nonobese severe septic patients.

Conclusion Obesity is associated with lower mortality rates at 30 and 180 days in patients diagnosed with severe sepsis. This survival benefit was not associated with lower cytokine production among obese patients. Further studies are needed to assess the mechanisms associated with the survival benefit related to obesity in patients with severe sepsis.

P48

Long-term outcome in COPD patients with pneumonic and nonpneumonic exacerbation: a 6-year prospective follow-up study

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Introduction Predicting long-term outcome in patients surviving a pneumonic or nonpneumonic COPD exacerbation remains challenging. This study investigates the association of clinical parameters and the prognostic blood marker pro-adrenomedullin (proADM) measured upon hospital discharge with 6-year mortality in well-defined cohort of COPD patients.

Methods We prospectively followed consecutive COPD patients from a previous Swiss multicenter trial (2006 to 2008) [1] over a 6-year follow-up and investigated all-cause mortality following hospital discharge. Patients and/or treating general practitioners were contacted by telephone interview to assess the vital status of patients. We used Cox regression models and the area under the receiver operating characteristics curve (AUC) to investigate associations of baseline predictors and mortality.

Results Overall mortality in the 469 included COPD patients was 55% (95% CI 0.5 to 0.6) with a 14% (95% CI 0.1 to 0.2) mortality incidence rate per year. Patients with pneumonic COPD exacerbation had a more pronounced inflammatory response compared with patients with nonpneumonic exacerbation with regard to levels of initial C-reactive protein levels (median 158 mg/dl vs. 39 mg/dl, $P < 0.0001$), procalctionin (median 0.4 µg/l vs. 0.1 µg/l, $P < 0.0001$) and proADM (median 1.3 nmol/l vs. 0.9 nmol/l, $P < 0.0001$), but long-term survival was similar (HR 1.0, 95% CI 0.8 to 1.2). In univariate regression models, proADM was significantly associated with mortality after 1, 3 and 6 years (HR 16.1 (95% CI 6.9 to 37.7), 10.5 (95% CI 5.7 to 19.6) and 10.4 (95% CI 6.2 to 17.7), respectively). There was no effect modification by type of exacerbation. A model including clinical parameters (age, coronary heart disease, heart failure, diabetes mellitus, chronic renal failure, neoplastic disease, pneumonia, smokers) and proADM showed good discrimination of long-term survivors from nonsurvivors with AUC of 0.74 (95% CI 0.6 to 0.7).

Conclusion Clinical parameters and discharge levels of proADM allow accurate long-term prognostication in COPD patients independent of initial type of exacerbation. The focus on the best use of long-term prognostic information to improve patient care and clinical outcomes seems promising/rational.

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P49

Frailty predicts need for medical review but not degree of organ support after complex orthopaedic surgery

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Introduction Based on expert opinion and case note review, the UK National Confidential Enquiry into Peri-operative Outcome has recommended provision of perioperative level 2 and 3 care to support major surgery in older people, and particularly those with comorbidity [1]. We wished to identify whether we could predict if the need was uniform and whether any factors could predict the degree of organ supports needed.

Methods A retrospective note review of all patients admitted to a level 2 critical care unit in the 12-month period from 1 January 2012 to 31 December 2012 undergoing revision hip surgery either as a two-stage or single-stage process. Surgery was undertaken at a national referral unit and chosen to represent an appropriate group of older, comorbid patients. Predefined preoperative and perioperative data were collected from chart review, along with postoperative physiological data whilst the patient was in critical care. This included frailty, comorbidities, operative blood loss, anaesthetic technique and level and duration or organ supports including the need for additional medical review whilst on the unit. Frailty was assessed preoperatively

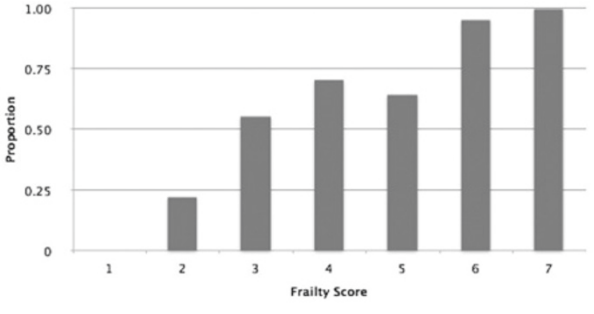

Figure 1 (abstract P49). Proportion of patients requiring additional medical review on critical care by degree of frailty.

using the Rockwood assessment tool by trained staff [2]. Data were analysed using Microsoft Excel for Mac 2011 and Stata/IC 11.2 for Mac.
Results A total of 182 patients with a mean age of 69.8 years (range 29 to 92) were identified. Frail patients were significantly more likely to need additional medical input in the postoperative period whilst on critical care (Figure 1, $P = 0.002$) but this was not significantly linked to need for vasopressors, evidence of sepsis or choice of anaesthetic technique.
Conclusion In complex revision orthopaedic surgery, the need for postoperative level 2/3 support cannot be predicted from any preoperative or intraoperative factors but patient frailty does indicate the need for medical input in the postoperative period.
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P50

Frailty measures in the critically ill: are we approaching a critical age? A systematic review

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Introduction As the general population ages, the proportion of critically ill patients in whom frailty may adversely affect outcome is likely to rise. The aim of this systematic review was to evaluate performance of frailty measures in predicting ICU, hospital and long-term outcomes following intensive care admission.
Methods We performed a literature search for original studies in: EMBASE, MEDLINE, Web of Knowledge, Cochrane database of systematic reviews, and Database of Abstracts of Reviews of Effects, using the terms 'frailty', 'frail elderly', 'critical care', 'critically ill', 'critical illness' and 'intensive care'. Our study inclusion criteria were that the study: included patients cared for in intensive care, captured data relating to premorbid frailty, and reported ICU, hospital and/or long-term outcome data.
Results Initial searches identified 606 reports, of which, following review of abstracts and removal of duplicates, 66 full-text papers were evaluated. Of these, 11 met inclusion criteria. A further 19 papers that met inclusion criteria were identified from relevant review articles and reference lists. There was huge variation in populations studied, methodology, frailty measures utilised and reported outcome measures. Of the 30 included studies, 11 studies evaluated patients undergoing major (including cardiothoracic) surgery, two studies specifically assessed patients with pneumonia, one study investigated patients in a burns ICU and one study restricted its investigation to former nursing home residents. The most commonly used measures of frailty were: measures of Activities of Daily Living ($n = 9$), which predicted need for long-term institutional care, 30-day, 90-day, 6-month and 12-month mortality; Clinical Frailty Score [1] ($n = 5$), which predicted ICU mortality, hospital mortality, 12-month mortality, quality of life and functional dependence; and Knaus score [2] ($n = 4$), which predicted ICU mortality, hospital and 12-month mortality.
Conclusion Measures of frailty appear to predict mortality and functional dependence following critical admission across a wide range of clinical conditions. However, comparative data regarding the relative accuracy and reliability of frailty measures in the intensive care population are currently deficient.
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P51

Prediction of 1-year mortality of patients treated for more than 72 hours in an ICU

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Introduction ICU or hospital mortality rates have been reported as the endpoint of ICU therapy for many years. The aim of this study was to determine the 1-year mortality after discharge from the ICU in patients who were treated in the ICU for more than 72 hours and to identify predictors for 1-year mortality.
Methods This study was conducted in a 20-bed mixed ICU of a teaching hospital. The study sample was extracted from a dataset of all ICU patients treated for more than 72 hours between 1 January 2007 and 1 October 2012. Demographic characteristics and clinical characteristics at admission and during the ICU stay were collected. Characteristics of patients alive 1 year after ICU discharge were compared with patients who died within the first year after ICU discharge. Descriptive statistics were calculated. Multivariate analysis of 1-year mortality was performed using a logistic regression model with backward elimination. Survival was analysed by the Kaplan–Meier method using the time interval from day of ICU discharge until death.
Results During the study period, 740 patients were treated for more than 72 hours in the ICU. The ICU mortality was 106/740 (14%). The data of 617 ICU survivors were further analysed (17 patients were lost to follow up). One-year mortality was 175/617 (28%), of which 85/175 (49%) patients died during hospital stay after ICU discharge. Independent predicting factors of 1-year mortality were: age at ICU admission (OR: 1.03; 95% CI: 1.01 to 1.05), APACHE IV predicted mortality score (OR: 1.02; 95% CI: 1.02 to 1.03), number of comorbidities (one or two co morbidities OR: 2.14; 95% CI: 1.42 to 3.23) (>3 comorbidities OR: 2.56; 95% CI: 1.16 to 5.62), readmission after ICU discharge within the same period of hospital stay (OR: 1.98; 95% CI: 1.13 to 3.46) and the diagnosis at admission (cardiovascular OR: 4.31; 95% CI: 1.73 to 10.76) (sepsis OR: 2.67; 95% CI: 1.50 to 4.77).
Conclusion Of patients being treated for more than 72 hours in the ICU, 28% died within 1 year after ICU discharge. One-half of them within the hospital stay after ICU discharge. High age at ICU admission, high APACHE IV predicted mortality score, high number of comorbidities, readmission and an admission diagnosis within the categories 'cardiovascular' and 'sepsis' are associated with an increased 1-year mortality after ICU discharge in this population. The burden of patients dying after ICU discharge underlines the necessity for clear ICU discharge criteria and post-ICU care.

P52

Long-term physical functioning and health-related outcomes in survivors of intensive care

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Critical Care 2014, **18(Suppl 1):**P52 (doi: 10.1186/cc13242)

Introduction The long-term impact of critical illness on survivors' physical and mental health remains unknown. Our aim was to create a follow-up clinic for survivors of critical illness in order to quantitatively examine muscle weakness, physical functioning and mental health and relate these findings to health-related quality of life (HRQL) and ICU risk factors.
Methods Study patients were selected from a 24-bed multidisciplinary ICU. Fifty-six patients who were ≥18 years old, stayed longer than 4 days in the ICU and did not have an acute brain injury were followed-up at 2 and 4 months post hospital discharge. Peripheral muscle strength (grip, triceps, biceps, hamstrings, quadriceps and dorsiflexors) and physical functioning were objectively assessed using hand-held dynamometry and the six-minute walk test (6MWT); both were compared with age/sex normative data. HRQL and mental health were assessed using the Short Form-36 (SF-36), EuroQol-5D (EQ-5D) and Hospital Anxiety and Depression Scale.
Results The median age of patients was 60 years, 68% were admitted for respiratory illnesses, they were severely ill (median APACHE II, 19) and had long ICU lengths of stay (median, 11 days). Muscle strength was significantly reduced when compared with normative data in all muscle groups at the 2-month and 4-month visits (2-month average indexed overall strength, 72%, $P < 0.05$). The median distance walked during the 6MWT was 382 m at 2 months (median percent predicted, 72%) and it did not significantly change at the 4-month visit. Reduced peripheral muscle strength was significantly correlated with lower distance walked during the 6MWT. Reported HRQL by the SF-36 was below national averages at both 2-month and 4-month visits (2-month

physical composite score (PCS) 36.2, mental composite score 48.1; 50 = national average). Reduced muscle strength was associated with low scores on the SF-36 physical function and general health domains. Performance on the 6MWT correlated with the SF-36 including the PCS (P = 0.001). Screening positive for anxiety was associated with both poor 6MWT performance and reporting dysfunction on the EQ-5D domains. ICU/hospital length of stay, number of days ventilated, severity of illness and organ dysfunction were not found to be predictive of muscle strength or physical functioning.

Conclusion Our study gives qualitative evidence that survivors of critical illness have reduced muscle strength, physical functioning and HRQL after hospital discharge. Also, we have shown muscle weakness is predictive of overall physical functioning, which in turn impacted HRQL and mental health. No ICU risk factors were identified that predicted deficits in muscle strength or physical functioning.

P53

Patients with prolonged stay on ICUs and the risk of mortality within 1-year of cardiac surgery

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Critical Care 2014, **18(Suppl 1):**P53 (doi: 10.1186/cc13243)

Introduction The aim of this study was to determine an appropriate risk model to identify patients at high risk of prolonged ICU stay and to aid patient consent prior to cardiac surgery.

Methods Data were prospectively collected on 5,440 consecutive cardiac surgery cases between April 2009 and March 2012. The primary outcome measure was the combined outcome of prolonged ICU stay (length of stay greater than 20 days) and/or in-hospital mortality. Logistic regression was performed to assess the predictability of logistic EuroSCORE against the primary outcome. Low-risk, medium-risk and high-risk groups were identified and subsequent risk of 1-year mortality assessed. Survival status was determined at 1 year.

Results A total of 192 (3.5%) patients had a prolonged ICU stay and 187 (3.4%) in-hospital deaths occurred, resulting in a combined primary outcome of 349 (6.4%). At 1 year, 371 (6.8%) deaths occurred. The risk of death in-hospital and at 1 year was significantly higher in patients with prolonged ICU stay (in-hospital mortality, 15.6% vs. 3.0%; P <0.001/1 year, 27.6% vs. 6.1%; P <0.001). The mean logistic EuroSCORE for all patients was 10.9. Patients with prolonged ICU stay had a significantly higher logistic EuroSCORE (20.3 vs. 10.6; P <0.001). The logistic EuroSCORE was a reasonable predictor of prolonged ICU/in-hospital mortality (OR 1.04, 95% CI 1.04 to 1.05, P <0.001) with a receiver operating characteristic (ROC) curve of 0.72. The relationship between a patient's logistic EuroSCORE and predicted risk of prolonged ICU is shown in the figure; including low-risk, medium-risk and high risk groups. Around 50% of the entire cohort of patients had a logistic EuroSCORE of 10 or less and an associated risk of prolonged ICU stay of 5% or less. See Figure 1.

Conclusion Using an existing risk prediction model, a patient's risk of prolonged ICU stay can be calculated using contemporaneous data. This information could be relevant for aiding in providing informed consent for cardiac surgery patients.

P54

Six-month outcomes in lung cancer patients surviving ICU admission: results from a multinational multicenter study

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Critical Care 2014, **18(Suppl 1):**P54 (doi: 10.1186/cc13244)

Introduction Information about lung cancer patients surviving critical illnesses is very scarce. Our aim was to evaluate the outcomes and continuing of anticancer treatments in lung cancer patients surviving ICU admission.

Methods Secondary analysis of a prospective multicenter study including patients admitted for >24 hours to 22 ICUs in six countries from Europe and South America during 2011. Readmissions and patients in cancer remission >5 years were excluded. Logistic regression was used to identify predictors for hospital mortality.

Results A total of 449 patients (small-cell (SCLC) = 55; non-SCLC = 394)) were admitted to ICUs, and out of them 275 (SCLC = 29; NSCLC = 246) were discharged alive from the hospital. Among them, 200 (73%) patients were alive and 72 (26%) had died at 6 months; three

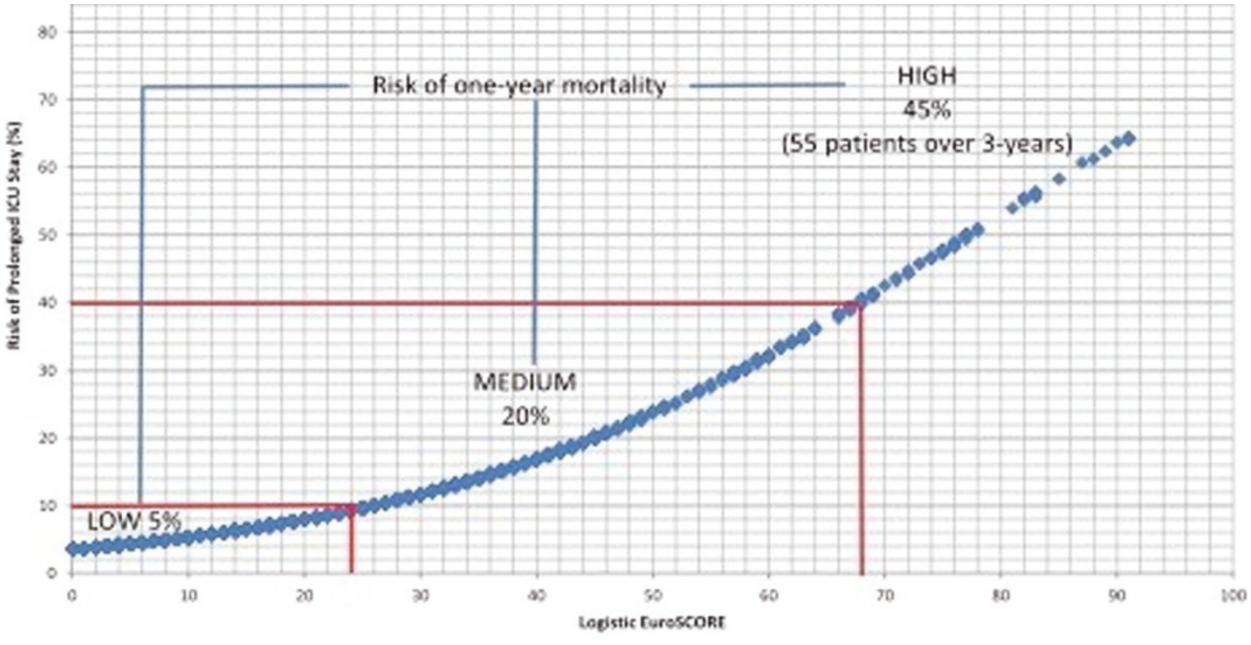

Figure 1 (abstract P53). Risk of long stay versus 1-year mortality.

(1%) patients were lost to follow-up. Mortality rates were far lower in the patient subset with nonrecurrent/progressive cancer and a good performance status (PS), even those with sepsis, multiple organ dysfunctions, and need for ventilatory support. Cancer recurrence or progression occurred in 53 (26%) hospital survivors. Anticancer treatments were recommended for 108 (39%) hospital survivors and administered to 102. Treatments used were variable combinations of surgical resection (7%), radiation therapy (34%), and chemotherapy (80%). The initial treatment plan required reduction or modification in 35 (34%) patients. Post-hospital mortality was nonsignificantly lower in the patients given the initial treatment plan than in the other patients (17% vs. 32%, $P = 0.065$). Poor PS was the only factor associated with a lower probability of receiving the initial treatment plan (OR = 0.20; 95% CI, 0.05 to 0.87; $P = 0.032$). At 6 months, 71% patients were at home, 15% were hospitalized, and 7% were in hospice care; the location was unknown for 6% patients. PS at 6 months was 3 to 4 in 19 (9.5%) survivors.

Conclusion Post-hospital mortality in critically ill lung cancer patients is relatively high and many patients require anticancer treatments after discharge. PS before ICU admission is a major determinant of both mortality and ability to receive optimal anticancer treatment in these patients.

P55

Survival and quality of life in patients acquiring acute kidney injury in the first 24 hours of ICU admission

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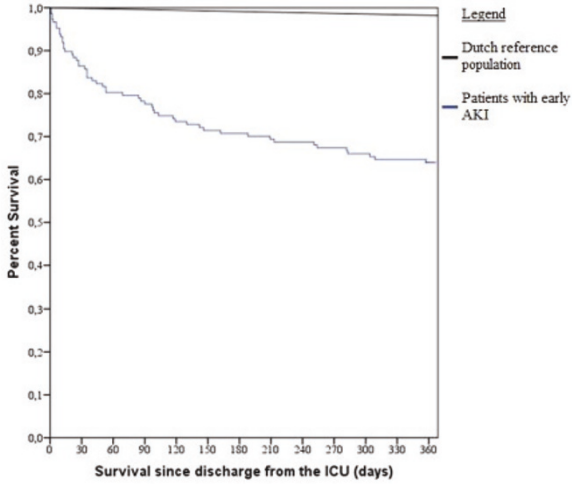
Introduction Survival and quality of life (QoL) in ICU patients with acute kidney injury (AKI) have been repeatedly reported as poor [1-3]. It is unknown whether early AKI, occurring during the first 24 hours of ICU treatment, is also a strong predictor of poor long-term outcome. Our aim was to describe the long-term outcomes of this specific group of ICU patients.

Methods All patients admitted to our mixed ICU from July 2009 to May 2012 with early AKI were included. All survivors received the EuroQoL EQ-6D-3L questionnaire. Early AKI was defined as creatinine >1.5 mg/dl and urine output <150 ml/8 hours. Poor ICU outcome was defined as either death or EuroQoL index <0.4 at 1-year follow-up.



Survival after ICU discharge	Baseline	6 months	1 year
	n (%)	n (%)	n (%)
Patients with early acute kidney injury	153 (100%)	104 (68.0%)	100 (65.4%)
Dutch reference population	153 (100%)	152 (99.3%)	150 (98.0%)

Figure 1 (abstract P55). Survival.

Results Out of 5,934 admissions, 269 patients were identified with early AKI. After ICU discharge a large and significant difference in survival between included patients and the Dutch population, matched for age and gender, was seen (P <0.001). The median QoL index in surviving patients was 0.65 (interquartile range (IQR) 0.45 to 1.00), versus 0.86 (IQR 0.84 to 0.89) in the Dutch population (P <0.001). Low QoL was found in 11/59 (18.6%) survivors. In total, poor ICU outcome was seen in 171/269 (63.6%) patients. See Figure 1.

Conclusion Patients developing AKI in the first 24 hours of ICU stay are prone to poor outcome. Future research into prognostic factors for ICU patients should include early AKI in their models.

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P56

Increasing age of patients admitted to intensive care, and association between increased age and greater risk of post-ICU death

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Critical Care 2014, **18(Suppl 1):**P56 (doi: 10.1186/cc13246)

Introduction The population of the UK is ageing, with the fastest increase in those ≥85 years. Increased age has been repeatedly associated with adverse outcome and it is uncertain to what extent this relates to the changes of ageing in themselves, or due to other considerations. Age is a key variable in the majority of scoring systems that relate patient characteristics to adverse outcome. We aimed to assess change in age distribution of patients admitted to our ICU over 20 years and examine the relationship between age of patient, mortality and length of stay (LOS).

Methods Data were extracted from electronic records (WardWatcher) and analysed using SPSS 20, GraphPad Prism 5.0 and Excel 2007.

Results ICU patients have become older by 4.4 months/year. By 2013 the median age was 66 and 15% of all patients are now ≥80 years – a 36% increase since 1993. Compared with the reference group (61 to 70 years), those in the older deciles have increased risk of ICU and hospital mortality (P <0.01). Fifteen per cent of all those 81 to 90 years old and 20% of those >91 years old who do not die on the ICU go on to die on the ward. It is unknown what proportion of these post-ICU deaths was unexpected. Older patients had prolonged hospital LOS (P <0.01) but not ICU LOS. See Figures 1 and 2.

Conclusion There are increasing numbers of older patients on ICUs in the UK. In analyses uncorrected for severity of illness or comorbidities, older patients are more likely to die on the ICU, and on the ward after ICU. They also spend longer in hospital prior to discharge.

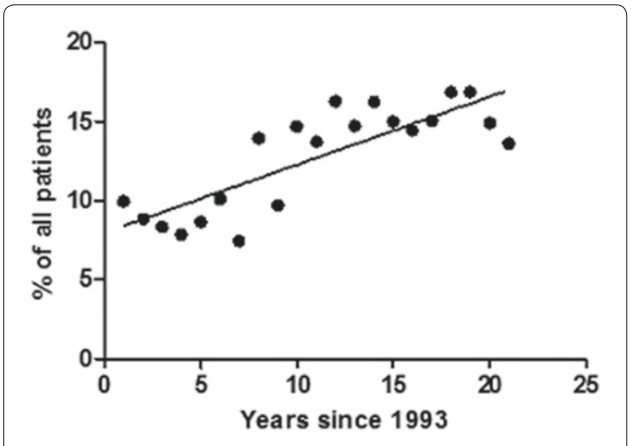

Figure 1 (abstract P56). Proportion of patients admitted to ICU aged >80 years, over time.

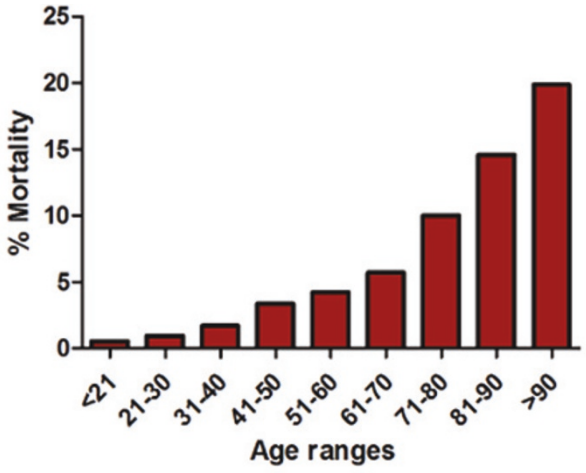

Figure 2 (abstract P56). Post-ICU in-hospital mortality, by age.

P57

Outcomes of military patients treated at the UK Royal Centre for Defence Medicine 2007 to 2013

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Critical Care 2014, **18(Suppl 1):**P57 (doi: 10.1186/cc13247)

Introduction UK military personnel injured overseas are repatriated to the Royal Centre for Defence Medicine (RCDM) based at the Queen Elizabeth Hospital Birmingham (QEHB) in Birmingham UK. We report the demographics and outcomes of military patients treated on the ICU at RCDM using data from the Intensive Care National Audit and Research Centre over a 6.5-year period.
Methods Data on 570 admissions of 527 patients to the ICU at RCDM/QEHB were analysed by ICNARC using standard methodology.
Results Some physiology and CCMDS data were missing for 175 patients. Age, sex and mortality are described in Table 1. A total of 90.9% of patients had traumatic injuries, 2.1% received CPR prior to ICU admission, 1.5% prehospital. A total of 20.6% had head, neck or spinal trauma. A total of 85.7% were transferred directly to the ICU from a military hospital overseas, others coming to the ICU following surgery at RCDM. Of the 382 patients with APACHE II score data the mean score was 11.0 (SD 4.9), probably reflecting stabilisation in military hospitals overseas or during aeromedical critical care transfer. The mean number of ICU days was Level 3: 7.6 (SD 11.6); Level 2: 2.0 (SD 2.8). A total of 70.4% of patients required advanced respiratory support for a mean of 7.5 days, and 33% required advanced cardiovascular support for a mean of 3.7 days.

Table 1 (abstract P57). Case mix, demographics and outcome

n	570
Male (%)	97.9
Age	25.7
Trauma (%)	90.9
Died (%)	6.8
LOS	8.8
MV (%)	70.4
CRRT (%)	10.9
Neuro (%)	24.8
CV (%)	33.2

Conclusion The data on resource utilisation for this group of patients may inform planning of critical care support for military operations overseas.

P58

Very old patients with cancer admitted to the ICU: outcome and predictive factors of mortality

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Critical Care 2014, **18(Suppl 1):**P58 (doi: 10.1186/cc13248)

Introduction The rate of very old patients (≥80 years old) admitted to intensive care has increased in the last years. Older age is associated with a higher prevalence of chronic diseases, including cancer [1]. The aim of the present study was to describe characteristics, outcomes and predictive factors of mortality in very old patients admitted to the ICU.
Methods We performed a retrospective analysis of all cancer patients who were 80 years or older admitted to the ICU between January 2009 and December 2012 in a tertiary reference cancer center. Data were collected from medical records.
Results A total of 597 patients with cancer were included in the analysis. Hospital mortality was 28.5%. These patients were more likely to have a solid tumor, a localized disease and underwent surgery, chemotherapy or radiotherapy recently. Variables associated with hospital mortality in these patients were: lung cancer, metastatic cancer and at ICU admission vasopressor requirements, acute respiratory failure, low hemoglobin levels, elevated creatinine levels, elevated bilirubin levels, acidosis and hyperlactatemia. By the multivariate analysis, the following factors were independent factors associated with hospital mortality: lung cancer (odds ratio (OR) = 6.3, 95% CI = 2.6 to 15.0, P <0.001), lactate levels on ICU admission (OR = 1.03, 95% CI = 1.02 to 1.04), P <0.001), bilirubin levels on ICU admission (OR = 1.16, 95% CI = 1.04 to 1.30, P = 0.007) and creatinine levels on ICU admission (OR = 1.58, 95% CI = 1.35 to 1.85, P <0.001).
Conclusion Very old patients with cancer present acceptable rates of survival after ICU admission. Similarly to younger patients, organ function evaluation in the first hours of ICU can predict outcomes in this specific population.
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P59

A retrospective review of mortality and complications following oesophagectomy in a large UK teaching hospital

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Critical Care 2014, **18(Suppl 1):**P59 (doi: 10.1186/cc13249)

Introduction Just over 1,200 curative oesophagectomies are carried out in the UK annually. Although in-hospital mortality rates have fallen (12 to 13% in 1998 to 2.5% 2013), complication rates remain high [1] with anastomotic failure and respiratory failure common postoperatively [2]. The aim of this retrospective review was to examine the outcomes in patients who underwent oesophagectomies in our unit between January 2010 and October 2012.
Methods We examined demographic data, survival (30 day and 1 year) and length of ICU and hospital stay. Case notes were reviewed to identify postoperative complications including anastomotic breakdown, reintubation and respiratory failure. Data were analysed to examine the relationship between the use of postoperative non-invasive ventilation and intraoperative fluid volume and the incidence of postoperative complications.
Results Seventy-two patients were identified as having undergone an oesophagectomy between January 2010 and October 2012. Median age was 65 and 82% were male. One patient died within 30 days (1.39%)

and nine patients had died by 1 year (12.5%). The median length of ICU and hospital stay was 4 days and 14 days respectively. Six patients had an anastomotic leak (of which two were chyle leaks). Use of non-invasive ventilation (in 23.1% of patients) was not associated with an anastomotic leak (chi-square $P = 0.53$), nor was the amount of fluid given intraoperatively (Mann–Whitney U $P = 0.410$). Six patients had to be reintubated and this was associated with a significantly increased length of both ICU and hospital stay (Mann–Whitney U $P = 0.01$ and 0.03 respectively). Lower P/F ratios were also associated with a significant increase in length of both ICU and hospital stay ($P = 0.007$ and 0.043).

Conclusion The overall mortality and morbidity rate was comparable with that seen nationally. Our data suggest that the use of non-invasive ventilation was not associated with anastomotic breakdown. A lower P/F ratio in the postoperative period was associated with prolonged ICU and hospital stay.

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P60

SwissScoring: a nationwide survey about SAPS II assessing accuracy

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Critical Care 2014, **18(Suppl 1):**P60 (doi: 10.1186/cc13250)

Introduction The first description of SAPS II dates back to 1993 [1], but little is known about the scoring accuracy in daily practice and factors possibly affecting it. The purpose of this study was to evaluate accuracy of SAPS II scoring by means of a nationwide survey.

Methods Twenty clinical scenarios, covering a broad range of illness severity, were randomly assigned to a convenience sample of clinicians or nurses of Swiss adult ICUs. They were asked to assign a SAPS II score (including details for each item of the score) for one scenario. Results were compared with a reference, as defined by five experienced researchers using a Delphi method, and cross-matched with data related to training and quality control for scoring, information on daily practice of scoring, and structural and organizational properties of each participating ICU.

Results Sixty-three (81%) of 78 adult ICUs participated in this survey. A perfect match with each single reference item was found in 27 (7.8%) of 345 scorings. The participants' mean SAPS II scoring was 42.6 ± 23.4, with a bias of +5.7 (95% CI 2.0 to 9.5) as compared with the reference score. There was no evidence of variation of the bias according to case severity, number of beds in the unit, number of residents during workshifts, linguistic area, profession (physician vs. nurse), experience, initial SAPS II training, and presence of a quality control system. The items with highest scoring accuracy were bilirubin, temperature and chronic disease (93%, 93% and 91% respectively), whereas the lowest agreement was found for urinary output and for the Glasgow Coma Scale (63% and 64%).

Conclusion This nationwide survey suggests a wide variability of SAPS II scoring results. On average, SAPS II was overestimated by more than 10%, irrespective of the profession or experience of the scorer or the structural characteristics of the ICUs. At least one person per unit involved in the scoring should be trained by the national society and should be responsible for the scoring quality.

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P61

Abandoning the National Early Warning Score in our district general hospital

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Critical Care 2014, **18(Suppl 1):**P61 (doi: 10.1186/cc13251)

Introduction Early Warning Scores (EWS) are used in UK hospitals to identify patients who are acutely unwell or needing urgent review. The National EWS (NEWS) [1] was implemented in our institution and led to a noticeable increase in the numbers of patients being triggered for escalation of medical care, although clinically this was thought unwarranted. This led to a potentially dangerous lack of faith in the NEWS by clinical staff. We assessed whether it was safe to move to VitalPAC™ EWS (ViEWS), a commercially available electronic EWS [2].

Methods All patients scored as 'high risk' by NEWS (with a score of 6 or more) in a snapshot audit of patients in our 500-bed acute district general hospital were identified and reviewed clinically. All of these patients were then recategorised using ViEWS. The clinical safety of this recategorisation was then assessed.

Results Forty-six patients were identified in our hospital at the time of the snapshot as being high risk according to NEWS. After recategorising this cohort of patients using ViEWS, 36 were classified as high risk (in this instance meaning a score of 5 or more). Subjectively the authors did not have any clinical concerns created by moving 10 patients out of the high-risk classification.

Conclusion ViEWS is more specific without being less sensitive. We have replaced NEWS with ViEWS and feel that this is clinically safe.

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P62

Endpoint resuscitation-based prediction model for early mortality of severe sepsis and septic shock

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Critical Care 2014, **18(Suppl 1):**P62 (doi: 10.1186/cc13252)

Introduction There is an unknown role for macrocirculation and microcirculation endpoint resuscitation, which are combined as the component of a prediction model for early mortality of patients with severe sepsis and septic shock [1,2]. The aim of this study is to develop a prediction model for early mortality (first 120 hours after onset [3]) of patients with severe sepsis and septic shock based on macrocirculation and microcirculation endpoint resuscitation.

Methods A retrospective cohort study was conducted in adult patients with severe sepsis and septic shock hospitalized in the ICU, Cipto Mangunkusumo Hospital, Indonesia. Patients' outcome and time to outcome were observed during the first 120 hours after severe sepsis and/or septic shock onset. Independent predictors for early mortality were identified by Cox's proportional hazard regression analysis and each was quantified to develop an early mortality prediction model. The calibration and discrimination abilities of the model were determined.

Results Subjects consisted of 268 patients. Early mortality developed in 70 patients. Two independent predictors for early mortality were: lactate clearance <10% (adjusted hazard ratio (HR) 11.81 (95% CI 6.50 to 21.46)) and number of organ dysfunctions (two organs, adjusted HR 1.47 (95% CI 0.58 to 3.72); >2 organs, adjusted HR 3.79 (95% CI 1.65 to 8.69)). A scoring system as the predictive model was performed by assigning 1 point for two organ dysfunctions, 6.5 points for >2 organ dysfunctions, and 12 points for lactate clearance <10%. This scoring system was stratified into two levels: low-risk (score <12, probability for early mortality 7.8%) and high-risk (score ≥12, probability for early mortality 72.3%) groups. The Hosmer–Lemeshow test revealed good precision ($P = 0.745$) and the area under the receiver operating characteristic curve showed very good discrimination ability (0.91 (95% CI 0.87 to 0.97)).

Conclusion A prediction model for early mortality of patients with severe sepsis and septic shock can be developed based on two parameters, lactate clearance and number of organ dysfunctions. A model has been developed to predict and classify mortality risk.

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P63

Is the Golden hour important? Looking at disability and health-related quality of life in a Portuguese trauma registry

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Critical Care 2014, **18(Suppl 1):**P63 (doi: 10.1186/cc13253)

Introduction The Golden hour (GH) complies the concept that definitive trauma care must be initiated within 60 minutes in order to improve outcome, but evidence is conflicting [1,2]. A variety of injury and health loss scores are used in post-impact care for assessing the injury severity, probability of survival and long-term loss of health [3]. The aim of this study is to establish a relationship between the concept of GH and disability or health-related quality of life (HRQoL) in trauma patients and to compare injury scores and health loss scores in this population.

Methods We analyzed patients from a trauma registry of a 700-bed university hospital between January 2003 and December 2007 who were alive 6 months after injury. A follow-up interview with the EQ-5D questionnaire was conducted. Data included patient demographics, type of injury, ISS, RTS and TRISS scores, ICU and hospital length of stay (LOS), mortality and EQ-5D domains.

Results There were 78% (n = 589) males and the average age was 44 ± 20 years. Most trauma cases originated from metropolitan areas and 91% (n = 688) of patients were managed within the GH. There was an association of mortality with older age and penetrating trauma. Mortality was higher for those with shorter length of stay. Those treated within the GH were less likely to die. In the HRQoL analysis, over one-half of the patients had moderate to severe problems in the Usual Activities domain. The median EQ-5D Index was 0.66 (0.47 to 0.98). There was no association of GH with HRQoL domains 6 months after discharge from the ICU. For the TRISS there was a lower probability of survival for the patients with severe problems in the physical health domains. The same results were obtained for association with age and LOS.

Conclusion The GH may be important as a survival outcome but not as a HRQoL outcome. Patients with severe problems in EQ-5D physical health domains showed lower probability of survival, were older and had a longer ICU LOS.

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P64

Predicting outcomes after blunt chest wall trauma: development and external validation of a new prognostic model

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Introduction Blunt chest wall trauma accounts for over 15% of all trauma admissions to emergency departments worldwide [1]. Reported mortality rates vary between 4 and 60% [2]. Management of this patient group is challenging as a result of the delayed onset of complications. The aim of this study was to develop and validate a prognostic model that can be used to assist in the management of blunt chest wall trauma.

Methods There were two distinct phases to the overall study; the development and the validation phases. In the first study phase, the prognostic model was developed through the retrospective analysis of all blunt chest wall trauma patients (n = 274) presenting to the emergency department of a regional trauma centre in Wales (2009 to 2011). Multivariable logistic regression was used to develop the model and identify the significant predictors for the development of complications. The model's accuracy and predictive capabilities were assessed. In the second study phase, external validation of the model was completed in a multicentre prospective study (n = 237) in 2012. The model's accuracy and predictive capabilities were re-assessed for the validation sample. A risk score was developed for use in the clinical setting.

Results Significant predictors of the development of complications were age, number of rib fractures, chronic lung disease, use of pre-injury anticoagulants and oxygen saturation levels. The final model demonstrated an excellent c-index of 0.97.

Conclusion In our two-phase study, we have developed and validated a prognostic model that can be used to assist in the management of blunt chest wall trauma patients. The final risk score provides the clinician with the probability of the development of complications for each individual patient.

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P65

Transplantation of bone marrow-derived mononuclear cells can improve the survival rate and suppress the inflammatory response in a rat crush injury model

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Introduction Crush syndrome is often encountered in natural disasters. It is a critical condition leading to multiple organ failure. However, the mechanisms by which the local traumatic injuries affect distant organs remain unknown. We paid attention to bone marrow-derived mononuclear cells (BMMNCs) as therapeutic strategy against crush injury. Transplantation of BMMNCs can elicit protection and regeneration against damaged organs through their paracrine properties and its clinical application has been realized to treat ischemia reperfusion-related various diseases. We have previously reported that multiple organ damage based on systemic inflammatory response is induced in crush injury and the pathogenesis is largely dependent on massive ischemia–reperfusion. We investigated whether BMMNCs could suppress systemic inflammation and improve mortality in a rat model of crush injury.

Methods To develop crush syndrome, both hind limbs of rats were compressed for 6 hours under weights (3.0 kg each). Rats in the treated group were intravenously administrated BMMNCs (1×10^7 cells in 1 ml phosphate-buffered saline (PBS)) immediately after weight removal (BMMNC group) and PBS alone was administered in the control group (CR group). The sham group underwent the same procedure without compression of hind limbs (SH group). The rats were observed over 7 days after the injury to evaluate survival. To estimate anti-inflammatory effects of BMMNCs, sera were collected 3 hours, 6 hours and 24 hours after the injury. The levels of interleukin 6 (IL-6) and tumor necrosis factor alpha (TNFα) were measured by ELISA and statistically analyzed.

Results The survival rate at day 7 in the BMMNC group was 80.0%, and that in the CR group was 47.6%, revealing that the 7-day survival

was significantly improved by the BMMNC injection (P <0.05). Crush injury-induced upregulation of serum IL-6 was significantly reduced by the BMMNC treatment at all time points (P <0.05). The level of TNFα decreased significantly in the BMMNC group compared with that in the CR group 24 hours after the compression release (P <0.05). These findings suggest that transplantation of BMMNCs has an ability to evade the devastating condition following crush injury by suppressing systemic inflammation.
Conclusion The administration of BMMNCs reduced production of inflammatory cytokines and improved survival rate in a rat model of crush injury. Cell therapy using BMMNCs might become a novel therapy against crush injury.

P66

Impact of a dedicated trauma desk in ambulance control on the identification of major trauma in Scotland

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Introduction In this study we determine the impact of a dedicated trauma desk on the identification of patients suffering from major trauma and on time to allocate critical care resources. Trauma is increasingly recognised as a serious global health problem and is the leading cause of death in those under the age of 45, accounting for 1,300 deaths in Scotland each year [1]. In addition, trauma causes considerable short-term and long-term morbidity and has personal, social and financial impact on the population [2]. Evidence and expert opinion strongly support the presence of appropriately trained, clinically active, personnel integrated and fundamental to the command and control structure in order to optimise the right resource being dispatched to the right patient at the right time.
Methods From October 2012 to April 2013 a trauma desk, staffed by experienced paramedics, was created in ambulance control with access to all emergency calls across Scotland. The operational hours of the desk were 08:00 to 18:00, 7 days a week. A customised database provided a data entry portal. Retrospective data were collated for comparison. Primary outcome measures were the number of emergency calls identified as potential major trauma and the time to allocation of critical care resources. Secondary outcome measures were the effects on stand-down rates of prehospital critical care teams.
Results There were 190 activations of critical care teams during the study period compared with 73 from the historical data from the same time frame in the previous year, representing a 160% increase in activations. The mean time from emergency call to allocation of critical care resource was 6 minutes compared with 19 minutes from historical data. The stand-down rate for prehospital critical care resource from emergency calls identified by trauma desk clinicians was 31.5% compared with 56% for those by nontrauma desk clinicians or dispatchers.
Conclusion A clinician focusing on major trauma in the ambulance control room improves activation times of prehospital critical care teams. The number of patients receiving life-saving and limb-saving interventions has substantially increased. The stand-down rate of teams following activation by the trauma desk is considerably reduced.
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P67

The Manchester Triage System in optimizing triage in adult general medical emergency patients: the Triage Project

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Introduction Some patients presenting to the emergency department (ED) currently face inacceptable delays in initial treatment due to suboptimal initial triage. Triage scores, such as the Manchester Triage System (MTS), have not been well validated in unselected medical patients. Herein, we performed a prospective cohort study to assess the prognostic potential of the MTS and the prognostic biomarker pro-adrenomedullin (ProADM) to identify patients at high initial treatment priority, patients with admission to the ICU, and patients who die within a 30-day follow-up.
Methods This is a prospective, observational cohort study including all consecutive medical patients seeking ED care between June 2013 and October 2013, except nonadult and nonmedical patients. We collected detailed clinical information including the initial MTS and measured ProADM levels on admission in all patients. Initial treatment priority was adjudicated by two independent, blinded physicians based on all available results at the time of ED discharge to the medical ward. To assess outcomes, data from electronic medical records were used and all patients were contacted by telephone 30 days after hospital admission. The prognostic performance of MTS and ProADM was assessed in multivariate regression models with area under the receiver operating curve (AUC) as an overall measure of discrimination.
Results We included a total of 1,452 patients (58% males, mean age 66.6 years). A total of 20.1% (n = 292) were classified as high treatment priority, 5.4% (n = 79) were admitted to the ICU and 4.4% (n = 64) died within 30 days. The initial MTS showed a good prognostic accuracy to predict treatment priority (AUC 0.75) and ICU admission (AUC 0.76), but not for mortality prediction (AUC 0.58). Initial ProADM levels were independent predictors for all three outcomes and significantly improved the MTS score to AUCs of 0.78 for treatment priority, 0.80 for ICU admission and 0.84 for mortality.
Conclusion Within this large cohort of consecutive unselected medical patients seeking ED care, the MTS instrument in combination with a prognostic biomarker (ProADM) allowed accurate initial risk assessment in regard to treatment priority, ICU admission and mortality. A combined score has the potential to significantly improve initial risk assessment in patients, which may translate into faster and more targeted care and better clinical patient outcomes.

P68

Introduction of the Kaifu telemedicine system for emergency medicine to ambulance services with improvement of the survival rates

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Introduction Our hospital has introduced the telemedicine system for emergency medicine (k-support) using a smart device to rectify health disparity and reduce the burden to general physicians since February 2013. We have expanded to the ambulance services' k-support toward further survival rate improvement.
Methods The registration device, patient information and image information such as magnetic resonance imaging and computed tomography taken in the hospital were transferred in real time to k-support using the smart device. Since September 2013, we newly developed k-support to the Kainan Fire Department Mugi branch office, Kainan Fire Department Hiwasa branch office, Kaifu Fire-fighting Union Kainan fire department, and Muroto Fire-Fighting Headquarters Touyou branch office, and reviewed our experience of this approach in the use of k-support during the first 3 months of the introduction.
Results k-support was used for 62 patients, and 13 (21.0%) of them were categorized as neurosurgical diseases. The detail of neurosurgical diseases consisted of six patients (46.1%) with head injury, followed by five patients (38.5%) with cerebral infarction, one patient (7.7%) with cerebral hemorrhage and one patient (7.7%) with miscellaneous diseases. We shared the information by ambulance services to tweet the patient information or transmit vital signs and electrocardiograms. We experienced a case that was diagnosed with cardiogenic embolism and tried the 'drip and ship' method of rt-PA. The outcomes were as follows: hospitalization, 28 (45.2%); discharge, 18 (29.0%); and transfer, 16 (25.8%).
Conclusion Introduction of k-support is the first trial in Japan. For emergency diseases such as ischemic heart diseases and stroke, we could perform responses earlier than ever by providing this system.

P69

Training to achieve coordination of rescue and ambulance and medical teams

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Introduction Japanese emergency medical technicians are not allowed to perform some advanced medical practices such as a tracheal intubation, establishment of an intravenous line, administration of a drug to a patient who retains their own circulation. So medical staff have to be dispatched to the accident scene to give a patient such medical practices. In Japan, we have developed and dispersed the educational course of the Disaster Medical Assistance Team since 2005. But the role of medical teams at the scene is not widely known among rescue workers. It is also distant for medical staff to coordinate rescue teams, because most of them do not work with rescue workers in their daily work. We have felt a need for practical training to achieve the coordination of rescue and medical teams.
Methods We held a disaster-relief training workshop from 2010 to 2013. Prior to starting the drill, we gave two lectures about the role of a medical team in a rescue site and the basic knowledge of rescue skills. The drill was organized for 1 to 1.5 hours. The scenario was secret for participants. Before and after the workshop, we had a questionnaire survey for attitude changes about a collaborative work between a rescue team and a medical team.
Results A total of 160 people participated in the workshop (63 rescue workers, 27 ambulance workers, 33 paramedics, 37 medical staff). At first, rescue workers tended to downplay the importance about the division of roles or the establishment of command and control system between rescue teams and medical teams, but their attitude changed after the drill (P <0.05). They also understood the need to know about basic trauma survey skills and some medical terms.
Conclusion To achieve mutual understanding, it is important to have drills in which both rescue teams and medical teams participate.

P70

Complementary cooperation of an ambulance helicopter and car with medical doctors: meaning of simultaneous dispatch

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Introduction Recently, the dispatch system with a medical doctor in pre-hospital care has made rapid progress in Japan. We usually use an ambulance helicopter or an ambulance car/rapid response car for dispatch. In this report, we analyzed the cases in which the medical doctors were dispatched using both means at the same time.
Methods We analyzed 29 cases with simultaneous dispatch with the medical doctors using ambulance helicopter and car during October 2012 to September 2013.
Results The average distance of dispatch was 25.6 km. The correspondence to the plural patients was three trauma cases. In nine cases, the ambulance car was first selected for the dispatch vehicle and the ambulance helicopter was added. In three cases, both devices were canceled on the dispatch way to the scene. In seven cases, the ambulance car was canceled. In 10 cases, the patients were transferred by the ambulance helicopter.
Conclusion In the selection of the dispatch means, the time to contact with the patient is the most important factor. However, the decision of the suitable means is occasionally quite difficult at the moment of first information. The ambulance helicopter and car were complementary to each other in the dispatch mean of the medical doctors.

P71

Evaluation and prevention of violence in the emergency department in Lebanon

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Introduction At the hospital we are faced with situations of violence, whether verbal or physical, especially in the emergency department (ED) [1]. The objective of this study is to evaluate the phenomenon of violence at hospitals in Lebanon, especially in the ED, and to recommend techniques to prevent it.
Methods A questionnaire consisting of 18 questions was sent to the caregivers in the ED of three randomly selected hospitals in Beirut, Lebanon in 2012. A total of 111 people (nurses, aides, doctors, interns, residents, social workers and security guards) responded to the survey questionnaire.
Results The majority of the surveyed people are young women (62%) aged between 20 and 40 years (78%) with a nursing degree (74%) and professional experience <5 years (48%). In total, 59% of respondents have experienced violence in the ED during the night (58%) from the patients (31%) or their companions (68%). The caregivers most affected by the violence are nurses (54%) and employees of reception (46%). Violence can be verbal (threats 47%, insults 36%, criticism 18%) or physical (hitting 43%, slapping 40%, stabbing 17%). The dissatisfaction of the patient in his care (42%) and his anxiety (33%) are the most important factors in the generation of violence that may have repercussions on the care workers and their psychological status.
Conclusion Violence in the ED may be due to the heavy workload of the caregivers causing a delay in care. Secondly, patients in the ED may feel insufficiently informed and heard by the nursing staff. The priority given to emergencies depending on the severity and not the order of arrival can be misunderstood [2]. Therefore, we recommend the following actions: encourage caregivers to improve their knowledge and training on the management of patients in emergency situations; train emergency caregivers to mediation, nonviolent communication and managing stressful situations; and increase the number of nurses and security guards in the ED and motivate them to ensure a better quality of care and minimize the delay in their care.
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P72

Epidemiology and critical care management of patients admitted after intentional self-poisoning

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Introduction Intentional self-poisoning is one of the most common presentations to acute medical units across the UK [1]. To our knowledge no studies have been published on incidence of admissions to critical care in England after overdose. Our aim was to investigate the epidemiology, clinical features and outcomes of patients admitted to critical care after intentional self-poisoning to establish patterns in our community.
Methods We performed a retrospective data collection using our critical care database 'Metavision' to select all patients admitted with a diagnosis of 'overdose'. Records were scrutinised to collect information on patient demographics, clinical features and medical management.
Results Thirty-eight patients (male:female ratio 1:1.53) were admitted to critical care over a 1-year period (September 2011 to 2012). This represented 2.45% of the total admissions to critical care during the same period. The sample had a significantly younger median age (45 years) than the standard patient population in critical care (68 years) during the same period (P <0.0001). Despite the young age and paucity of comorbidities, there was no difference in length of stay between overdose patients (2.0 days) and all other patients on critical care (1.58 days, P = 0.3). The median number of agents ingested was three

(1 to 7) with 84.2% ingesting ≥2 agents. Hypnotics and antidepressants made up 45% of the agents ingested. A total 92.1% of the sample was admitted out-of-hours or at weekends. Fifty per cent had a past history of overdose, 25% had a history of alcohol misuse. A total of 79% of patients were referred to critical care due to a low conscious level but only 50% required IPPV and 20% received vasopressors/inotropes. The mortality rate was 2.6%, with one further death 6 months after discharge due to alcoholic liver disease. Estimated financial cost was £80,555 or £2,119 per patient (57 level 3 bed-days, 35 level 2 bed-days).
Conclusion Intentional self-poisoning mortality rates are low in spite of the number of patients admitted. Despite the young age of patients and lack of comorbidities, their length of stay is similar to the average length of stay for all patients admitted to the unit, representing a significant financial cost. Self-poisoning requiring critical care support is more common out-of-hours when less senior expertise is available. Education of junior doctors into management of overdose is therefore vital to ensure the early identification and appropriate treatment of these patients.

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P73

Price per unit: the cost of alcohol-related admissions to a regional ICU

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Introduction A number of studies have demonstrated the significant and increasing morbidity and mortality associated with alcohol-related disease in the UK, and the corresponding impact this has on critical care services [1]. This study was designed to similarly evaluate the current burden of alcohol-related disease on admission rates to a regional ICU, but also to calculate the financial costs of such admissions.
Methods Data-entry fields derived from recommendations in a public heath publication [2] were introduced to the local electronic records system to enable prospective data collection for all admissions that were either wholly or partially attributable to alcohol consumption. Using locally defined values for the cost per day of an admission to the ICU, depending on the maximum level of organ support required during the admission, it was possible to calculate the total expense incurred by the unit for each alcohol-related admission.
Results In 1 year from December 2012 to November 2013 inclusive, the ICU recorded 84 alcohol-related admissions, accounting for approximately 9% of annual unplanned admissions. With an average length of stay (5.8 days) similar to that of all other unplanned admissions, this totalled 534 ICU bed-days. A total of 86% of patients with alcohol-related conditions were male with an average age of 46.4 years (range 15 to 83 years), and the majority (42%) presented with chronic conditions partially attributable to alcohol consumption. The number of admissions per month varied from zero in May to a peak of 14 in November, with the majority (40%) of admissions occurring over the autumn months (Figure 1). Eighty-nine per cent of patients with alcohol-related conditions required support for at least two organ failures, which subsequently equated to an overall cost to the unit of £725,308 and 12% of an approximate £6 million annual budget.
Conclusion The results of this study support the hypothesis that alcohol-related disease contributes considerably to admissions to this ICU. Furthermore, they have shown that the financial impact was proportionally greater than the percentage number of admissions attributable to alcohol consumption, reflecting the high frequency of multiorgan failure in this patient cohort.

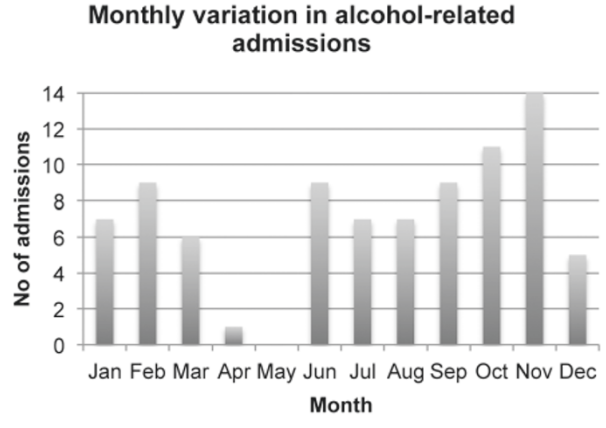

Figure 1 (abstract P73).

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P74

Clinical research of patients with multiple organ dysfunction syndrome induced by severe heat stroke: nine case reports and literature review

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Introduction The objective was to analyze the clinical features of multiple organ dysfunction syndrome (MODS) induced by severe heat stroke, and to investigate the pathogenesis, diagnosis and prevention strategies in patients with MODS caused by severe heat stroke.
Methods We retrospectively studied nine cases of MODS caused by severe heat stroke, and systemically reviewed the relevant literature.
Results (1) Nine patients with MODS caused by severe heat stroke were all exposed in hot and humid environments. All nine patients are severe heat stroke, including seven cases of classic heat stroke (77.8%) and two cases of exertional heat stroke (22.2%). (2) Among nine cases of MODS caused by severe heat stroke, eight patients met the diagnostic criteria for SIRS. In addition, there was a significant increase in blood PMN proportion and serum CRP of all nine patients. Of note, there was also a marked increase in serum IL-6 (average (36 ± 19) pg/ml; reference range (0 to 5.9 pg/ml)); and TNFα level (average (21 ± 10) pg/ml; reference range (0 to 8.1 pg/ml)), while IL-8 was normal (average (22 ± 25) pg/ml; reference range (0 to 62 pg/ml)). (3) There were 34 organ damages involved in all nine patients with MODS induced by severe heat stroke. The kidney, circulatory and liver accounted for 58.8% of all these organ dysfunctions. The incidence of severe heatstroke-induced organ dysfunction in turn was the kidney, circulation, liver, blood coagulation, metabolism, brain, lungs, and gastrointestinal tract. (4) During hospitalization, the common complication was pulmonary infection in patients with MODS caused by heat stroke. (5) After early intensive care of organ supportive treatment, there was a quick improvement and recovery in most cases in several days. Seven patients survived, and the average length of stay in hospital was 9.5 days.
Conclusion Severe heat stroke results in significant abnormal changes in inflammatory markers in patients with MODS induced by heat stroke. The types of organ dysfunction in heat stroke-induced MODS are usually distinct from those of infection and trauma. After active cooling and intensive organ function supportive treatment, most patients recovered in a relatively short period.
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P75

Effect of low-dose hydrocortisone on gene expression profiles after severe burn injury

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Introduction The systemic effect of inflammatory mediators released after severe burn is a severe cardiovascular dysfunction called burn

shock. Patients need vasopressor infusion to maintain adequate delivery of oxygen but it could have deleterious effects on skin perfusion and worsen the burn depth. This shock could result from the interplay of the initial hypovolemia and the release of multiple inflammatory mediators [1]. It has been shown that a low-dose of hydrocortisone could reduce the shock duration but the mechanisms involved remain unclear. We investigated the systemic genomic response after severe burn injuries and determine whether patterns of gene expression could be associated with a low dose of glucocorticoids.

Methods Thirty burn patients with over 30% of total body surface area were enrolled into a randomized double-blind clinical study. Fifteen patients were treated with a low dose of hydrocortisone and 15 patients were treated with placebo. Whole blood samples were collected after shock onset (S1) before any treatment, 1 day after treatment beginning (S2), and 120 hours and 168 hours after the burn injury (S3/S4). Blood samples of 13 healthy volunteers were collected. Pangenomic expression was evaluated with Affymetrix HG-U133plus 2.0 microarrays. Moderated *t* tests and *F* test were used to compare burn patients with controls and gene expression profiles between the two groups (B–H correction, $P < 0.05$).

Results Severe burn injury induced the deregulation of a considerable number of genes ($n > 2{,}200$ at S1) in comparison with controls with an increased number of deregulated genes over time. Within burn patients, more than 300 genes were deregulated by hydrocortisone over time. The treatment had a rapid effect on gene expression, 339 and 627 genes were differentially expressed at S2 and S3 respectively. However, the number of these genes decreased drastically at S4 (only 24 genes significant). The genes identified at S2 were mostly related to the decrease of growth, development and quantity of leukocytes but these biological processes were not found significant at S3, indicating that the action of glucocorticoid in the response to burn injury is short lived and time dependent.

Conclusion This study is an informative overview of the genomic responses after burn injuries. More importantly, it is the first study providing information about mechanisms involved in glucocorticoid's reduced shock duration after burn.

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P76

Care of Burns in Scotland: 3-year data from the Managed Clinical Network National Registry

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Introduction The Managed Clinical Network for Care of Burns in Scotland (COBIS) was launched in April 2007. Primary aims included establishing and maintaining a registry of complex burn injury in Scotland and setting mechanisms to regularly audit outcome of burn treatment against nationally agreed standards of care. On behalf of COBIS, we present 3-year incidence and mortality data of Scottish patients admitted with a complex burn injury in this abstract.

Methods From January 2010 onwards, data were prospectively collected for all patients in Scotland with complex burn injury admitted to Scottish burns units. Data collection was initially on a paper *pro forma*, but subsequently evolved into a web-based audit data capture system to securely link hospital sites involved in the delivery of care of complex burns. Data collected included extent and mechanism of burn, presence of airway burn or smoke inhalational injury, comorbidities, complications, length of stay, interventions and mortality. Quality, completeness and consistency of data collection are audited with feedback to the individual units.

Results In a population of approximately 5.3 million, the annual incidence of complex burn injury is 499 to 537 (9 to 10 per 100,000). The incidence of a major burn is 5% of burn admissions. The hospital mortality from a burn is 1 to 2.2%. See Table 1.

Table 1 (abstract P76). Numbers of complex burns in Scotland 2010 to 2012

	2010	2011	2012
Adult	304	392	399
Paediatric	195	185	138
Adult >15%	27	28	26
Paediatric >15%	0	2	4
Mortality	5	7	13

Conclusion From these data, Scotland now has comprehensive national figures for complex burn injury. This allows for benchmarking against other international indices, few of which provide comprehensive data. COBIS data can now also be correlated with other mortality data sources. As data quality improves, detailed analysis of mortality data will allow COBIS to identify contributing issues affecting burns patients. Some issues identified already are that patients with burns often die soon after their discharge from hospital of other related and unrelated causes. Subsequent analysis of this will allow COBIS to identify and address issues that may be contributing to these statistics.

P77

Low socioeconomic status, ethnicity and geographical location confers high risk of significant accidental burns injuries in London

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Introduction The majority of burns injuries are considered accidental, although previous studies have identified demographic factors associated with higher risk of burns such as socioeconomic deprivation [1] and being from ethnic minority groups [2]. This study aims to identify population subgroups in London at high risk of burns injuries requiring admission to a burns centre through geographic mapping and socioeconomic statistics.

Methods Records of all paediatric and adult inpatients admitted to the burns centre at Chelsea and Westminster Hospital were retrospectively reviewed for age, ethnic group and deprivation score of residence, as measured by the English Index of Multiple Deprivation 2010. Corresponding population data for London were obtained.

Results In total, 2,195 patients from London were admitted between January 2009 and August 2013, with 1,963 (89.4%) classified as having accidental injuries. A total 1,725 (87.8%) of accidental burn injuries occurred in the patients' own homes. Patients from ethnic minorities have the highest rate of burn injury at 7.1 per 100,000 population per annum ($P < 0.0001$). Patients below the median for socioeconomic deprivation in London are more likely to suffer burn injuries ($P < 0.0001$). Patients from the most deprived quartile are more likely to suffer burns injuries of >10% TBSA ($P = 0.04$), and have a trend towards higher rates of ICU admission ($P = 0.144$). Domestic accidental burns were mapped to their respective administrative wards, and the rate of burns per 100,000 was calculated and divided into quintiles. The areas with the top quintile of burn injury rate, of up to 18.8 per 100,000 population per year, were almost four times the national average.

Conclusion Ethnicity, socioeconomic deprivation and geographical location appear to be risk factors for burn injuries. Identifying such groups may allow the development of targeted preventative strategies.

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P78

Effectiveness of noncontrast abdominal multidetector CT for evaluating the patient with renal insufficiency in the emergency department

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Introduction Contrast-enhanced abdominal multidetector CT (MDCT) is an important and accurate diagnostic approach for acute abdominal

symptoms or searching for an infection focus such as sepsis. But contrast dye can cause renal damage especially in critically ill patients. Noncontrast CT can be alternative options but few studies have shown the effectiveness of noncontrast MDCT. We want to evaluate the effectiveness of noncontrast abdominal MDCT in the emergency department.

Methods This is a retrospective chart review study conducted in a single tertiary academic hospital from January 2011 to April 2012. Patients were enrolled if they visited the emergency department with acute abdominal symptoms or infection signs, had elevated serum creatinine level, and received noncontrast 16-channel MDCT.

Results During study period, 78 patients with renal insufficiency received noncontrast abdominal CT. Causes of CT were infection focus (48, 61.5%), abdominal pain (21, 26.9%), GI bleeding (4, 5.2%), abnormal labs (3, 3.9%), ureter stone (1, 1.3%) and abdominal distension evaluation (1, 1.3%). Any abnormal CT findings were detected in 61 (78.2%) patients. For 42 (53.8%) patients, noncontrast CT findings showed diagnostic abnormal findings. For excluding abdominal pathology, 35 (44.9%) were helpful. In one (1.6%) case with hematochezia, noncontrast CT showed no benefit for patient diagnosis. Additional contrast-enhanced CTs were performed in 32 (41%) and additional findings were found in five cases (6.4%). There were 40 patients with severe sepsis or septic shock. Abnormal CT findings were found in 30 (75%) cases. Additional contrast enhanced CT was done for 13 (32.5%) patients but no additional information was detected.

Conclusion Performing noncontrast abdominal MDCT to the patient with renal insufficiency for evaluating acute abdominal symptoms, severe sepsis or septic shock in the emergency department was feasible and effective.

P79

Antipyretics in the emergency department – intravenous paracetamol versus intramuscular diclofenac: a comparative study

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Introduction Fever is a common problem in adults visiting the emergency department (ED) [1]. Although it is important to treat the cause of fever, symptomatic management of fever is also necessary. Multiple studies are available on the efficacy of various antipyretics in children, but very little has been done in adults [1,2]. Hence we aimed to compare the antipyretic efficacy of intravenous (i.v.) paracetamol and intramuscular (i.m.) diclofenac in adult patients presenting with fever to the ED.

Methods In this parallel-group, open-label trial, participants aged 14 to 75 years who had a temperature more than 38.5°C were enrolled and treated in the ED, Alkhor, Hamad Medical Corporation, during the period June 2008 to December 2011. Patients were randomly assigned to receive either 1,000 mg i.v. paracetamol or 75 mg i.m. diclofenac. The primary outcome was degree of reduction in mean oral temperature at 90 minutes and the secondary outcomes were degree of reduction at 30, 60 and 120 minutes. The efficacy of drugs was assessed by a superiority comparison. Analysis was done using intention-to-treat (ITT) principles.

Results In total, 139 patients received i.v. paracetamol and 150 received i.m. diclofenac. The mean age was 35.5 ± 14.24 and 36.4 ± 14.98 years in the i.m. diclofenac and i.v. paracetamol groups respectively. The majority of the patients were males in both groups. After 90 minutes both groups showed a significant reduction in mean temperature, i.m. diclofenac showing a greater reduction (–1.44 ± 0.43(95% CI –1.4, –2.5)) than i.v. paracetamol (–1.35 ± 0.46 (95% CI –1.3, –3.1) P <0.0001). After 120 minutes, a significant difference was observed in the mean change from the baseline temperature between the groups, –1.81 ± 0.46 (95% CI –1.7, –2.9) in i.m. diclofenac versus –1.63 ± 0.55 (95% CI –1.5, –4.1) in the i.v. paracetamol group (P <0.0001). Significant changes in temperature were observed in favor of i.m. diclofenac over i.v. paracetamol at each time point from 60 minutes through 120 minutes inclusive.

Conclusion Both i.m. diclofenac and i.v. paracetamol showed significant antipyretic activity, with diclofenac having a greater effect. In view of ease of administration, i.m. diclofenac can be used as a first-choice antipyretic in febrile adults in the ED.

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P80

Survey of severe sepsis and septic shock management in Thailand: THAI-SHOCK SURVEY 2013

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Introduction A pragmatic survey of shock management in Thai physicians is unavailable. The objective of this study is to identify shock management patterns for severe sepsis and septic shock in Thailand.

Methods Two thousand questionnaires were sent to physicians involved in caring for shock patients across Thailand. The frequency scale was defined as five levels by patient proportion estimation at routine practice.

Results Between April and August 2013, a total of 533 questionnaires (26.7%) were returned. For severe sepsis and septic shock management, a total of 406 physicians (76.2%) reported their routine usage of quantitative resuscitation protocols. Urine output, mean arterial pressure and central venous pressure are more frequently used than central venous oxygen saturation and lactate as the resuscitation endpoint. Nearly 80% of these had an 'often and always' resuscitation goal within 6 hours. Most physicians (65.3%) never used procalcitonin. The antimicrobial empirical treatments were started within 1 hour for 87.7% and these were continued less than 5 days in 67.3% before de-escalation. Crystalloid was the common initial fluid therapy in 98.9%. The most common used vasopressor was norepinephrine (69.6%). The median of cortisol threshold level for steroid replacement therapy was 15 (interquartile range, 5 to 19) mg/dl. Almost all of the physicians used hydrocortisone (96.4%). The median daily dose of hydrocortisone was 300 mg (interquartile range, 200 to 300). Nearly 50% divided the dose every 8 hours and 31.8% infused continuously. The duration for tapering was varied (33.6% in 2 to 3 days). Central venous pressure (CVP) and fluid challenge test were more frequently used for preload evaluation than new fluid responsiveness methods. Less than 15% still used a pulmonary artery catheter in their routine practice.

Conclusion Most physicians manage shock with protocols. Hemodynamic endpoints are preferred to tissue perfusion targets. Early antimicrobial therapy and de-escalation are routine practices without use of infective biomarkers. Crystalloid is preferred rather than colloid at initial resuscitation. CVP and fluid challenge are still more popular than new fluid responsiveness methods on preload assessment. Hydrocortisone is the most common steroid prescription in septic shock but the threshold of initiation, frequency and discontinuation are varied.

P81

Laboratory early warning score versus clinical early warning score as a predictor of imminent cardiac arrest

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Introduction NCEPOD reported in 2012 that 75% of patients had warning signs for cardiac arrest present prior to their arrest [1]. NICE recommends a vital sign-based early warning score (EWS) to identify patients at risk of deterioration or death [2]. In our trust, audit has

shown that only 20 to 35% of patients trigger the clinical EWS prior to cardiac arrest. Jarvis and colleagues proposed that an EWS based on common laboratory findings can predict patient mortality [3]. The aim of this study, as part of a wider review of cardiac arrests in our hospital, was to determine whether the laboratory early warning score (LEWS) might be of use identifying patients at risk of cardiac arrest in our trust.
Methods Retrospective data collected identified cardiac arrest calls that lead to CPR or defibrillation over 6 months. The LEWS was calculated according to the formula devised by Jarvis and colleagues [3]. LEWS ≥4 for males and ≥5 for females was taken as being a 'trigger' as suggested by Jarvis and colleagues [3].
Results Eighty-nine cardiac arrest calls lead to CPR and/or defibrillation in this time period. Of these, 65 patients had had blood tests within the last 24 hours. Median LEWS was 6 for females and 7 for males (range 1 to 12). Most patients (77%) had a LEWS trigger (≥4 for females and ≥5 for males).
Conclusion The collected data suggest that more patients at risk of cardiac arrest in our hospital might be identified using a LEWS rather than a clinical EWS. It is evident that for a clinical EWS regular observations need to be taken and are subject to user error. Clinical EWS could also not be sensitive enough or there is a failure to implement it successfully. LEWS can be generated automatically when bloods are taken. The downside is that it relies on bloods being done. It is beyond the scope of this study to examine the sensitivity/specificity of LEWS or suggest that LEWS should replace EWS. We suggest that LEWS may compliment EWS by identifying a different group of patients. The ongoing data collection aims to correlate the clinical EWS for each patient directly with their LEWS to confirm the initial findings.
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P82

Hospital mortality predictive factors following Rapid Response Team activation

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Introduction The Rapid Response Team (RRT) represents an important advance in the management of deteriorating ward patients and is recommended as a patient safety measure. Most studies on RRT evaluate the effects of its implementation on rate reduction of cardiopulmonary arrest outside the ICU and hospital mortality, with limited information on the criteria for RRT calls and predictive factors associated with hospital mortality [1,2]. Therefore, our objective was to determine what factors are associated with hospital mortality for patients seen by the RRT at the Hospital Israelita Albert Einstein (HIAE).
Methods A total of 1,051 patients assessed by RRT between January and December 2012 at the HIAE, a general hospital with 650 beds, were included in this study. Multivariate analysis was used to evaluate what variables were associated with hospital mortality. Early RRT call was defined as RRT activation <48 hours from hospital admission and late RRT call if it happened >48 hours from hospital admission.
Results The mean age was 64 ± 19.8 years and 48% (n = 513) were male. There were 513 (48.9%) early calls and 537 (51.1%) late calls. The main reasons for RRT activation were respiratory failure in 18.2% (n = 191) and severe sepsis/septic shock in 13.1% (n = 138). The distribution of RRT activation was uniform over the 24-hour period, with 50.5% (n = 531) of calls during the day (7:00 a.m. through 7:00 p.m.) and 49.5% (n = 520) overnight (7:00 p.m. through 7:00 a.m.). A total of 460 patients (43.7%) were admitted to the ICU. The multivariate analysis showed the following variables as significantly associated with hospital mortality: age (OR 1.03; 95% CI 1.01 to 1.04), late (>48 hours) RRT call (OR 2.73; 95% CI 1.79 to 4.71), acute change in oximetry saturation to <90% (OR 1.94; 95% CI 1.28 to 2.95) and acute change in respiratory rate to <8 or >28 breaths/minute (OR 1.79 95% CI 1.09 to 2.94).
Conclusion In this study, hospital mortality predictive factors for patients seen by the RRT were: age, acute respiratory failure and late RRT call.

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P83

Long-term outcome of the Emergency Response Team system in in-hospital cardiac arrest

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Introduction To improve early detection and the mortality rate of in-hospital cardiac arrest, the Emergency Response Team (ERT) system was planned and implemented since June 2009 to detect pre-arrest conditions and for any concerns. The ERT consisted of on-duty physicians and nurses from emergency department. ERT calling criteria [1,2] consisted of acute change of HR <40 or >130 beats per minute, systolic blood pressure <90 mmHg, respiratory rate <8 or >28 breaths per minute, O_2 saturation <90%, acute change in conscious state, acute chest pain or worried about the patients. From the data on ERT system implementation in our hospital in the early phase (during June 2009 to 2011), there was no statistical significance in difference in in-hospital cardiac arrest incidence and overall hospital mortality rate. Since the introduction of the ERT service in our hospital, we have conducted a continuous educational campaign to improve awareness in an attempt to increase use of the service.
Methods To investigate the outcome of the ERT system in in-hospital cardiac arrest and the overall hospital mortality rate, we conducted a prospective, controlled before and after examination of the long-term effect of an ERT system on the incidence of cardiac arrest. We performed chi-square analysis to find statistical significance.
Results Of a total 623 ERT cases from June 2009 until December 2012, there were 72 calls in 2009, 196 calls in 2010, 139 calls in 2011 and 245 calls in 2012.The number of ERT calls per 1,000 admissions in year 2009 to 2010 was 7.69, 5.61 in 2011 and 9.38 in 2013. The number of Code Blue calls per 1,000 admissions decreased significantly from 2.28 to 0.99 per 1,000 admissions (P <0.001). The incidence of cardiac arrest decreased progressively from 1.19 to 0.34 per 1,000 admissions and was significant in difference in year 2012 (P <0.001). The overall hospital mortality rate decreased by 8% from 15.43 to 14.43 per 1,000 admissions (P = 0.095).
Conclusion ERT system implementation was associated with progressive reduction in cardiac arrests over the 3-year period, especially statistically significant in difference in the fourth year after implementation. We also found an inverse association between number of ERT use and the risk of occurrence of cardiac arrests, but we found no difference in overall hospital mortality rate.
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P84

Epidemiology of unplanned intensive care admissions through in-hospital referrals at a tertiary referral centre university hospital

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Introduction The provision of intensive care has lagged behind demand [1]. Intensive care services in the UK have significant resource restriction. Although rationing of beds has been a priority, equally important is to establish patient safety and also identify strategies to prevent admissions [2], which echoes the importance of early recognition of deteriorating patients and prompt intervention. This study evaluates the epidemiology of unplanned admissions to the ICU

in order to identify the associative trends that led to the admission and hence to mitigate the processes of interventional strategies.
Methods A prospective observational evaluation of ICU unplanned admission through in-hospital ward referral over a 3-month duration. Anonymised data collection included baseline demographics, timing and grade of referral, Modified Early Warning Score (MEWS) at time of referral, clinical reason for referral, senior review prior to referral, MEWS trend 24 hours prior to referral, if appropriate basic intervention commenced, time delay between referral and assessment by the ICU team, organ failure score, length of stay (LOS) and survival status.
Results So far 22 patients have been enrolled, of which 60% of the unplanned admissions were 'out of hours', 60% of admissions were from medical wards and 33% from surgical wards. Pneumonia was the main reason for referral and admissions were due to respiratory failure requiring advanced ventilator care. Twenty per cent of the patients did not have senior medical review for at least 4 hours prior to the ICU referral. Basic interventions such as antibiotics and intravenous fluids were not started in a few patients (13%) prior to admission. The mean ICU review time from referral was 70 minutes and the mean MEWS at the time of referral was 8.
Conclusion The study is due to be completed by mid-January 2014. With the limitation of incompleteness, the findings so far have alluded that there is a necessitation for change and education for early identification and intervention in deteriorating patients. The completed study with outcomes (that is, survival rates and ICU LOS) will help us identify whether delay or deficiency in the early management had a causal relationship.
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P85

Use of low-dose CT KUB: is it becoming the easy way out?

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Introduction In 1995, Smith and colleagues first proposed the use of low-dose CT KUB for the diagnosis of ureteric colic [1]. Since then, popularity of this imaging modality has increased due to a number of reasons: a sensitivity of 94 to 97%, a specificity of 96 to 99%, lack of intravenous contrast injection and speed of examination. The UK College of Emergency Medicine considers CT KUB as best practice for radiological investigation of renal colic. A review of the literature suggests that the true positive rate (number of patients diagnosed with an obstructing or symptom causing calculus) should be between 47.5 and 67% and alternative diagnoses should be confirmed in approximately 10% of patients imaged [2].
Methods All patients over the age of 18 years who had a CT KUB requested from the emergency department of the Homerton University Hospital, London over a period of 3 months, between May 2012 and July 2012, were identified. Individual case notes were examined and data were collected on an Excel spreadsheet. Data were analysed and results were divided into positive for renal colic (true positive), positive for other pathology (other significant diagnoses) and negative results.
Results A similar previous audit carried out in 2009 at the same hospital demonstrated a true positive rate of 48.5%. The 2012 audit examined the outcome of 124 consecutive scans and a true positive rate of 29% ($P = 0.0006$) was identified. Alternative diagnoses were 10% in 2009 compared with 17% in 2012 ($P = 0.02$).
Conclusion The true positive rate of CT KUB for renal colic has decreased significantly. We are getting more negative scan results and more scans diagnosing other significant pathology. The authors believe clinicians' thresholds for imaging may have decreased due to the apparent low-dose radiation of CT KUBs. Furthermore, there is a perceived ease of access to CT KUB imaging and hence this modality appears to be being used to identify other significant pathology.
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P86

Bled dry? An audit of blood sampling practices on an adult intensive therapy unit

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Introduction The aim of this audit was to evaluate whether guidelines produced in a local intensive therapy unit (ITU) with regard to blood sampling practices were being adhered to. The volume of blood taken and cost was also evaluated.
Methods A retrospective audit investigating the number of routine blood tests ordered on an ITU in January 2013 was performed. There were no exclusion criteria. Computer-based data collection systems were used to gather data with regard to patient details and when blood tests were processed. The collection bottles used were examined to see how much blood was needed to fill them. Thirty nurses were asked how much 'dead space' blood they discarded, and an average was recorded. The cost of the blood tests was also calculated. Following a period of education regarding the contents of the guidelines, this was re-audited in July 2013 retrospectively.
Results The initial audit examined 901 patient-days. Urea and electrolytes (U&Es) and full blood counts (FBC) were requested in line with the guidelines. Liver function tests (LFTs), bone profile, magnesium and a clotting screen were ordered approximately four times more than advocated. It was shown that many bone profiles and magnesium tests were probably inappropriate requests. Moreover, twice as much blood was taken from patients compared with that recommended by guidelines (almost 16 litres in total in January). The cost of the routine blood tests in January was €11,019. If guidelines had been followed, the estimated yearly saving would be €65,588. During the repeat audit, 731 patient-days were examined. The amount of times a U&E or FBC were requested was largely unchanged, but the amount of times a LFT, bone profile, magnesium and clotting screen were ordered reduced by approximately 50%. Almost one-third more blood was taken from patients when compared with the suggested volume in the guidelines. The cost of the blood tests done in July was €5,423. Despite an improvement in the frequency of blood testing, an estimated €21,907 per year could still be saved.
Conclusion The results underline that the unit's guidelines were not being followed. The re-audit does show an improvement in adherence. Patients are being exposed to unnecessary blood tests, which not only is implicated in iatrogenic anaemia, but also places a significant financial burden on the department. Continued staff education and encouragement are required in order to aid the transition from current to recommended practice.

P87

Decreasing central-line blood draws by consolidation of phlebotomy timing: results of a quality improvement project

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Introduction The direct central line entry rate is believed to be a major contributor to the risk of central line infections. At Mayo Clinic there was historically no schedule for obtaining blood for analysis in the pediatric ICU. A policy was implemented in May 2013 to restrict blood draws to three times daily for nonemergent blood draws only. We subsequently conducted this study to determine whether implementation of this policy was associated with a reduction of blood draws as well as central-line unique entries.
Methods Data from the laboratory as well as database for Central Line Unique Entry were analyzed at baseline and after implementation of the policy change for identification of any decrease in line entry/blood draw rate. As per Mayo Clinic policy, IRB approval was not required for a QI project.
Results In the pre-implementation phase there were a total of 4,602 blood draws in 5,227 total patient-days, (0.88 blood draws/patient-days). After consolidation, there were 1,095 blood draws in 1,491 patient-days (0.73 blood draws/patient-day; 17% reduction). Of these line entries, 24.7% were arterial line entry, 50.5% central line entry and

12.5% were by peripheral venipuncture. After policy implementation, these numbers were 10.9%, 49.7%, and 23.8%, respectively. The average central line unique entry after blood draw consolidation decreased from 10 to 6 line entries/central line-day. Consolidation of blood draws was associated with a cost saving of $7,200/year.
Conclusion Consolidating time frames for blood draws in the PICU was associated with decreased central line entries, decreased utilization of vascular access teams, and decreased phlebotomy cost. We hypothesize that this policy will be associated with a decreased incidence of CLABSI when more patients are included for analysis.

P88

Introducing an arterial non-injectable connector into clinical practice

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Introduction The standard arterial system for blood withdrawal provides no impediment to intra-arterial injection [1] and bacterial contamination. We assessed the probability of inadvertent intra-arterial injection, transmission of bacterial contamination and surveyed the nursing staff following introduction of a non-injectable connector (NIC).
Methods The simulation study data were descriptive. Fifteen junior doctors managed a case of bradycardia. A simulated patient had a peripheral intravenous cannula, central venous catheter and brachial arterial cannula. Atropine was available on request. A laboratory controlled trial compared a transmission of bacteria through standard arterial ports against the NIC when attached to an arterial sampling hub. The colonization rates were compared using a two-tailed Fisher's exact test. A closed-circuit arterial sampling system was designed. A contaminated syringe tip was inserted into the conventional arterial hub or the NIC to take an arterial sample. Transducer flush fluid flowing to the patient bloodstream was cultured. In a survey the nursing staff were asked questions regarding the NIC system, including its manual handling, sampling of the blood and its durability.
Results In the simulation study 10/15 clinicians (67%) injected atropine directly into arterial cannula via a three-way tap. Five of 15 doctors (34%) injected safely. In the laboratory study, swabbing of the arterial hubs showed bacterial contamination of all of the samples in the standard group (20/20) and no contamination in the NIC group (0/20), P <0.0001. Eighty-five per cent (17/20) of samples in the standard arterial group showed onward transmission of pathogens to the patient circulation, and none of the patient samples taken from the NIC group were contaminated (0/20), P <0.0001. In the survey, 80% of the nurses found manual handling of a new device equally simple and 20% even simpler. Sampling of the blood was equally challenging for 87% participants. Ninety-four per cent found similar durability of the new device and better protection against accidental intra-arterial injection. Sixty-six per cent of the nursing staff would replace the standard system with a NIC.
Conclusion Most of the doctors would inject the drug intra-arterially. Currently, no other device is available to eliminate accidental intra-arterial injection or bacterial transmission. The nursing staff found the management of the NIC equally challenging.
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P89

Novel hemostatic technique using a silicone gel dressing for tangential excision in burn surgery

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Introduction The purpose of this study is to demonstrate the efficacy of our novel hemostatic technique for burn surgery. Significant bleeding remains a challenge in tangential excision of the burn wound. Although various techniques to reduce intraoperative blood loss have been described, there is an absence of uniformity and consistency in their application. In the literature, the blood loss in burn surgery is estimated to be at least 123 ± 106 ml per percentage body surface area excised [1]. Recently we developed a novel hemostatic technique using a silicone gel dressing (SI-AID®; ALCARE Co., Ltd, Tokyo, Japan) to stop intraoperative bleeding. Briefly, soon after tangential excision with the Humby knife, the wounds were sprayed with thrombin and with 1:100,000 adrenalin solution and wrapped tightly with SI-AID® for a full 10 minutes. Burn wounds on limbs were tangentially excised under tourniquet control and wrapped with SI-AID® before deflation of the tourniquet. After deflation of the tourniquets, we waited for a full 10 minutes. When the SI-AID® was removed, any major bleeders were cauterized, and the grafts were applied after rinsing the wounds with warm saline.
Methods This is a prospective observational study. From 1 January to 31 October 2013 we collected preoperative and 24-hour postoperative hemoglobin levels from the patients who underwent tangential excision for burn injury, and calculated blood loss in the perioperative period. The data for amounts of blood transfusion, excised area, and harvest area were also collected.
Results Nine patients, 13 operations were included. The mean excised area was 8.3 ± 4.6% body surface area. Estimated blood loss was 35.3 ± 38.3 ml per percentage body surface area excised. Intraoperative transfusion requirements were 86.2 ± 134.5 ml per case. The mean skin graft take rate was 4.5 ± 2.2%.
Conclusion The application of our new technique during burn excision and grafting resulted in a remarkable reduction in blood loss and transfusion requirements.
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P90

Should we avoid invasive treatment in cancer patients with pericardial tamponade?

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Introduction Patients with cancer now live longer due to advances in oncologic treatment. ICU admission is progressively more frequent in this population due to complications of both disease and therapy. Pericardial effusion leading to tamponade and hemodynamic compromise is a common finding in the advanced stages of disease and results in death if not treated on an urgent basis. However, we do not know midterm outcomes of these patients after pericardial drainage. The aim of this study was to evaluate prospectively cancer patients with pericardial tamponade regarding mortality in 6 months.
Methods We evaluated consecutively 105 patients with cardiac tamponade consecutively admitted to the ICU of the Cancer Institute, a reference cancer hospital, during a 3-year period. Baseline characteristics and clinical data were collected prospectively. Patients were followed during a 6-month period.
Results Fifty-three patients (50%) were female. Most patients had a previous diagnosis of lung neoplasia (46%), followed by breast neoplasia (15%) and hematological neoplasia (15%). The mean Karnofsky performance status of patients was 70. All these patients underwent surgical drainage in a mean time of 1.5 hours since ICU admission until surgery. Length of ICU stay was 8 days (2 to 15) and of hospital stay was 16 days (8 to 31). ICU mortality was 75.2%, hospital mortality was 83% and at 3 months 92% of patients were dead.
Conclusion Cardiac tamponade is a serious complication in cancer patients. Despite adequate treatment, high rates of mortality are observed. Prospective studies are needed to better define whether in these patients end-of-life discussion should be implemented early in the diagnosis, avoiding futility.

P91

Goal-directed hemostatic therapy using rotational thromboelastometry in patients requiring emergent cardiovascular surgery

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Introduction Massive bleeding remains a leading cause of potentially preventable death after cardiovascular surgery [1]. Conventional coagulation tests (CCT) fail to characterize the multiple hemostatic abnormalities observed in surgical patients and are further limited by their slow results and poor correlation with transfusion requirements. We assessed the clinical impact of goal-directed coagulation management based on rotational thromboelastometry (ROTEM) in patients undergoing an emergent cardiovascular surgical procedure.
Methods Over a 2-year period, data from 71 patients were collected prospectively and blood samples were obtained for coagulation testing. Administration of packed red blood cells (PRBC) and hemostatic products was guided by an algorithm using ROTEM-derived information and hemoglobin level. Based on the amount of PRBC transfused, two groups were considered: high bleeders (≥5 PRBC; HB) and low bleeders (<5 PRBC; LB). Data were analyzed using the chi-square test, unpaired *t* test and ANOVA as appropriate.
Results Preoperatively, the HB group (n = 31) was characterized by lower blood fibrinogen and decreased clot amplitude at ROTEM compared with the LB group (n = 40). Intraoperatively, larger amounts of fibrinogen, fresh frozen plasma and platelets were deemed necessary to normalize the coagulation parameters in the HB group. Postoperatively, the incidence of major thromboembolic and ischemic events did not differ between the two groups (<10%) and the observed in-hospital mortality was significantly less than expected by the POSSUM score (22% vs. 35% in HB group and 5% vs. 13% in LB group).
Conclusion ROTEM-derived information is helpful to detect early coagulation abnormalities and to monitor the response to hemostatic therapy. Early goal-directed management of coagulopathy may contribute to improve outcome after cardiovascular surgery.
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P92

Thromboelastometric examination on the ICU before elective procedures

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Introduction In critically ill patients a number of elective procedures with a potential risk of bleeding are performed. In this population, coagulation disorder is frequently observed according to the commonly used laboratory parameters of APTT (activated partial thromboplastin time), INR (international normalized ratio) or platelet count. Thromboelastometric examination (ROTEM) evaluates coagulation of whole blood and thus allows the testing of all components of secondary hemostasis.
Methods Identification of patients with pathological values of INR, APTT and platelet count before the planned intervention. Through a questionnaire we found a potential correction of coagulopathy carried out by the physician. Performed ROTEM methodology: ExTEM (external pathway thromboelastometry). Inclusion criteria: normal curves and values, CT (clotting time), MCF (maximum clot firmness). In those patients with normal values according to ExTEM examination, no blood products were administered.
Results During March 2013 to November 2013, 40 patients were identified as relevant, 26 men of average age 53 years and 14 women of average age 59 years. Central venous cannulation, 12 cases; surgical revision, nine cases; thoracic drainage, six cases; percutaneous endoscopic gastrostomy, five cases; nephrostomy, two cases; epidural catheter, two cases; tracheostomy, two cases; permanent pacemaker, one case; and bronchoscopy, one case. INR normal values were 0.8 to 1.2. The average measured value of INR in men was 1.50, and in women was 1.35. APTT normal values were 0.8 to 1.2. The average measured value of APTT in men was 1.09, and in women was 1.14. Platelet count was 150×10^9/l to 300×10^9/l level of platelets; in men was 252.57, in women was 226.78. ExTEM CT normal values at 41 to 74 seconds: measured value of CT in men was 62.58 and in women was 62.07. MCF normal values were 50 to 72 mm; the measured value of MCF in men was 69.88, and in women was 73.28. Considered administration of blood derivatives: fresh frozen plasma, 123 transfusion units (TU); platelets, 4 TU. In the examined cases no blood products were administered to avoid the risk of bleeding before the elective procedure. No periprocedural bleeding was observed.
Conclusion Examination EXTEM in these patients proved to be effective and efficient in predicting bleeding complications in relation with interventions routinely performed on the ICU. Also, these specific cases proved not indicated and thus ineffective administration of blood products.

P93

ROTEM: Multiplate monitoring in the ICU and outcome scores

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Introduction Hemostatic disorders are common in intensive care patients and can be used as prognostic markers. The aim of this prospective clinical study was to study platelet function in intensive care patients using point-of-care viscoelastic and platelet aggregometry instruments and platelet count (PLC). Our hypothesis was that measurement of platelet function would give more information about disseminated intravascular coagulation (DIC), morbidity and mortality than PLC alone.
Methods Patients admitted to the ICU were monitored with ROTEM viscoelasticity and a new Multiplate platelet aggregometer; routine coagulation analyses; International Society of Thrombosis and Haemostasis and Japanese Association for Acute Medicine DIC calculated scores; Sequential Organ Failure Assessment scores, Simplified Acute Physiology Score III – Expected Mortality Rate; and real in-hospital mortality. Nonparametric tests were chosen for all statistical evaluation. P <0.05 was considered significant.
Results A total of 128 patients with different diagnoses were studied, with 330 sampling events. Multiplate analyses correlated significantly with PLC and ROTEM. However, there were more test results below normal limits for Multiplate analyses than for ROTEM in patients with thrombocytopenia. Multiplate, ROTEM and PLC results were low in patients with high SOFA scores and in patients with overt DIC scores. These test results at admission to the ICU did not differ between survivors and nonsurvivors, and did not correlate with the length of stay in the ICU. Only EMR differed between survivors and nonsurvivors and correlated with ICU length of stay.
Conclusion In this study, Multiplate and ROTEM did not provide any more information than PLC about DIC, morbidity and mortality. Multiplate showed lower platelet function in more patients with low platelets than ROTEM. In patients without thrombocytopenia, all patients had normal ROTEM results, but 36% of Multiplate measurements were low. This higher sensitivity of the Multiplate to measure lowered platelet function needs to be linked to real bleeding in larger patient series to define its clinical significance.

P94

Retrospective observational study of interventional radiology and critical care coagulopathy

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Introduction Estimation of bleeding risk in critical care patients undergoing interventional radiological procedures is often made on the basis of coagulation tests. If these tests are abnormal, fresh frozen plasma (FFP) is often given to reduce the risk of bleeding, despite

a poor evidence base for this practice [1]. There is a relatively better evidence base for prophylactic platelet transfusion [2] but clinical practice is inconsistent. Through a retrospective study we aimed to establish the thresholds triggering use of FFP and platelet transfusion prior to percutaneous drain insertion in critical care patients.

Methods We identified 68 consecutive chest, abdominal or pelvic drain insertions in 54 critical care patients between 1 January 2008 and 11 October 2012 at the John Radcliffe Hospital, Oxford. The prothrombin time (PT), activated partial thromboplastin time (APTT) and platelet counts prior to each procedure were recorded to demonstrate triggers used for FFP and platelet transfusion. In patients who underwent transfusion, the next PT, APTT and platelet count post transfusion were recorded.

Results Patients who received FFP had a mean PT of 18.5 seconds while those who did not receive FFP had a mean PT of 16.7 seconds (unpaired *t* test, $P = 0.275$). In the nine patients given FFP, the pre-transfusion mean PT was 18.5 seconds whereas the post-transfusion mean PT was 17.1 seconds (paired *t* test, $P = 0.235$). The pre-transfusion mean APTT was 41.6 seconds compared with a post-transfusion mean APTT of 38.1 seconds (paired *t* test, $P = 0.127$). No patient had platelet levels below the recommended transfusion threshold [2], but one patient nevertheless received a double-dose platelet transfusion. One patient had a recorded immediate bleeding complication. Their PT was 15.6 seconds and APTT was 40.9 seconds and they did not receive FFP. One patient had an anaphylactic reaction whilst receiving FFP.

Conclusion This study demonstrates inconsistent use of FFP, with no significant difference in PT between patients who were transfused and those that were not. The lack of effect of FFP transfusion on PT and APTT creates additional confusion for its prophylactic usage. There is a need for further clarification around coagulopathy and interventional radiology in the critical care setting. The low absolute incidence of bleeding complications and risk of complications from transfusion lends further support to the view that FFP should be used therapeutically rather than as prophylactic 'cover' [1].

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P95

Monitoring of treatment with low molecular weight heparins using viscoelastic devices

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Introduction Few studies have investigated the use of viscoelastic devices for monitoring of treatment with LMWHs and to our knowledge there are no studies comparing different LMWHs or different visocoelastic methods.

Methods Enoxaparin (Klexane) and tinzaparin (Innohep) were added to 2 ml citrated blood from 10 intensive care patients to obtain plasma concentrations of 0, 0.5, 1.0 and 1.5 IU/ml enoxaparin and tinzaparin, respectively. The study was approved by the local ethics committee and with written consent (relatives). Clot formation and clot retraction was studied using ROTEM and ReoRox.

Results ROTEM analysis showed prolonged clot formation (CT) with increasing concentrations of enoxaparin and tinzaparin (more so). ReoRox analysis showed that the initiation of clot formation (COT1) increased with increasing doses of enoxaparin and tinzaparin (more so), as did the progression of clot formation (COT2 – COT1), thus resulting in a prolongation until complete clot formation (COT2). See Table 1.

Conclusion Clot initiation was prolonged with both drugs and detected by both ROTEM and ReoRox. Clot formation was more decreased with tinzaparin than enozaparin and only detected by ReoRox.

P96

Heparin stability in parenteral nutrition bags prepared in a neonatal ICU

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Introduction Heparin is commonly given in our neonatal ICU (NICU) by continuous intravenous infusion. Heparin is diluted in parenteral nutrition bags and administered over a period of 24 hours with in-line filtration. However, there are no data on heparin stability in parenteral nutrition bags, especially on its compatibility with 50% dextrose mainly present in bags. The aim of our *in vitro* study was to determine heparin stability in parenteral nutrition bags prepared in a NICU after 24-hour infusion and to assess its interaction or not with 50% dextrose.

Methods We prepared both types of bag: parenteral nutrition bags whose composition was defined in the unit, including sodium heparin (77 UI/ml); and bags containing only sodium heparin diluted in 50% dextrose (193 UI/ml). These bags ($n = 6$ per type) were infused over a period of 24 hours with and without in-line filtration. Heparin activity was measured using a chromogenic anti-Xa method in bags just being prepared (references for other measures) and after 24-hour infusion and in effluents at the end of infusion line after 24 hours.

Results Our results show values of heparin activity measured in bags and effluents with and without in-line filtration after 24-hour infusion for both types of bag assessed (Tables 1 and 2). Results are expressed as median values (minimum to maximum) in percent.

Table 1 (abstract P95). ROTEM and FOR variables for enoxaparin and tinzaparin

		Enoxaparin			Tinzaparin		
	0 IU/ml	**0.5 IU/ml**	**1.0 IU/ml**	**1.5 IU/ml**	**0.5 IU/ml**	**1.0 IU/ml**	**1.5 IU/ml**
ROTEM							
CT (seconds)	175 ± 38	191 ± 89*	214 ± 109	249 ± 94*	223 ± 53*	289 ± 84*	326 ± 125*
CFT (seconds)	77 ± 23	87 ± 21	85 ± 16	83 ± 22	74 ± 27	84 ± 45	80 ± 21
Angle (°)	75 ± 4	74 ± 4	75 ± 3	74 ± 4	75 ± 5	73 ± 5	73 ± 4
MCF (mm)	62 ± 5	61 ± 7	63 ± 5	63 ± 6	68 ± 7*	64 ± 8	65 ± 6*
MCL (%)	8 ± 4	6 ± 3+	5 ± 4	2 ± 5*	5 ± 4*	6 ± 4	2 ± 4*
ReoRox							
COT1 (seconds)	30 ± 5	35 ± 7*	39 ± 8*	38 ± 11*	36 ± 4*	45 ± 9*	48 ± 15*
COT2 (seconds)	65 ± 11	76 ± 13*	82 ± 14*	85 ± 20*	74 ± 5*	91 ± 16*	108 ± 29*
COT2 – COT1 (seconds)	34 ± 10	41 ± 8*	43 ± 9*	46 ± 10*	37 ± 4	46 ± 11*	51 ± 15*

Data presented as median (SD). *P <0.05 compared with 0 IU/ml LMWH.

Table 1 (abstract P96). Results of heparin activity in parenteral nutrition bags

	Bags at T0	Bags at T0 + 24 hours	Effluent at T0 + 24 hours
With filtration	100 (84.09 to 109.09)	95.45 (79.55 to 102.27)	97.73 (75.00 to 104.55)
Without filtration	100 (90.48 to 114.29)	97.62 (83.33 to 107.14)	97.62 (83.33 to 114.29)

Table 2 (abstract P96). Results of heparin activity in bags with sodium heparin in 50% dextrose

	Bags at T0	Bags at T0 + 24 hours	Effluent at T0 + 24 hours
With filtration	100 (77.45 to 108.82)	95.10 (90.20 to 109.80)	98.04 (95.10 to 100.98)
Without filtration	100 (85.44 to 107.77)	92.23 (88.35 to 100.00)	94.17 (86.41 to 108.74)

Conclusion We conclude that there is no loss of heparin activity when drug is infused over 24 hours for both types of bag prepared, with and without in-line filtration, showing heparin activity remains stable during this period and there is no interaction of drug with other nutrient components of bags, especially 50% dextrose.

P97

Bivalirudin or heparin: which anticoagulation strategy for critically ill cardiac surgery patients?

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Introduction Anticoagulation with unfractionated heparin in cardiac surgery patients has several limitations, and above all the risk of heparin-induced thrombocytopenia. Bivalirudin is a direct thrombin inhibitor, use of which in cardiac surgery patients has expanded in recent years. The aim of the study was to analyze two strategies for introducing bivalirudin in this setting (as secondary drug switching from heparin or as primary anticoagulant) and to evaluate clinical outcomes.
Methods Data from 100 propensity matched patients who received heparin (Group H, $n = 50$) or bivalirudin (Group B, $n = 50$), from January 2009 to January 2012, in a cardiac surgery ICU of a university hospital were analyzed. Bivalirudin was administered as either first-line or second-line drug after heparin discontinuation if heparin-induced thrombocytopenia was presumed.
Results Bivalirudin treatment was associated with a reduction of major bleeding ($P = 0.05$) compared with the control group. Interestingly, in an intention-to-treat analysis, patients receiving primary bivalirudin showed a significant reduction in minor bleeding ($P = 0.04$), and mortality ($P = 0.01$) compared with the secondary bivalirudin group, and similarly if compared with UFH and secondary bivalirudin patients ($P = 0.01$ and $P = 0.05$ respectively). Predictors of hospital mortality at multivariate analysis included urgent admission (OR = 2.7; 95% CI, 1.03 to 7.2; $P = 0.04$), septic shock (OR = 8.0; 95% CI, 2.26 to 28.7; $P < 0.005$) and primary therapy with UFH (OR = 19.2; 95% CI, 2.2 to 163.9; $P = 0.007$).
Conclusion Novel anticoagulant strategies might play a crucial role in critically ill cardiac surgery patients. In a propensity-matched population, our study showed that primary bivalirudin anticoagulation may reduce bleeding complications and mortality. Further studies are therefore warranted.

P98

Reversal of edoxaban-induced anticoagulation by the four-factor prothrombin complex concentrate Beriplex® in a rabbit model

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Introduction The oral direct and selective factor Xa inhibitor edoxaban (Daiichi Sankyo) is currently available in Japan for the prophylaxis of venous thromboembolism (VTE) in patients undergoing major orthopedic surgery and is undergoing investigation in phase III trials for the prevention of stroke in patients with atrial fibrillation and the treatment and secondary prevention of VTE. The primary complication of any available anticoagulant therapy is the risk of bleeding. Rapid reversal of anticoagulation may be necessary in patients requiring emergency treatment due to uncontrolled bleeding. Prothrombin complex concentrates (PCC) are frequently used to reverse the effect of vitamin K antagonists such as warfarin and have also been suggested to be potentially effective in reversing the effects of the new oral anticoagulants. The present study was therefore designed to determine whether the four-factor PCC Beriplex® can effectively reverse bleeding and normalize coagulation following edoxaban administration in a rabbit kidney injury model.
Methods Rabbits were treated with a high intravenous bolus dose of edoxaban (1,200 µg/kg) followed by the administration of Beriplex® (25 to 75 IU/kg). Bleeding was assessed based on the time to hemostasis and the total blood loss after induction of a standardized kidney injury. In parallel, the following biomarkers of hemostasis were determined: factor Xa inhibition, prothrombin time (PT), activated partial thromboplastin time (aPTT), whole blood clotting time (WBCT), and thrombin generation (TGA).
Results The results confirmed increased and prolonged bleeding of edoxaban-treated animals following standardized kidney injury compared with vehicle administration. Parallel monitoring of biomarkers of hemostasis showed a prolongation of PT, aPTT, WBCT, and changes in thrombin generation parameters. Subsequent administration of Beriplex® resulted in a dose-dependent reversal of edoxaban-induced bleeding as indicated by reduced time to hemostasis and total blood loss. Both parameters achieved statistical significance compared with placebo at the Beriplex® dose of 50 IU/kg under fully blinded study conditions. The biomarkers correlating best with Beriplex®-mediated edoxaban anticoagulation reversal included PT, WBCT and endogenous thrombin potential.
Conclusion In summary, Beriplex® treatment effectively reversed edoxaban-induced anticoagulation in an animal model of acute bleeding at clinically relevant dose levels.

P99

Use of a specific antidote to dabigatran (idarucizumab) reduces blood loss and mortality in dabigatran-induced and trauma-induced bleeding in pigs

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Introduction The reversal of the anticoagulant effects of the new oral anticoagulants in severely bleeding patients requires new therapeutic strategies. This study investigated the effectiveness of a specific antidote for idarucizumab to reverse bleeding in a dabigatran anticoagulated pig trauma model.
Methods After ethical approval, male pigs ($n = 30$) were given dabigatran etexilate for 3 days (30 mg/kg bid p.o.), and the sham group ($n = 6$) received placebo. To achieve supra-therapeutic anticoagulation, dabigatran was infused prior to injury on day 4 in anesthetized pigs, and the sham group received placebo. A standardized blunt liver injury was inflicted and blood loss (BL) was recorded 10 minutes post trauma. The

dabigatran-treated animals were randomized (n = 6/group) to a single injection of idarucizumab at 30, 60 or 120 mg/kg i.v. or vehicle (control animals). Blood loss and hemodynamic variables were monitored over 4 hours or until time of death. Data were analyzed by ANOVA (± SD) and by the log-rank test.

Results Dabigatran levels were 1,147 ± 370 ng/ml with no differences between groups prior to injury. BL in sham animals was 409 ± 53 ml 10 minutes after injury and 700 ± 107 ml after 4 hours (survival rate 100%). Anticoagulation with dabigatran (control animals) resulted in significantly higher BL 10 minutes after injury (801 ± 66 ml, P <0.05). Mortality in these animals was 100%, with a mean survival time of 121 minutes (range: 90 to 153 minutes; P <0.05 vs. sham and idarucizumab-treated animals). Total BL in dabigatran-treated animals was 2,977 ± 316 ml. In contrast, treatment with idarucizumab was associated with a dose-dependent reduction in BL. The lowest dose of 30 mg/kg resulted in 17% mortality (1/6 animals) and BL was reduced by 50% (1,586 ± 619 ml). BL was further reduced in animals receiving 60 (1,077 ± 103 ml) or 120 mg/kg idarucizumab (1,137 ± 121 ml; both 100% survival). Hemodynamic parameters and markers of shock were similar to pre-trauma levels in latter groups receiving idarucizumab.

Conclusion This study demonstrates for the first time that anticoagulation with dabigatran can be reversed effectively and safely by idarucizumab. Even under supra-therapeutic dabigatran concentrations, the antidote decreased blood loss and mortality in this lethal pig animal model. Thus, data from clinical studies are warranted to confirm the findings of this study.

P100

Primary bivalirudin anticoagulation for patients with an implantable ventricular assist device

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Critical Care 2014, **18(Suppl 1):**P100 (doi: 10.1186/cc13290)

Introduction Bivalirudin is a direct thrombin inhibitor that is increasingly used in patients undergoing mechanical circulatory support as it presents many advantages compared with heparin. The aim of this study was to describe our experience with bivalirudin as primary anticoagulant in patients undergoing ventricular assist device (VAD) implantation.

Methods An observational study on the 12 consecutive patients undergoing VAD implantation from October 2011 at out institution. Five patients were implanted the Heart Mate II LVAD (Thoratec Corp., Pleasanton, CA, USA), six patients the Heartware HVAD (HeartWare Inc., Miramar, FL, USA), and one patient a Cardiowest Total Artificial Heart (Syncardia Systems Inc., Tucson, AZ, USA). Patients received a continuous infusion of bivalirudin, with a starting dose of 0.025 μg/kg/hour. The target activated partial thromboplastin time (aPTT) was between 45 and 60 seconds.

Results Patients never received heparin during hospitalization nor had a prior diagnosis of HIT. Preoperative platelets count was 134,000 ± 64,000 platelets/mm^3. The bivalirudin dose was 0.040 ± 0.026 mg/kg/hour, and the duration of therapy was 5 (5 to 12) days. The lowest platelet count during treatment was 73,000 ± 23,000 platelets/mm^3. No thromboembolic complications occurred. Two episodes of minor bleeding from chest tubes which subsided after reduction or temporary suspension of bivalirudin infusion were observed. Six patients required blood red cell transfusions, and one patient had one fresh frozen plasma transfusion. No platelet transfusions were performed during treatment. The ICU stay was 8 (7 to 17) days, and the hospital stay 25 (21 to 33) days.

Conclusion Bivalirudin is a valuable option for anticoagulation in patients with VAD, and can be easily monitored with aPTT. The use of a bivalirudin-based anticoagulation strategy in the early postoperative period may overcome many limitations of heparin, and above all the risk of HIT which is higher in patients undergoing cardiac surgery. Bivalirudin should no longer be regarded as a second-line therapy for anticoagulation in patients with VAD.

P101

Plasma-free hemoglobin and microvascular response to fresh or old blood transfusion in septic patients

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Introduction Free hemoglobin (fHb) can scavenge nitric oxide and induce vasoconstriction [1]. The fHb content may be higher in older blood bags. We studied whether old red blood cell (RBC) transfusion increases plasma fHb in septic patients and if this affects the microvascular response.

Methods Twenty septic patients randomly received either fresh (<10 days storage) or old (>15 days) RBC transfusion. Plasma fHb was measured before and 1 hour after transfusion; the sublingual microcirculation was assessed with sidestream dark-field imaging. The perfused boundary region (PBR) was measured as an index of glycocalyx damage [2]. The thenar Tissue Hb index (THI) was measured (near-infrared spectroscopy).

Results fHb increased in the old RBC group (Figure 1). THI increased in both groups, while SDF parameters were unaltered. Negative correlations were found between ΔfHb and changes in total vessel density (r = –0.57, P <0.01; Figure 2) and THI (r = –0.71, P <0.001). These relations were lacking in patients with PBR <2.68 μm.

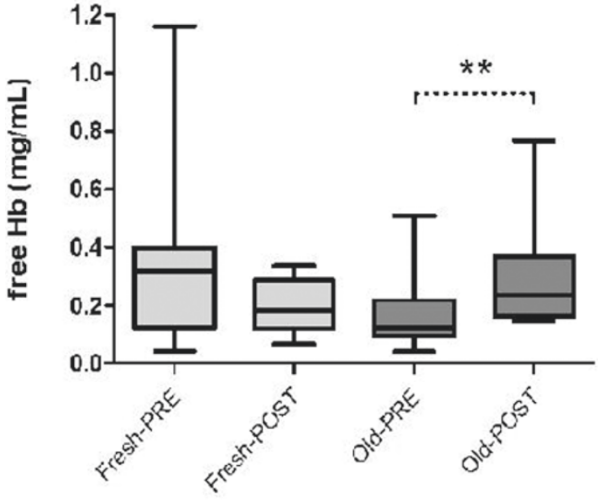

Figure 1 (abstract P101). Changes in fHb.

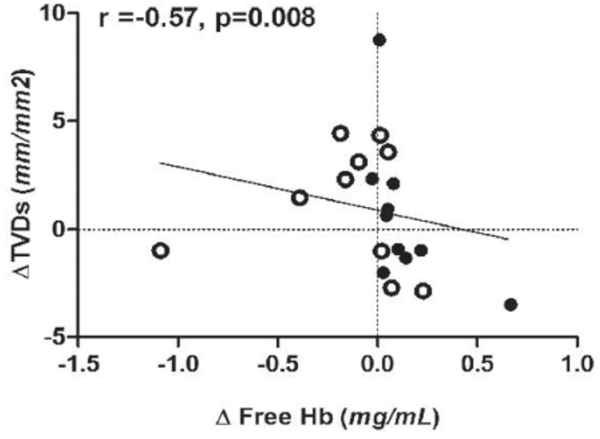

Figure 2 (abstract P101). Relation between changes in fHb and TVD.

Conclusion Old RBC transfusion increased plasma fHb in septic patients. Increasing plasma fHb levels after transfusion were associated with decreased microvascular density and lower increase in tissue Hb content. This relation might be blunted when the glycocalyx is preserved.

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P102

Fatty acid composition of blood plasma in multiple organ dysfunction syndrome

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Critical Care 2014, **18(Suppl 1):**P102 (doi: 10.1186/cc13292)

Introduction The aim of study was to assess the fatty acid (FA) composition of blood plasma in multiple organ dysfunction syndrome (MODS).

Methods The objects of the study were 18 people with multiple organ failure (35.6 ± 8.7 years) of various etiologies. The blood of 16 healthy volunteers aged 37.7 ± 3.2 years served as control. There were also analyzed blood plasma and fragments of artery luminal part from patients who died from different causes. Analysis of FA was conducted using capillary gas–liquid chromatography. Quantitative evaluation of individual FA content was made as a mass percentage of their total. Statistical analysis was performed using the Mann–Whitney U test (P <0.05).

Results Normalized contents of oleic and palmitoleic monounsaturated FA increase in patients with MODS, while the levels of stearic saturated FA and polyunsaturated FA decrease, as compared with the control. Considering these results, we conclude that blood plasma FA composition in MODS biased towards composition of FA characteristic of adipose and muscle tissue triglycerides, which quantitatively predominant monounsaturated FA, and stearic and polyunsaturated FA have a significantly lower level [1,2]. Thus, the composition of the FA in MODS reflects the degree of lipolysis activation in fat depots. As a result of these processes there should occur an imbalance in vascular endothelial cells between monounsaturated and polyunsaturated FA and, as a consequence, changes in metabolism of eicosanoids and other lipid vasoactive mediators should develop. One should note that in plasma of people who died in a hospital environment due to various reasons, similar changes in FA blood composition are observed. The degree of change of FA composition in postmortem blood samples presumably primarily depends on severity and duration of a previous critical and serious condition. Postmortem changes presumably exert some influence on blood plasma FA composition. Moreover, the composition of FA in blood plasma in the case of MODS is similar to that of FA in the luminal part of the artery wall. This suggests a decrease in the influence of intertissue differences in lipid composition on metabolic processes.

Conclusion Given that the monounsaturated FAs in the case of MODS enter the bloodstream primarily from adipose and muscle tissues, one can assume that their blood plasma level reflects the degree of hypermetabolism processes in the organism.

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P103

Response of coagulation and fibrinolysis system was different between older and nonolder patients with severe sepsis

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Introduction The present study investigated the relationship between age [1] and biomarkers of coagulation and fibrinolysis [2] and their impact on outcome in severe sepsis patients.

Methods A prospective observational study of adult patients with severe sepsis was conducted in a single academic hospital. Plasma was analyzed for coagulation and fibrinolysis markers on days 1, 2, and 3. Patients were stratified according to the age 67 years, which was the point of the Youden index (maximum sensitivity + specificity – 1) in a receiver operation characteristics plot for a logistic regression model of in-hospital mortality.

Results For the in-hospital survival rate, that of older sepsis patients was significantly lower than younger patients, 9/15 (60.0%) versus 27/28 (96.4%), P <0.05. Older patients had markedly higher total plasmin activator inhibitor-1 (TPAI-1) on day 1, thrombin–antithrombin complex (TAT) on days 2 and 3, and fibrin monomer complex on day 2, and markedly lower plasminogen (PMG) on day 3 and alpha-plasmin inhibitor (αPI) on days 2 and 3 compared with younger patients (all P <0.05). Age was an independent predictor of high TAT on days 2 and 3, high fibrin monomer complex on day 2, low PMG on day 3, and low αPI on days 2 and 3 after adjusting for some cofactors and covariables. TPAI-1 on day 2, TAT on day 2, and PMG on day 3 were risk factors of in-hospital mortality in older sepsis patients (Table 1).

Table 1 (abstract P103). Univariate analysis of logistic regression for in-hospital mortality

	HR	95% CI	*P*
PAI-1 day 2	1.02	1.0 to 1.06	<0.01
TAT day 2	1.49	1.02 to 19	<0.05
PMG day 3	0.64	0.1 to 0.95	<0.01
SOFA day 1	1.2	0.9 to 1.69	0.21
IL-6 day 1	0.99	0.9 to 1.00	0.21

Conclusion In severe sepsis, older patients displayed a biomarker profile suggestive of enhanced response of coagulation and fibrinolysis system compared with younger patients. Change of some markers depended on age and may contribute to the poor outcome in older patients.

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P104

ε-Aminocaproic acid does not increase adverse effects in cardiac surgery: an analysis of 2,852 cases

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Introduction Antifibrinolytic drugs recently have been associated with adverse outcomes in patients undergoing cardiac surgery. We reviewed our experience with prophylatic ε-aminocaproic acid in patients undergoing cardiac surgery at InCor – Heart Institute.

Methods We retrieved data on 2,852 consecutive patients undergoing cardiac surgery at revascularization at Duke between 1 January 2004 and 31 December 2008. We compared patients receiving or not prophylatic ε-aminocaproic acid in coronary artery bypass graft surgery, or valve procedures or combined ones. We evaluated baseline characteristics, intraoperative data and severe clinical endpoints during 30 days.

Results A total of 2,852 patients were included in the analysis and 1,389 (48.7%) received prophylactic ε-aminocaproic acid. The others did not receive any antifibrinolytic. In the risk-adjusted model, survival was similar among patients treated with aminocaproic acid or not treated (1.9 vs. 1.6%, P = 0.48). Bleeding in 24 hours was reduced in the treated group as compared with the nontreated (391 vs. 472 ml, P = 0.012). There were no differences regarding acute renal failure, stroke and infection in 30 days.

Conclusion In cardiac surgery, prophylactic use of aminocaproic acid reduces bleeding and does not result in higher incidence of acute complications.

P105

Eculizumab treatment of atypical haemolytic uraemic syndrome: results from the largest prospective clinical trial to date

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Introduction Atypical haemolytic uraemic syndrome (aHUS) is a rare, life-threatening disease in which patients experience uncontrolled complement activation leading to systemic thrombotic microangiopathy (TMA). We report on the effect of eculizumab (Ecu), a terminal complement inhibitor approved for the treatment of aHUS, in the largest prospective clinical trial in aHUS.
Methods Adult aHUS patients (≥18 years) with platelets <150×10^9/l and LDH ≥1.5 ULN were recruited into a 26-week single-arm, phase 2 study evaluating Ecu treatment. Patients with STEC-HUS (Shiga toxin and *E. coli*) and severe ADAMTS13 deficiency (activity <5%) were excluded. Identification of complement mutation was not required for enrolment. The primary endpoint was complete TMA response (platelet and LDH normalisation (>150×10^9/l and <ULN, respectively) and <25% increase in serum creatinine from baseline (BL)). Other efficacy evaluations measured platelet counts and eGFR improvement (by MDRD).
Results Forty-one patients were enrolled (mean (SD) age 40.3 (15.3) years; 28 (68%) females), 30 (73%) of whom with first presentation of aHUS (median 2 weeks before Ecu). BL mean (SD) platelets and eGFR were 119 (66.1) ×10^9/l and 17.3 (12.1) ml/minute/1.73 m^2, respectively. Thirty-eight (93%) patients received Ecu for 26 weeks. Table 1 shows improvements in outcomes. Dialysis was discontinued in 20 (83%) among the 24 patients requiring dialysis at inclusion. Ecu was generally well tolerated, with no deaths or unexpected safety concerns. Meningococcal infections occurred in two patients, one of whom continued treatment.

Table 1 (abstract P105). Outcomes at 26 weeks in adult aHUS patients receiving Ecu

Complete TMA response, *n* (%) patients	30 (73); 95% CI 57 to 86
Platelet count normalisation, *n* (%) patients	40 (98); 95% CI 87 to 100
Mean (SD) platelet count increase from baseline, ×10^9/l	135 (114); *P* <0.0001
Mean (SD) eGFR increase from baseline ml/minute/1.73 m^2	29.3 (23.6); *P* <0.0001

Conclusion Results from this large prospective clinical trial in adult patients with aHUS confirm prior trials with Ecu to inhibit complement-mediated TMA, improve renal and haematological outcomes and show the benefit of early diagnosis and treatment. There were no unexpected safety concerns. The trial is ongoing.

P106

Variation in red blood cell transfusion thresholds in critically ill patients

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Introduction Restrictive transfusion practice in recent randomized trials and systematic reviews continues to have favorable outcomes [1]. Despite this, substantial variability in transfusion practice persists [2]. It is important to identify contemporary variability, and which patient, provider, and institutional factors drive this variability. Therefore, we performed a retrospective analysis hypothesizing that red blood cell (RBC) transfusion practice remains variable and is influenced by patient characteristics and institutional transfusion culture.
Methods We performed a multicenter retrospective analysis within the ongoing prospective randomized, Age of Blood Evaluation (ABLE) trial. The patient population included patients admitted to the ICU with an anticipated length of invasive or non-invasive mechanical ventilation >48 hours and who required a first RBC transfusion during the first 7 days of ICU admission. As of March 2013, completed and verified data from 45 sites in Canada, France, and the UK were included. Sites with at least 12 patients were included in site analysis. The primary outcome is the association of enrolling centers on the median hemoglobin prior to transfusion.
Results As of March 2013, there were 1,288 patients randomized in the ABLE study. The median patient age was 63 years (IQR 50 to 74). The majority of patients were emergent admissions (97%) with nonoperative diagnoses (85%), including respiratory illness (27%) and sepsis (18%). Bleeding was infrequent (0.4%). At least one comorbidity was common (43%), frequently significant cardiac disease (14%) and diabetes (12%). There is significant variability in the median pre-transfusion hemoglobin across different sites (P <0.05). The median pre-transfusion hemoglobin by site was 75 g/l (IQR 71 to 77). Six of 24 sites had a significantly higher, and four had a significantly lower, median transfusion threshold compared with the median. Significant variability in the median pre-transfusion hemoglobin remained in multivariate analysis, after adjustment for age and type of ICU.
Conclusion There was a 16 g/l difference in median hemoglobin between the lowest and highest site and wide inter-site variation. These differences may be due to transfusion education, monitoring and blood-bank enforcement practices. Site, not country, remains a significant predictor of transfusion. Future directions in transfusion best practices should focus on local transfusion culture. Significant and nonevidence-based variability persists in transfusion thresholds for critically ill patients.
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P107

A liberal strategy of red blood cell transfusion reduces cardiovascular complications in older patients undergoing cardiac surgery

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Introduction Owing to their high risk in cardiac surgery, it is essential to define which transfusion strategy results in a lower rate of cardiovascular complications in older patients [1]. The aim of this study was to compare clinical outcomes after the implementation of either a restrictive or a liberal transfusion strategy in patients aged 60 years and above.
Methods This study was a substudy of the Transfusion Requirements After Cardiac Surgery study. In this subgroup analysis we included all patients aged 60 years and above randomized to a restrictive or a liberal strategy of RBC transfusion. A composite endpoint for cardiovascular complications was used and defined as a combination of 30-day all-cause mortality and severe cardiovascular morbidity.
Results The primary composite endpoint – all-cause 30-day mortality, cardiogenic shock, or myocardial infarction – occurred in 9.6% of patients in the liberal strategy group and in 18.4% in the restrictive strategy group (P = 0.041). The incidence of cardiogenic shock was 5.2% in the liberal group and 12.8% in the restrictive group (P = 0.031) and of myocardial infarction was 2.2% in the liberal group and 5.6% in the restrictive group (P = 0.203). There was no significant difference between transfusion strategies in 30-day mortality rates (4.4% vs. 8%, respectively; P = 0.23).
Conclusion In this prospective, randomized clinical trial, older patients submitted to a restrictive strategy of RBC transfusion had a rate of cardiovascular complications in 30 days after cardiac surgery twice as high than a liberal strategy. In this group of patients, probably

untreated anemia would be more harmful than in a younger or healthier population undergoing cardiac surgery.

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P108

Anemia and high hematocrit are associated with in-hospital mortality in emergency department patients with suspected infection

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Introduction Anemia and its association with mortality among emergency department (ED) patients with suspected infection has to our knowledge never been investigated. We hypothesize that anemia as well as high hematocrit increases the risk of in-hospital death among these patients.

Methods A prospective observational study of adult ED patients with suspected infection presenting to an urban, academic medical center ED at Beth Israel Deaconess Medical Center, Boston, MA, USA. Inclusion criterion was clinically suspected infection at ED presentation. Patients were enrolled over a 1-year period. Laboratory and clinical data were collected at enrollment. Primary outcome was in-hospital mortality. Logistic regression was performed determining the independent mortality odds adjusting for confounders.

Results A total of 4,952 patients were enrolled with an in-hospital mortality rate of 4% and a mean age of 58 ± 21 years. In total, 4,683 (95%) patients had their hematocrit measured: 3,857 (82%) patients had a normal hematocrit (30 to 44%), 413 (8.8%) patients had 25 to 29% hematocrit, and 66 (1.4%) patients ≤24% hematocrit. A total of 248 (5.3%) had a high hematocrit (≥45%). After adjusting for age, present or prior cancer, diabetes I and II, end-stage renal disease, AIDS and liver disease, anemia remained an independent predictor of in-hospital mortality with odds ratios of respectively 1.7 and 2.5 with worsening anemia as well as high hematocrit, with odds ratio 2.3 (Table 1). The AUC for the model was 0.78.

Table 1 (abstract P108). Effect of severity of anemia or high hematocrit on in-hospital mortality

Hematocrit	Mortality OR	*P* value
≥45%	2.3(1.3 to 4.1)	0.007
30 to 44%, ref.	1.0	
25 to 29%	1.7(1.1 to 2.6)	0.019
< 20%	2.5(1.1 to 5.8)	0.032

Conclusion Anemia and elevated hematocrit seem to be associated with in-hospital mortality among patients with suspected infection. Treatment of high or low hematocrit as a part of the ED resuscitation could be a subject for further investigation.

P109

New simplified criteria for predicting massive transfusion in trauma

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Introduction Several predicting models have been described to identify the necessity for massive transfusion (MT) for trauma patients [1]. The purpose of this study is to validate the simplified scoring systems reported previously and establish new criteria at emergency and in the ICU in Japan.

Methods We retrospectively analyzed trauma patients transported to our center for the recent 2 years. Patients transferred from other hospitals with minor injuries or confirmed cardiac arrest at the scene were excluded.

Results A total of 297 trauma patients were included in this study. Thirty-one (10.4%) patients required MT. Sensitivity and specificity for the Assessment of Blood Consumption (ABC) score were 48% and 99%, respectively. Because blunt injuries account for most trauma patients in Japan, we established new simple criteria using significant factors that were derived from the examination on arrival. If trauma patients met any of the following conditions – that is, shock index (SI) >1, base excess (BE) <–3 mmol/l, and positive focused assessment of sonography for trauma (FAST) – sensitivity and specificity was 97% and 80%, respectively. The area under the receiver operating characteristic curve of ABC and the new criteria was 0.889 (95% CI, 0.815 to 0.963) and 0.927 (95% CI, 0.881 to 0.974), respectively.

Conclusion We suggest new criteria for early predicting MT in trauma using SI, BE, and FAST. This method may be valid especially in such areas because blunt injuries are the major cause of trauma in Japan.

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P110

Evaluation of the implementation of a massive transfusion protocol

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Introduction A massive transfusion protocol (MTP) aims to provide standardized and early delivery of blood products and prohemostatic agents by keeping pre-thawed fresh frozen plasma (FFP) available. Implementation of MTP is assumed to result in transfusion with higher ratios of FFPs and platelets to red blood cells (RBCs). Pre-thawing may also result in waste of FFPs. These MTP benefits or disadvantages have not yet been demonstrated. The aim of this study was to evaluate efficacy of a MTP 1 year after implementation in our level I trauma center in an academic hospital.

Methods A retrospective analysis of an electronic blood bank transfusion database comparing massive transfusion before (January to December 2011) and after (January to December 2012) implementation of MTP. Activation of MTP consists of delivery of packages of 6 units of RBC, 6 units of pre-thawed FFP and 2 units of platelets collected from five donors. Massive bleeding was defined as transfusion ≥10 units of RBCs. Statistics by *t* test and Mann–Whitney *U* test.

Results In 2012, a total of 101 MTP activations was registered. Accurate prediction of massively bleeding patients (n = 30) was 29.7% of MTP activations. Of all massively bleeding patients in 2012, MTP was not activated in 55.2%. In patients for whom MTP was activated, the RBC:FFP ratio was 1:0.9. In patients for whom MTP was activated and who were massively bleeding, the RBC:FFP ratio was 1:0.9, which was significantly higher compared with 1:0.6 in massive bleeders in 2011 (n = 70) (P = 0.001). The median of blood products administered was 12.5 (6 to 21) in massive bleeding after MTP implementation, compared with 8 (3 to 13) in 2011 (P <0.001). In patients for whom MTP was activated, 9.7% of thawed FFPs were not transfused and wasted. When massive transfusion was accurately predicted, the waste of FFPs was 4.8% versus a waste of 16.2% in the group of unjustified MTP activation.

Conclusion Implementation of MTP is associated with an increase of blood products transfused and a significant shift of RBC:FFP ratio to 1:1. However, MTP is also associated with a 9.7% waste of FFP. Improving prediction for massive bleeding patients may result in a decrease of wasted, costly blood products.

P111

Blood product transfusions in septic patients are associated with mortality, ARDS, and more days on mechanical ventilation

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Introduction The objective of this study was to determine whether septic patients requiring blood product transfusions have worse

outcomes compared with those who do not require transfusions. It is not uncommon for patients with sepsis to require blood product transfusions. The need for transfusions may be indicative of inflammatory consumption of blood cells, active blood loss, or impaired hematopoiesis. Regardless of the etiology, need for transfusion may be an indicator of a more severely ill patient and a valuable prognostic factor.

Methods This retrospective cohort study included all patients over the age of 40 years with a confirmed diagnosis of sepsis and an ICU stay at our academic medical center from 1 January 2005 to 31 March 2011. Use of blood product transfusion, patient demographics, and APACHE II score at the time of sepsis were collected from patient charts. Outcomes of interest were in-hospital mortality, development of acute respiratory distress syndrome (ARDS), days on mechanical ventilation, hospital cost, and length of stay.

Results We identified 824 patients who met the inclusion criteria for this study. Of those patients, 543 (66%) received at least 1 unit of blood products during hospitalization. Patients receiving blood products had significantly higher in-hospital mortality (36.1% vs. 26.9%; $P = 0.003$) and a higher rate of development of ARDS (45.3% vs. 27.1%; $P < 0.001$) compared with patients not receiving blood products. Patients receiving packed red blood cells (PRBCs) (60%) did not demonstrate a significant increase in mortality (35.1% vs. 28.8%; $P = 0.058$), while patients receiving platelets (20%) did have higher mortality (45.1% vs. 29.5%; $P < 0.001$). Transfusions of PRBCs or platelets were both associated with a higher development of ARDS ($P < 0.001$ for both). There was a significant increase in days on mechanical ventilation (7.0 days vs. 2.3 days; $P < 0.001$), hospital cost ($88,331 vs. $35,047; $P < 0.001$), and length of stay (17.3 days vs. 9.7 days; $P < 0.001$) for patients receiving blood products, regardless of the type. These differences were seen despite the mean APACHE II score being similar (22.8 vs. 22.5; $P = 0.645$).

Conclusion Patients with sepsis receiving blood products, particularly platelets, were significantly more likely to develop ARDS, had more days on mechanical ventilation, and had higher mortality. The lack of an increase in mortality associated with PRBC transfusion may be due to the benefit in oxygen delivery or sample size.

P112

Transfusion requirements in septic shock patients: a randomized controlled trial

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Critical Care 2014, **18(Suppl 1):**P112 (doi: 10.1186/cc13302)

Introduction Perioperative red blood cell transfusion is commonly used to address anemia, an independent risk factor for morbidity and mortality in critically ill patients [1]; however, evidence regarding optimal blood transfusion practice in septic shock is lacking. The aim of this study was to define which is the best transfusion strategy in septic shock patients regarding 28-day mortality and clinical outcomes: restrictive or liberal.

Methods The Transfusion Requirements After Cardiac Surgery (TRACS) study is a prospective, randomized, controlled clinical noninferiority trial conducted between February 2009 and February 2010 in an ICU at a university hospital cardiac surgery referral center in Brazil. Consecutive adult patients ($n = 502$) who underwent cardiac surgery with cardiopulmonary bypass were eligible; analysis was by intention to treat.

This is a randomized controlled parallel-group trial, which included 300 patients admitted to a cancer ICU with diagnosis of septic shock. Patients were randomly assigned to a liberal strategy of blood transfusion (to maintain hemoglobin >9 g/dl) or to a restrictive strategy (hemoglobin >7 g/dl). Mortality in 28 days was the main outcome. Secondary outcomes were clinical complications days free of organ dysfunction, ICU and hospital length of stay, adverse effects of transfusion and 60-day mortality.

Results A total of 136 patients were included in the first part of the trial. Mean age was 62 ± 14 years, SAPS 3 at admission was 65 ± 15 and all patients had the diagnosis of solid neoplasm. Sixty-three patients (46.3%) were included in the liberal strategy and 73 patients (53.7%) in the restrictive strategy. Occurrence of 28-day mortality was similar between groups (54% in liberal group vs. 56.2% in restrictive group; $P = 0.395$).

Conclusion Among cancer patients with septic shock, the use of a restrictive perioperative transfusion strategy compared with a more liberal strategy resulted in similar rates of 28-day-mortality.

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P113

Inflammatory properties of microparticles in stored red blood cell transfusion products

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Introduction Blood transfusion is associated with increased morbidity and mortality in the critically ill [1]. Adverse effects of transfusion may be mediated by changes in the blood product that accumulate with storage time [2]. The mechanisms, however, are largely unknown. Erythrocyte-derived microparticles (MPs) have been found in transfusion bags [3,4] and their concentration increases with storage duration [5]. We hypothesize that accumulation of MPs during storage induces a proinflammatory state in the recipient.

Methods Microparticles were isolated by high-speed centrifugation from red blood cell transfusion bags stored for 41 or 42 days. Whole blood from healthy volunteers was incubated for 24 hours with supernatant from the bags either containing MPs or depleted from MPs. Controls were incubated with medium or LPS (10 ng/ml). TNFα, IL-10 and IL-6 were measured in supernatant by ELISA. Data are expressed as median and range.

Results MP-depleted supernatant induced a modest increase in median levels of TNFα (9.2 (2.3 to 22.2) pg/ml) and IL-6 (2,140.7 (1,507 to 2,199) pg/ml) compared with the negative controls (2.3 (2.3 to 2.3) pg/ml and 94.4 (64.7 to 124.1) pg/ml, respectively), while IL-10 levels were not affected. Addition of MP-containing supernatant resulted in highly increased levels of TNFα (699 (687 to 742) pg/ml), IL-6 (37,443 (26,493 to 40,967) pg/ml) and IL-10 (1,201 (1,178 to 1,533) pg/ml) compared with negative controls. This MP-induced increase in cytokine production was comparable with the increase observed after the addition of LPS.

Conclusion Erythrocyte-derived MPs from aged red blood cell transfusion bags induce a strong inflammatory response *in vitro*, which is largely negated when MPs are removed. Whether MPs mediate adverse effects of blood transfusion in the critically ill remains to be determined.

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P114

Influenza A (H1N1): the first hit for transfusion-related acute lung injury?

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Introduction Transfusion-related acute lung injury (TRALI) is the leading cause of transfusion-related fatalities [1]. A two-hit hypothesis has been proposed for TRALI. The first hit is underlying patient factors, resulting in adherence of primed neutrophils to the pulmonary endothelium, such as severe pneumonia due to influenza A H1N1. The second hit is caused by mediators in the blood transfusion that activate the endothelial cells and pulmonary neutrophils, resulting

in capillary leakage and subsequent pulmonary edema [2]. TRALI is a clinical diagnosis with the following criteria: acute onset within 6 hours of blood transfusion, PaO_2/FIO_2 ratio <300 mmHg, or worsening of the P:F ratio, bilateral infiltrative changes on chest radiograph, no sign of hydrostatic pulmonary edema (pulmonary arterial occlusion pressure ≤18 mmHg or central venous pressure ≤15 mmHg) and no other risk factor for acute lung injury [2].

Methods We describe a fatal TRALI in a patient with influenza A (H1N1), suggesting a relationship between a first-hit lung injury followed by the second lung impairment after blood transfusions.

Results We report a 57-year-old female, without a previous medical record. She had an acute onset of fever, cough, muscle pain and progressive dyspnea leading to acute respiratory distress syndrome. The test for influenza A H1N1 was positive. She was recovering, but on day 12 of admission, after 1 hour of platelet transfusion, she started with intensive tachycardia, dyspnea and hypoxemia. Her mechanical ventilation parameters increased dramatically. She was in plan for extubation with FiO_2 of 30% and positive end-expiratory pressure of 8, which became 100% and 14 respectively. The P:F ratio dropped to 62. Her leukocytes were 10.6×10^9/l a few hours earlier and went down to 1.5×10^9/l after the onset. Previous lactate was normal, but jumped to 42 mg/dl. She was free of vasopressors and after the offending transfusion went through refractory shock and died approximately 24 hours after the blood transfusion.

Conclusion For our knowledge this is the first case reported of TRALI in an influenza A (H1N1) patient. Although blood transfusion can be life saving, it also can be a life-threatening intervention. Prevention is still the best hit.

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P115

Prothrombin complex concentrate restores haemostasis in a dabigatran anticoagulated polytrauma pig model

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Introduction Prothrombin complex concentrate (PCC) has been suggested as a measure to terminate trauma and dabigatran-induced bleeding. Owing to the conflicting data concerning such therapy, we investigated the impact of a four-factor PCC to terminate massive bleeding following the infliction of multiple trauma in dabigatran anticoagulated pigs.

Methods After ethical approval, 24 male pigs were administered dabigatran etexilate (30 mg/kg bid p.o.) for 3 days. On day 4, dabigatran in anaesthetised animals was infused prior to injury to achieve supra-therapeutic levels. Twelve minutes after infliction of bilateral femur fractures and standardised blunt liver injury, animals randomly received PCC (25, 50 or 100 IU/kg; $n = 6$) or placebo ($n = 6$). Time-adjusted blood loss as primary endpoint (observation period 300 minutes) and a panel of coagulation variables were continually measured. Data were analysed by two-way ANOVA. Data are mean ± SEM.

Results Concentrations of dabigatran prior to infliction of trauma was comparable between groups (590 ± 40 ng/ml). Anticoagulation with dabigatran and trauma caused severe coagulopathy as shown by prolonged TEM variables (CT, CFT), PT and aPTT. Following PCC application these effects were partially reversed. Due to ongoing blood loss both PT and TEM variables prolonged over time in PCC 25 IU/kg substituted animals. Accordingly, no-PCC (38.5 ± 4.7 ml/minute) and PCC 25 IU/kg (22.6 ± 5.5 ml/minute) animals showed highest blood loss (P <0.05 vs. PCC 50 IU/kg and PCC 100 IU/kg) with a mean survival time of 106 minutes (no-PCC animals) and 204 minutes for PCC 25 IU/kg animals, respectively. All animals of the PCC 50 IU/kg and PCC 100 IU/kg group survived. Blood loss in both groups was comparable (PCC 50 IU/kg: 5.9 ± 0.2 ml/minute; PCC 100 IU/kg 6.0 ± 0.3 ml/minute).

Conclusion The use of high doses of PCC reversed the anticoagulant effects of dabigatran, which was associated with a significant reduction of blood loss. However, the results of this study show that sufficient concentrations of PCC are necessary to overcome thrombin inhibition.

P116

Effect of a fixed dose of fresh frozen plasma on systemic inflammation and endothelial damage in nonbleeding critically ill patients

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Introduction Fresh frozen plasma (FFP) is associated with onset of acute lung injury [1], the mechanism of which is largely unknown. On the other hand, FFP may be beneficial, as a higher ratio of FFP to red blood cells decreases mortality in bleeding trauma patients [2] and is associated with an endothelial stabilizing effect *in vitro* [3]. We investigated the effect of transfusion with FFP on host response and markers of endothelial damage in nonbleeding critically ill patients.

Methods This was a substudy of a multicenter trial in which nonbleeding critically ill patients with an increased International Normalized Ratio (1.5 to 3.0) were randomized to omitting or administering a prophylactic transfusion of FFP (12 ml/kg) prior to an invasive procedure. In 38 patients randomized to receive FFP transfusion, we measured levels of factor VIII, von Willebrand factor, and markers of proinflammatory response before and after transfusion. Data are presented as medians.

Results FFP transfusion resulted in a significant decrease of TNFα (from 12.3 to 3.1 pg/ml, $P = 0.01$), von Willebrand factor (from 475 to 424%, P <0.01) and factor VIII (from 246 to 244%, P <0.01). FFP did not alter levels of IL-1β, IL1-RA, IL-8, IL-10, MCP1, MIP1A or sCD40L. Patients had some degree of lung injury at baseline as reflected by a lung injury score of 2 (0.8 to 2.5), which did not change following transfusion. None of the patients developed TRALI.

Conclusion FFP transfusion is not associated with a proinflammatory response in the critically ill. Rather, FFP seemed to have an endothelial stabilizing effect.

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P117

Application of damage control resuscitation strategies to patients with severe traumatic hemorrhage: review of plasma to packed red blood cell ratios at a single institution

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Introduction When treating trauma patients with severe hemorrhage, massive blood transfusions are often needed. Damage control resuscitation strategies can be used for such patients, but an adequate fresh frozen plasma:packed red blood cell (FFP:PRBC) administration ratio must be established.

Methods We retrospectively reviewed the medical records of 100 trauma patients treated with massive transfusions from March 2010 to October 2012. We divided the patients into two groups according to the FFP:PRBC ratio: a high-ratio group (≥0.5) and a low-ratio group (<0.5). The patient demographics, fluid and transfusion quantities, laboratory values, complications, and outcomes of both groups were analyzed and compared.

Results There were 68 patients in the high-ratio group and 32 in the low-ratio group. There were statistically significant differences between groups in the quantities of FFP, FFP:PRBC, platelets, and crystalloids administered, as well as the initial diastolic blood pressure. When comparing the incidence of complications, bloodstream infections were noted only in the high-ratio group, and the difference was statistically significant ($P = 0.028$). Kaplan–Meier plots revealed that the 24-hour survival rate was significantly higher in the high-ratio group (71.9% vs. 97.1%, P <0.001). The 30-day survival rate was also higher in the high-ratio group (56.2% vs. 67.6%), but the difference was not statistically significant ($P = 0.117$).

Conclusion For treating patients with severe hemorrhagic trauma, raising the FFP:PRBC ratio to 0.5 or higher may increase the chances of survival (especially the 24-hour survival rate). Efforts to minimize bloodstream infections during the resuscitation process must be increased.

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P118

In a trauma experimental pig model prothrombin complex concentrates and a specific antidote (idarucizumab) are effective to reverse the anticoagulant effects of dabigatran

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Introduction Strategies to reverse the anticoagulant effects of the new oral anticoagulants in severely bleeding patients remain challenging and conflicting results have been presented regarding the efficacy of PCCs to alter dabigatran-induced coagulopathy. Thus, this study assessed the ability of PCC, activated PCC (aPCC), recombinant FVII (rFVIIa) and idarucizumab to reverse the anticoagulant effects of dabigatran in a porcine model of trauma.
Methods Studies were performed in five pigs. Dabigatran etexilate (DE) was given orally for 3 days (30 mg/kg bid) and on the 4th day dabigatran was infused 90 minutes (30 minutes: 0.77 mg/kg/hour; 60 minutes 0.52 mg/kg/minute) prior to blunt liver injury. Blood samples were taken before and after dabigatran infusion and 60 minutes post injury. Two doses of PCC (30, 60 IU/kg), aPCC (30, 60 IU/kg), rVIIa (90, 180 µg/kg) and idarucizumab (30, 60 mg/kg) were added to blood samples *ex vivo*. Coagulation was assessed by thromboelastometry, PT and diluted TT. One-way analysis of variance with the Dunnett *post-hoc* test for multiple comparisons was used for statistical analysis. Data are presented as mean ± SD.
Results Oral DE prolonged clot formation (CFT: 159 ± 39 seconds) and PT (27 ± 9 seconds). Following the 90-minute infusion of dabigatran, the mean plasma levels of dabigatran increased to 1,423 ± 432 ng/ml. This supra-therapeutic level was associated with a further prolongation of PT, aPTT, and the EXTEM variables CT and CFT. These changes in coagulation parameters were compounded by blood loss following trauma (total blood loss at 60 minutes: 1,978 ± 265 ml). Sixty minutes after trauma, four out of five animals had no measurable clot formation (EXTEM CFT ≥4,000 seconds) and clot strength (EXTEM MCF) had reduced to 11 ± 7 mm. Both PCCs and aDabi-Fab, but not rFVIIa, reversed the effects of dabigatran on thromboelastometry parameters (clotting time and clot formation time) and PT at all time points. In contrast, aPTT was only normalised by idarucizumab. Plasma concentrations of dabigatran remained elevated after PCC therapy, but were not measureable after idarucizumab.
Conclusion Both PCC and aPCC are effective in reducing coagulopathy in a porcine trauma model with dabigatran anticoagulation. The *ex vivo* addition of idarucizumab fully corrected all coagulation measures and significantly decreased plasma concentrations of dabigatran. No significant effects on haemostasis were observed after the application of rFVIIa.

P119

Attenuation of ischemia–reperfusion injury in swine resuscitated for hemorrhagic shock by low-dose inhaled nitrite or carbon monoxide

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Critical Care 2014, **18(Suppl 1):**P119 (doi: 10.1186/cc13309)

Introduction Fluid resuscitation of hemorrhagic shock is frequently associated with reperfusion injury and secondary organ damage. Studies suggest that low doses of both nitrite and carbon monoxide may protect tissues and organs from this reperfusion injury by limiting mitochondrial free radical production. We explored the effects of very small doses of nitrite and carbon monoxide on tissue injury in a porcine model of hemorrhagic shock.
Methods Fluid resuscitation of hemorrhagic shock is frequently associated with reperfusion injury and secondary organ damage. Studies suggest that low doses of both nitrite and carbon monoxide may protect tissues and organs from this reperfusion injury by limiting mitochondrial free radical production. We explored the effects of very small doses of nitrite and carbon monoxide on tissue injury in a porcine model of hemorrhagic shock.
Results Although no increase in blood nitrite concentrations was observed after inhalation, nitrite was associated with significant decreases in blood, muscle, and peritoneal fluid lactate concentrations (P <0.05), whereas both nitrite and carbon monoxide were associated with significant decreases in glycerol in peritoneal fluid (P <0.05). Following resuscitation, the muscle mitochondrial respiratory control ratio was preserved in the nitrite and carbon monoxide groups and reduced in the control group. Adjuvant drugs had no effects on any gross hemodynamic parameters.
Conclusion We conclude that at low doses, nebulized sodium nitrite and inhaled carbon monoxide are associated with tissue protection during resuscitation from severe hemorrhagic shock.
Acknowledgement This work was supported in part by DoD grant W81XWH-11-2-0049, NHLBI HL07820, and 2013121 from The South-Eastern Norwegian Health Authorities.

P120

Validation of inflationary non-invasive blood pressure monitoring in emergency room patients

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Introduction Currently, most non-invasive blood pressure (NIBP) monitoring is based on the oscillometric method and determines the blood pressure during cuff deflation [1]. On the other hand, a measurement during cuff inflation may be advantageous, as cuff inflation requires lower cuff pressure and shorter duration than deflation. In surgical patients during anesthesia, the inflationary NIBP has reasonable accuracy compared with conventional deflationary NIBP [2]. Few studies have reported NIBP monitoring using the inflationary NIBP in ER patients with various unstable conditions. A purpose of this study is to verify the usefulness of the inflationary NIBP monitoring in the emergency department.
Methods A total of 2,981 NIBP data were collected from 174 patients (age; 56.5 ± 22.2 (7 to 92) years) who have been accommodated in the resuscitation area of the ER at Keio University Hospital, using alternately two algorithms with a standard monitor (BSM-6000; Nihon Kohden Inc., Tokyo, Japan). One algorithm consists of continuous inflationary and deflationary measurement in a single cycle (dual algorithm, 1,502 data) performed in order to verify a success rate and a precision of data. The deflationary algorithm (1,479 data) consists of only conventional deflationary measurement performed in order to verify the duration of the measurement cycle.
Results The success rate of the inflationary NIBP (completed only by inflationary method) was 69.0%. The bias and precision of systolic pressure and diastolic pressure (difference of systolic and diastolic pressure between inflationary and deflationary NIBP) were –0.6 ± 8.8 and 3.5 ± 7.5 mmHg, respectively (Figure 1). Inflationary NIBP could also determine NIBP more quickly compared with deflationary NIBP (16.8 vs. 29.1 seconds, median) (Figure 2).
Conclusion These data suggest that inflationary NIBP has reasonable accuracy and sufficient rapidity compared with deflationary NIBP in emergency room patients.

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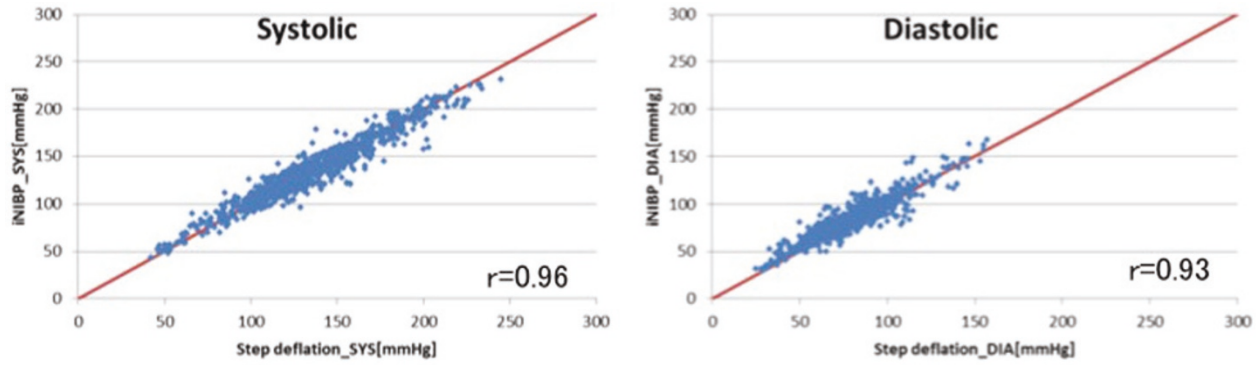

Figure 1 (abstract P120). Precision of measurements between inflationary and deflationary NIBP.

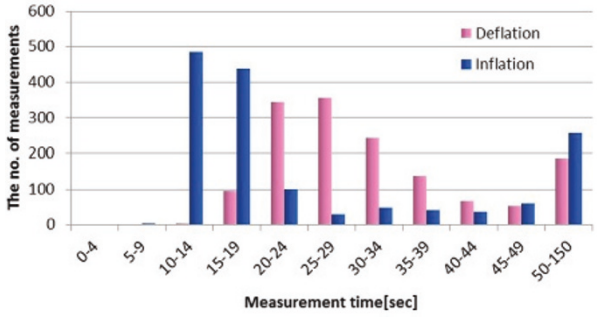

Figure 2 (abstract P120). Frequency histogram of measurement time.

P121

Influence of the oscillometric calibration method on accuracy and precision of continuous non-invasive arterial pressure measurements using the CNAP™ device

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Introduction The CNAP™ system (CNSystems Medizintechnik AG, Graz, Austria) provides continuous non-invasive arterial pressure (AP) measurements based on the volume clamp method using a finger cuff. Finger AP values are calibrated to oscillometric upper-arm AP measurements. In the present study we investigated the influence of the calibration approach based on oscillometric upper-arm cuff measurements on the accuracy and precision of the CNAP™ device in comparison with invasively obtained AP measurements.
Methods The datasets of simultaneously recorded invasive (via arterial catheter) and non-invasive (using the CNAP™ system) AP measurements in 43 patients treated in the medical ICU of a university hospital were analyzed in this study. The following comparative analyses between the two AP measurement techniques were performed: (1) comparison of CNAP™-derived AP values with invasive AP (IAP) measurements; (2) comparison of the CNAP™ oscillometric AP values used for the calibration of finger AP with IAP measurements; and (3) computer-aided calibration (CAC) of the CNAP™ finger AP values to IAP values instead of calibration to oscillometric upper-arm AP measurements with IAP measurements.
Results (1) The comparison of CNAP™-derived AP values with IAP measurements revealed a mean difference (± standard deviation) for mean AP, systolic AP, and diastolic AP of +0.6 mmHg (±10 mmHg), +11 mmHg (±17 mmHg), and −6 mmHg (±9 mmHg), respectively. (2) The comparison between the oscillometric AP values used for calibration of the CNAP™ device and the corresponding IAP values resulted in a mean difference (± standard deviation) of −0.8 mmHg (±8 mmHg), −5 mmHg (±14 mmHg), and +10 mmHg (±9 mmHg), respectively. (3) CAC of the CNAP™ finger AP values to IAP values instead of calibration to oscillometric upper-arm AP measurements resulted in a mean difference (± standard deviation) of +4 mmHg (±8 mmHg), +5.5 mmHg (±14 mmHg), and +3 mmHg (±7 mmHg), respectively. The accuracy of CAC-CNAP™-derived systolic and diastolic AP compared with the CNAP™-derived AP calibrated to oscillometric AP was significantly higher ($P = 0.004$ and $P < 0.001$, respectively).
Conclusion When using the CNAP™ system, calibration to oscillometric upper-arm AP values integrated into the CNAP™ system is a relevant source of difference between CNAP™-derived continuous non-invasive AP measurements and invasively assessed AP values.

P122

Arterial pulse waveform as an n-soliton evolution of the left ventricular pressure pulse

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Introduction The time profile of the arterial pulse is known to have features such as the dicrotic notch and subsidiary peaks. Such features may provide useful information about the vascular system and are traditionally explained in terms of aortic valve closure or multiple reflections from impedance mismatches within the arterial system. However, experimental evidence of such reflections has been elusive. It has been proposed that arterial dynamics may obey a nonlinear equation [1]. This model predicts the existence of multipeaked solitons which can travel long distances without dissipation. We demonstrate that within the soliton model it is not necessary to model valve closure or wave reflection: single or multiple notches arise *de novo* even from featureless theoretical LV pressure pulse profiles. We show that a number of clinically relevant features of the invasive blood pressure are reproduced by the soliton model and examine the role of LV pulse energy on pulse wave shape and progression.
Methods A model for the arterial pressure is given by solutions to a KdV equation with constants depending on the properties of the artery [1]. This can be solved with the initial condition of a parabolic left ventricular pressure pulse.
Results The evolution of the arterial pulse along the arterial tree is shown in Figure 1. We also predict arterial pulses for increasing left ventricular ejection energies.
Conclusion Our simple model explains many features of the arterial pulse observed in clinical practice such as the development of the dicrotic notch, the change in shape along the arterial tree and the steepening and acceleration with hypertension. Some phenomena that have traditionally been attributed to arterial wave reflections or resonance of the invasive arterial pressure measurement can instead be explained by intrinsic properties of the arterial pulse.

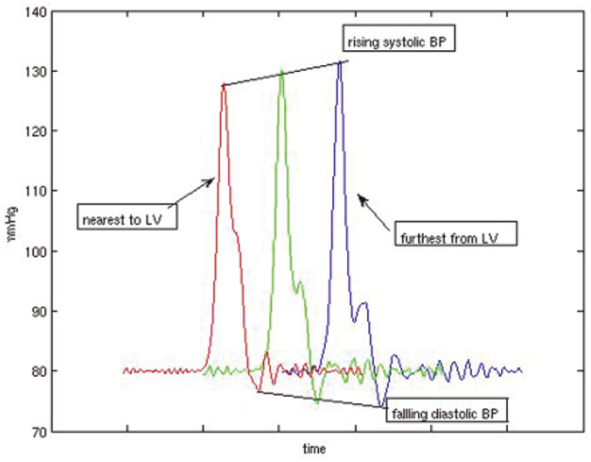

Figure 1 (abstract P122).

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P123

Tackling the burden of postsurgical complications in the USA: would perioperative goal-directed therapy help?

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Introduction Pay-for-performance programs and economic constraints call for solutions improving the quality of healthcare without increasing costs. Many studies have shown decreased morbidity in major surgery when perioperative goal-directed therapy (PGDT) is used. We assessed the clinical and economic burden of postsurgical complications in the University HealthSystem Consortium (UHC) in order to predict potential savings with PGDT.
Methods Data from adults who had 10 major surgical procedures in 2011 were screened in the UHC database. Thirteen postsurgical complications were tabulated. In-hospital mortality, hospital length of stay and costs from patients with and without complications were compared. The risk ratios reported by the most recent meta-analysis were used to estimate the potential reduction in postsurgical morbidity with PGDT. Potential cost savings were calculated from the actual and anticipated morbidity rates.
Results A total of 75,140 patients met the search criteria. In total, 8,421 patients developed one or more postsurgical complications (morbidity rate 11.2%). In-hospital mortality was 12.42% and 1.39% (P <0.001), mean hospital length of stay was 20.48 ± 20.09 days and 8.05 ± 7.11 days (P <0.001), and mean direct cost was $47,284 ± 49,170 and $17,408 ± 15,612 ($P$ <0.001) in patients with and without complications, respectively. With PGDT, morbidity rate was projected to decrease to 6.5 to 9.0%, yielding gross costs savings of $50 million to 151 million for the study population or $670 to $1,406 per patient.
Conclusion Postsurgical complications have a dramatic impact on mortality, hospital length of stay and costs. Potential cost savings resulting from PGDT are substantial. PGDT may be recommended to improve quality of care and decrease costs.

P124

Radiological control of central venous catheter (CVC) versus electrocardiogram-guided control inserted CVC: confirm with transesophageal echocardiography

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Introduction The placement of a central venous catheter (CVC) is now common practice. Control of the seat of the tip occurs through the antero-posterior radiograph of the chest (RX). New techniques have been developed to control the seat of the CVC, to avoid complications during the procedure and the RX control post insertion. The aim of this study is to demonstrate the ECG's P-wave amplitude (PWA) increases as we approach the atrio-caval junction (ACJ) by recording the intra-cavity and show that this method is more sensitive and specific compared with RX control. To confirm this, we use the direct view of the tip by transesophageal echocardiography (TEE), a method which has the most recognized high sensitivity and specificity [1].
Methods In 55 adult patients, hospitalized in the ICU, a CVC was placed. We excluded patients with cardiac arrhythmias or pacemaker wearers. All CVCs were placed with an ultrasound-guided puncture technique of the internal jugular vein (IJV) or subclavian vein (SV). The CVC was introduced by the Seldinger technique. Introducing the CVC along the Seldinger guide links to the same terminal on the cable connection as the intra-cavity derivation ECG (set CVC Certofix B; Braun), in turn connected to the adapter for ECG (Certodyn Universaladapter B; Braun). Then the detection mode of the adapter is converted by the ECG trace outside (through surface electrodes) to the ECG mode intra-cavity and an increase of PWA confirmed the CVC in the vicinity of the ACJ. Through the TEE with esophageal average scan at 120° we measured the distance between the tip and the ACJ. The results were expressed as mean with standard deviation.
Results Forty-five CVCs were placed in the IJV while 10 were in the SV. No complications or arrhythmias were detected during the procedure. All CVCs produced an increase in PWA. Where the PWA increased by 25% compared with normal, the TEE scanning tip was 2.5 ± 1.3 cm from the ACJ. Where the PWA increased by 33%, the TEE scanning tip was 1.9 ± 1.1 cm from the ACJ. Where the PWA increased by 50%, the TEE scanning tip was 1.3 ± 0.6 cm from the ACJ. The RX reports have described briefly the presence of the catheter in the superior vena cava without making explicit the exact position relative to the ACJ.
Conclusion We have shown the increase in PWA by detecting that the endo-cavity, as we proceed with the insertion of the CVC, corresponds to higher proximity to the ACJ. These results canceled the need for RX control in the future.
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P125

Impact of the neutral position and rotation of the head in ultrasound-guided internal jugular vein catheterization on duration of procedure and complications

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Introduction In internal jugular vein (IJV) catheterization, neck rotation may enhance the visibility of anatomical landmarks; however, it may increase the risk of carotid artery (CA) puncture by replacing the position of the IJV in relation to the CA. In our study, during US-guided IJV catheterizations, we investigated the effects of changing the position of the IJV by the CA depending on the neutral position and 45° rotation of the head on duration of procedure and complications.
Methods After obtaining hospital ethics committee approval, 100 intensive care patients aged >18 years were included in the study. Patients were randomly selected and catheterization was performed in a neutral position of the head (n = 50) and by turning the head 45° to the opposite side (n = 50). The US-guided catheterization procedure was performed in accordance with general principles. Once the needle entered the IJV and blood was aspirated, the US probe was released from the hand, and the catheter was placed and fixed according to the Seldinger technique. The data of the intervention side for each process, the count number of successful catheter insertion, whether there is arterial access or not and the duration of procedure (from skin contact of the needle to catheter insertion) were recorded.
Results The localization of the IJV in relation to the CA is 66% anterolateral, 4% anterior and 30% lateral in a neutral position, and 62% anterolateral, 28% anterior, 10% lateral position in 45° rotation. So while there is no change in a significant proportion of patients in

the localization of the IJV in relation to the CA, the anterior placement rate increasing the risk of CA puncture was significantly higher in a position of rotation compared with the neutral position ($P = 0.001$). No significant difference was found between procedure durations. Complications were recorded when observed.
Conclusion In our study, it has been shown that anterior placement of the IJV in the neutral position is less but this has no advantage in avoiding arterial puncture. The smaller area of procedure in a neutral position can cause difficulties in practice. However, the processing times between each head position were not different. Nevertheless, further studies evaluating whether there are comparable complication rates and the same duration of procedure in emergency and trauma patients in whom head rotation cannot be possible are needed.

P126

Anthropometric formulas versus intracavitary ECG for optimal tip position of central venous catheters

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Introduction Peres [1] and more recently Lum [2] developed some anthropometric formulas to correlate patient's height (H) and ideal length of central venous catheter (CVC) in order to identify optimal tip position. The aim of this study is to compare the reliability of the anthropometric formulas with the method based on intracavitary ECG.
Methods We enrolled patients admitted to our ICU candidate to elective CVC insertion, who had a detectable P wave on surface ECG. Intracavitary ECG was used to identify the optimum tip location since a maximal P wave indicates the cavo-atrial junction [3]. Post-insertion chest X-ray (CXR) was performed in all patients to verify the tip position. Assuming that the cavo-atrial junction is about 3 cm from the carina [4], the tip position was considered correct between 1 and 5 cm from the carina (between the lower 1/3 of the superior vena cava and the upper 1/3 of the right atrium). For each patient we retrospectively evaluated whether the catheter length calculated with Lum's and Peres' formulas on an estimated height would have been acceptable.
Results Sixty-five CVCs were placed: 51 in the right internal jugular vein (IJV), 14 in the left IJV. The mean catheter length by intracavitary ECG was significantly deeper than predicted by Lum's formulas (18.2 ± 1.9 vs. 16.7 ± 1.7 cm, $P < 0.001$) and not different from Peres' formulas (18.2 ± 1.9 vs. 18.2 ± 1.7 cm, $P = 0.8$).
At post-procedural CXR, 88% of the tips were in the target zone. In three cases (5%) the catheter went in the wrong direction but was immediately corrected during the procedure since the intracavitary P wave did not change its amplitude. Compared with the intracavitary ECG, the incidence of malposition would have been significantly higher with Lum's formulas (48% vs. 12%, $P < 0.001$) and Peres' formulas (51% vs. 12%, $P < 0.001$).
Conclusion The intracavitary ECG was associated with a lower incidence of tip malposition than Peres' and Lum's formulas. It is also the only technique allowing one to immediately correct a primary malposition during catheter insertion.
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P127

Residents learning ultrasound-guided catheterization are not sufficiently skilled to use landmarks

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Introduction An ultrasound-guided (UG) technique is the recommended procedure for central venous catheterization (CVC). But ultrasound may not be available in emergency situations, and therefore guidelines also propose that physicians remained skilled in landmark (LM) placement. We conducted this prospective observational study to determine the learning curve of the LM technique in residents only learning the UG technique.
Methods During the first 3 months of their rotation in our ICU, residents inexperienced in CVC used only the real-time UG technique. During the following 3 months, residents were allowed to place CVC by means of the LM technique when authorized by the attending physician.
Results A total of 172 procedures (84 UG and 88 LM) were performed by the inexperienced residents during the study. The success rate was lower (72% vs. 84%; $P = 0.05$) and the complication rate was higher (22% vs. 10%; $P = 0.04$) for LM compared with UG procedures. Comparison between the five last UG procedures and the first five LM procedures performed demonstrated that the transition between the two techniques was associated with a marked decrease of the success rate (65% vs. 93%; $P = 0.01$) and an increase of the complication rate (33% vs. 8%; $P = 0.01$). After 10 LM procedures, residents achieved a success rate and a complication rate of 81% and 6%, respectively.
Conclusion Residents who only learn the UG technique will not be immediately able to perform the LM technique, but require specific training based on at least 10 LM procedures. Whether the LM technique should still be taught when an ultrasound device is not available must therefore be addressed.

P128

Development of a standardized method of peripherally inserted central catheter (PICC-line) bedside installation

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Introduction Bedside insertion of peripherally inserted central catheters (PICCs) results in tip malposition in up to 48% [1], with catheters frequently terminating in the internal jugular vein (IJV) or in peripheral veins [2]. In an attempt to reduce tip malposition, we developed a standardized approach to PICC installation. This study aims to validate that method.
Methods From a 34-bed adult ICU, we retrospectively reviewed PICC insertions over a 6-month period before the intervention program (control group). We designed a prospective interventional pilot study on 40 consecutive patients (intervention group). Patients in the intervention group were positioned in a standardized fashion and the PICC length was measured from easily identified anatomic landmarks. During PICC insertion, the patient's head was either rotated ipsilaterally to the site of PICC insertion or the ipsilateral IJV was manually compressed, depending on the patient's capacity to collaborate. Once the PICC was inserted, an ultrasound survey was conducted to identify the catheter in the subclavian vein (SC) and ensure its absence in the ipsilateral IJV. The primary endpoint was defined as PICC tip position, obtained from the post-procedural chest X-ray. A catheter was considered to be in an optimal position if the tip resided in the distal third of the superior vena cava (SVC), adequate if it resided between the subclavian vein (SC) and the distal third of the SVC, and aberrant if in any other location.
Results In the retrospective control arm, 105 PICCs were reviewed for tip position. Optimal, adequate, and aberrant positions were found in 22 (21%), 49 (47%), and 34 (32%) respectively, in comparison with 17 (43%), 15 (38%), and eight (20%) in the intervention group ($P < 0.05$ between both groups). In the control arm, 11 (10%) PICCs terminated outside the central venous system, whereas none failed to achieve central venous access in the intervention arm.
Conclusion Using the standardized method described above, PICC tip positioning can be greatly improved. In our results, 100% of catheters placed using the standardized method allowed for central venous access. This pilot study paves the way for a larger, multicentric evaluation of the bedside installation method of PICC.
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P129

Is chest X-ray necessary after central venous catheter insertion?

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Critical Care 2014, **18(Suppl 1):**P129 (doi: 10.1186/cc13319)

Introduction According to the European Society of Parenteral and Enteral Nutrition guidelines [1], post-insertion chest X-ray (CXR) is not necessary if the location of the tip has been verified during the procedure and if pleura-pulmonary damage has been ruled out by other methods. The aim of this study is to assess feasibility and safety of an echo-ECG-guided method of central venous catheter (CVC) insertion and to evaluate whether post-insertion CXR can be avoided.
Methods We enrolled only patients admitted to our ICU and candidate to elective CVC insertion, who had a detectable P wave on surface ECG. Our insertion protocol included: preliminary ultrasound (US) scan of central veins and pleural space; US-guided puncture and US control of the correct direction of the guidewire; intracavitary ECG method for tip location (cavo-atrial junction (CAJ) = maximal P wave); and US scan of pleural space to rule out pneumothorax (PNX). Post-insertion CXR was performed in all patients to rule out PNX and verify tip location close to the CAJ (CAJ = 3 cm below the carina [2]). Tip location between 1 and 5 cm below the carina – in the lower 1/3 of the superior vena cava (SVC) or in the higher 1/3 of the right atrium (RA) – was considered acceptable [1].
Results Eighty CVCs were placed in 78 patients, either by residents in training or by attending doctors. The vein was selected by US scan: right internal jugular (IJ) 64%, left IJ 17%, right axillary 11%, left axillary 4%, right innominate 4%. One pre-existing PNX was identified by US before the procedure. Accidental arterial puncture occurred in three cases (two by residents). In five cases, the wrong direction of the wire was detected by US and corrected during the procedure. The mean number of attempts was 1.65 (1.35 for attending vs. 1.95 for residents, P <0.02) and mean insertion time was 10.4 minutes (8.72 for attending vs. 12.11 for residents, P <0.005). Pleural US scan ruled out puncture-related PNX in all patients. At post-procedural CXR: no PNX was detected, 90% of tips were in the target zone, 5% were in the middle 1/3 of SVC and 5% were in the middle 1/3 of RA (all CVC with tips out of the target zone were inserted by residents).
Conclusion Our insertion protocol was safe and effective, with minor differences between experienced versus nonexperienced operators. Our data suggest that immediate CXR is not necessary soon after CVC insertion, since PNX can be ruled out by US and since the intracavitary ECG method allows tip location in the SVC and RA in all cases.
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P130

Diagnostic value of chest ultrasound after cardiac surgery: a comparison with chest X-ray and auscultation

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Introduction Chest auscultation and chest X-ray are commonly used to detect postoperative abnormalities and complications in patients admitted to intensive care after cardiac surgery [1,2]. The aim of the study was to evaluate whether chest ultrasound represents an effective alternative to bedside chest X-ray to identify early postoperative abnormalities.
Methods A total of 151 consecutive patients (103 male and 47 female) were studied by chest auscultation, ultrasound and X-ray upon admission to intensive care after cardiac surgery. Six pathologic entities were explored by each method: postero-lateral pleural effusion and/or alveolar consolidation (PLAPS), alveolar-interstitial syndrome (AIS), alveolar consolidation (AC), pneumothorax (PTX), pleural effusion (PE), and pericardial effusion with or without cardiac tamponade. Positions of the endotracheal tube and central venous catheter were also checked.
Results Ninety-four of the 151 patients included (62%) showed abnormalities on chest X-ray (AC 9%, AIS 25%, PLAPS 42%, PE 3.3%, PTX 2%). Compared with chest X-ray, chest ultrasound had a sensitivity of 86% and a specificity of 99% for AC, a sensitivity of 95% and a specificity of 100% for AIS, a sensitivity of 97% and a specificity of 98% for PLAPS, a sensitivity of 99% and a specificity of 100% for PE, and a sensitivity and specificity of 100% for PTX. Furthermore, chest ultrasound detected all pericardial effusions while neither chest X-ray nor chest auscultation were able to identify them. Chest ultrasound identified all cases of endotracheal tube (two patients) and central venous catheter (two patients). There was a highly significant correlation between abnormalities detected by chest ultrasound and X-ray (k = 0.90), but a poor correlation between chest auscultation and X-ray abnormalities (k = 0.15).
Conclusion Chest auscultation may help identify endotracheal misplacement and tension pneumothorax but it may miss most of major abnormalities. Chest ultrasound represents a valid alternative to chest X-ray to detect all postoperative abnormalities and misplacements.
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P131

Ultrasound measurement of carotid flow time changes with volume status

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Introduction Assessment of volume status and responsiveness guides resuscitation strategy. Non-invasive techniques are desirable. Changes in carotid flow time have been proposed as a marker of volume status, but few data support their use. We sought to determine whether carotid flow time decreased in the volume-depleted state of acute blood loss, and whether volume-depleted individuals would demonstrate an increase in carotid flow time after a passive leg raise (PLR) maneuver.
Methods Volunteers aged 18 to 55 presenting to the hospital's blood donor center for whole blood donation were eligible to participate. Individuals with a history of aortic or carotid artery disease, atrial fibrillation, or a contraindication to blood donation were excluded. Prior to blood donation, an investigator performed an ultrasound of the right common carotid artery with a high-frequency linear transducer, obtaining a Doppler tracing of carotid artery flow. Measurements of peak velocity, systole time, and carotid flow time were obtained. A PLR was performed for 30 seconds, followed by repeat measurements of carotid velocity and flow time. Whole blood was then collected according to the blood donor center's protocol. Immediately after blood donation, repeat measurements of carotid flow and velocity were obtained in the supine position and after a PLR. Carotid flow times corrected for heart rate (FTc) were analyzed with Student's t test. The institutional review board approved the study.
Results Eighty donors were screened for participation by two investigators; 68 consented and completed donation (60.3% female, mean age 31). Donors had mean blood loss of 450 ml. The mean FTc supine after blood donation was 296 ms; this was significantly different from the FTc prior to donation (supine = 320 ms, PLR = 323 ms; P <0.0001). The mean FTc following blood donation and PLR was 321 ms, significantly different from the supine position after donation (P <0.0001), but not pre-donation measurements.
Conclusion Ultrasound measurement of carotid flow time was significantly decreased in the setting of acute blood loss. An auto-bolus by PLR after blood loss restored FTc to pre-donation levels. Further investigation of FTc as a non-invasive predictor of volume responsiveness is warranted.

P132

Real-time ultrasound-guided subclavian vein cannulation in cardiac surgery: comparison between short-axis and long-axis techniques

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Introduction Central venous catheters play an important role in patient care; however, their use is associated with various complications and more frequently through the subclavian vein (SCV) route. A previous study showed that ultrasound-guided cannulation of the SCV in critical care patients is superior to the landmark method and should be the method of choice in these patients [1]. The aim of this study was to compare short-axis and long-axis approaches for ultrasound-guided subclavian vein cannulation with respect to indicators of success.
Methods Eighty-three patients undergoing cardiac surgery and requiring central venous cannulation were randomized to receive long-axis or short-axis ultrasound-guided cannulation of the subclavian vein by a skilled anesthesiologist. First-pass success, unsuccessful placement, number of attempts, number of needle passes, skin and vessel puncture, time to successful catheterization and complications were considered as outcomes.
Results The subclavian vein was successfully cannulated by ultrasound-guided techniques in all patients. Central venous cannulation failed in two and 10 cases respectively with short-axis and long-axis view and the other view was used successfully. The first-pass success rate was significantly higher in the short-axis group (73%) compared with the long-axis group (40%) (P = 0.005). The procedure time, number of attempts, needle redirection, and skin and vessel punctures were significantly lower in the short-axis than long-axis group (P <0.05). The overall number of complications did not differ significantly between groups even if artery puncture and hematoma occurred more frequently in the long-axis group. Moreover, the need to change the ultrasound-guided insertion technique was more frequent in the long-axis group.
Conclusion Ultrasound-guided subclavian vein cannulation by an experienced operator has a higher first-pass success rate and lower access time using the short-axis than long-axis approach.
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P133

Transthoracic echocardiography used in conjunction with passive leg raising for assessment of fluid responsiveness in severe sepsis or septic shock patients

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Introduction During passive leg raising (PLR), we need a real-time device to demonstrate the hemodynamic change [1-3]. This study investigates the ability of transthoracic echocardiography (TTE) to predict fluid responsiveness (FR) in terms of detecting change of stroke volume (ΔSV) after PLR compared with the transpulmonary thermodilution technique (TPTD) ΔSV after volume expansion (VE).
Methods A prospective study was carried out in a medical ICU. Eligible patients were age ≥18 years without necessarily full adaptation to the ventilator with hemodynamic instability who were considered for VE. SV assessment using the subaortic velocity–time measurement was obtained by TTE simultaneously with other hemodynamic parameters derived from TPTD at baseline, within 2 minutes of PLR and following VE (250 ml fluid in 10 minutes). A fluid responder was defined by ΔSV ≥15% after VE by TPTD.
Results Preliminary reports on 16 patients with satisfactory cardiac windows were analyzed. ΔSV-TTE after PLR ≥13.6% predicts FR with sensitivity of 83.33%, specificity of 70% and AUC of 0.78 (95% CI: 0.54 to 1.00). Initial PPV ≥11% predicted FR with sensitivity of 83.33% with lower specificity of 60% and AUC of 0.64 (95% CI: 0.35 to 0.93) (Figure 1). The Bland–Altman plot showed 95% limits of agreement from –8.96 to +8.83% and mean difference (bias) of –0.07% (Figure 2).
Conclusion We may use %ΔSV measured by TTE after PLR to predict FR, which is noninvasive and less time-consuming than other invasive techniques.
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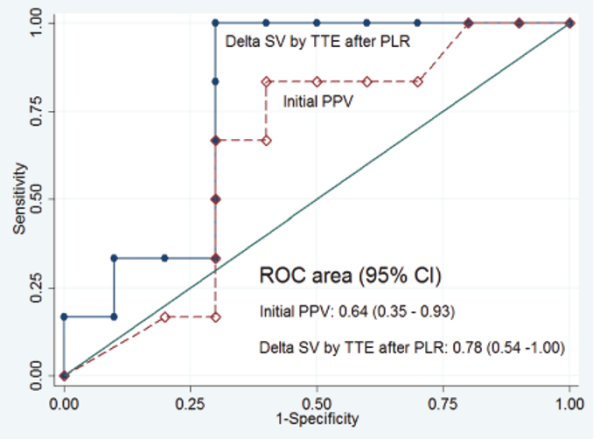

Figure 1 (abstract P133). ΔSV-TTE after PLR≥13.6% may predict fluid responsiveness with sensitivity of 83.33%, specificity of 70% and AUC of 0.78 (95% CI: 0.54 to 1.00). Initial PPV ≥11% predicted fluid responsiveness with sensitivity of 83.33%, lower specificity of 60% and AUC of 0.64 (95% CI: 0.35 to 0.93).

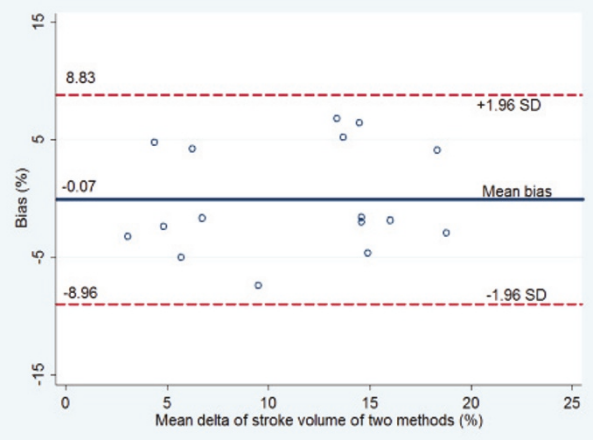

Figure 2 (abstract P133). Bland–Altman plot, comparing two methods, showing 95% limits of agreement from –8.96 to +8.83%ΔSV and the mean difference (bias) of measurement is –0.07%ΔSV. Dashed lines, upper and lower limits of agreement (95% CI for repeated measurements).

P134

Transoesophageal echocardiography and extracorporeal membrane oxygenation: fancy for enthusiasts or indispensable tool?

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Introduction Echocardiography is commonly used during both veno-arterial (V-A) and venovenous extracorporeal membrane oxygenation

(ECMO). In many circumstances, transoesophageal echocardiography (TOE) is the preferred monitoring tool. It can aid in cannula positioning, especially during double-lumen cannula placement for V-V ECMO, weaning of V-A ECMO and diagnose causes of high-access pressures and circuit flow problems. We use TOE as our preferred monitoring equipment before, during and after establishing ECMO. We sought to investigate how often information gained from TOE imaging had a major impact on management decisions.

Methods A single-centre observational study at a tertiary referral institution. All patients supported with V-A or V-V ECMO during an 18-month period were included. Routine procedures such as wire position checks during cannulation or information gained to assist weaning from V-A support were not included.

Results Twenty patients were supported with either V-A (all peripheral) or V-V ECMO during the observation period. In 12 patients (60%) TOE was instrumental in diagnosing potentially fatal complications or altered clinical management. In three patients on V-A support, afterload reduction and modulation of inotropic support was necessary due to extensive spontaneous echo contrast formation in the left ventricle and stagnant pulmonary blood flow; two out of these three patients, immediately after establishing support, required intra-aortic balloon counterpulsation to reverse clot formation around the aortic valve and root. Further diagnosis were Avalon cannula misplacement in the blind end of a piggyback cava following liver transplant, collapsing right atrial free wall with 'sucking down' into the access cannula ($n = 3$), pericardial clot formation and tamponade ($n = 1$), persistent left superior vena cava making planned cannula placement into the right atrium impossible or potentially fatal, diagnosis of patent foraminae ovale providing left atrial decompression and appropriate drainage cannula positioning during liver transplantation on ECMO.

Conclusion In our practice, TOE is an indispensable tool for safe ECMO practice, both during V-A and V-V support.

P135

Accuracy of synthesized right-sided/posterior chest lead electrocardiograms

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Introduction Right-sided precordial leads (V3R to V5R) and posterior chest leads (V7 to V9) provide important information for the right ventricle and posterior wall. These additional lead electrocardiograms (ECGs) improve diagnostic value in acute coronary syndrome patients [1]. However, these additional electrocardiograms are not routinely recorded due to the time-consuming procedure involved. Recently these synthesized six additional lead ECGs using the standard 12-lead ECG system (Nihonkoden Co. Ltd) have been developed [2,3]. But the accuracy is not clear. The purpose of the present study was to evaluate the accuracy of synthesized ECGs at the ST part.

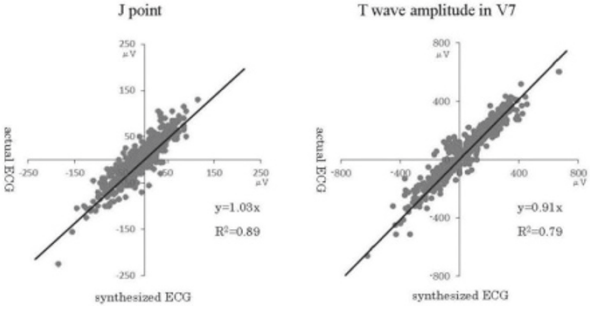

Figure 1 (abstract P135). Correlation between actual and synthesized ECG at V7.

Methods Standard 12-lead and actual V3R to V5R, V7 to V9 lead ECGs at Tokyo Medical University Hospital were successfully recorded and compared with synthesized ECGs at the J point, M point that was defined for the point after 1/16 RR interval and T wave amplitude. ECGs of the complete right branch block, complete left branch block and pacing rhythm were excluded.

Results A total of 1,216 ECGs were correctly recorded. The differences of actual and synthesized at the J point, M point and T wave amplitude were very small. Means of the difference ± 2SD were V3R/V4R/V5R/V7/V8/V9: J point, 17 ± 1/14 ± 1/13 ± 1/12 ± 1/15 ± 1/18 ± 1 μV; M point, 15 ± 1/13 ± 1/12 ± 1/12 ± 1/12 ± 1/13 ± 1 μV; and T wave amplitude, 20 ± 3/32 ± 2/16 ± 2/37 ± 2/39 ± 2/43 ± 3 μV. There were positive correlations between all actual and synthesized ECGs of J point, M point and T wave amplitude (Figure 1).

Conclusion The ST part of synthesized V3R to V5R and V7 to V9 lead ECGs appears to be highly reliable. Synthesized additional lead ECGs might be useful to diagnose ischemic heart disease.

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P136

Aortic stiffness in patients with early sepsis

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Introduction Acute and chronic systemic inflammatory conditions are associated with aortic stiffening. Carotid–femoral pulse wave velocity (PWV), a marker of aortic stiffness, increases in patients with inflammatory diseases and independently correlates to levels of C-reactive protein (CRP). The effects of massive inflammatory response in early sepsis on mechanical properties of the aorta have not been investigated. The objective of the current study was to prospectively assess aortic stiffness in patients with early severe sepsis and septic shock and relate it to inflammatory and haemodynamic variables and outcome.

Methods We recruited patients meeting criteria for severe sepsis and septic shock within 24 hours of admission to ICU. After haemodynamic stabilisation, PWV was recorded at inclusion and after 48 hours using dual-channel plethysmography. Severity of illness was assessed with APACHE II and serial SOFA scores, haemodynamic and inflammatory parameters (CRP, procalcitonin and fibrinogen) recorded. A 28-day follow-up was performed to distinguish between survivors and nonsurvivors.

Results Twenty consecutive general ICU patients (six with severe sepsis and 14 with septic shock) were enrolled in the study; median age 59 years (IQR 56.5 to 72), APACHE II score 17 (13 to 20.5), SOFA score 5 (IQR 4 to 9). At 28 days, six patients had died. Median initial PWV was 10.4 (IQR 6.9 to 12.1) m/second in patients with severe sepsis, and 6.8 (IQR 5.3 to 7.5) m/second in patients with septic shock ($P = 0.13$). After 48 hours, PWV in the severe sepsis and septic shock groups had become similar, 9.3 (IQR 7.3 to 11.1) m/second and 9.2 (IQR 7.8 to 13) m/second respectively ($P = 0.96$). PWV had significantly increased in survivors (7.8 to 12.3 m/second) ($P = 0.04$) versus nonsurvivors (6 to 7.8 m/second) ($P = 0.69$). Higher PWV correlated with increasing systolic pressure and lower CRP levels ($r = 0.73$, $P = 0.01$).

Conclusion In early sepsis, aortic stiffness is decreased in patients with greater disease severity, and in survivors increases to median levels within 48 hours. The main factors associated with lower pulse wave velocity are lower systolic pressure and higher CRP levels. The association of high serum CRP levels with low aortic stiffness in patients with sepsis does not match data described in the literature [1].

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P137

Novel technology for non-invasive thoracic fluid measurement: an animal model comparative study

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Introduction Approximately 15 million people worldwide suffer from congestive heart failure (CHF). The most severe symptom of CHF is pulmonary congestion – an acute increase in extravascular lung fluid due to acute decompensation of heart failure. To date, no direct, reliable, simple and non-invasive method is available for assessment of thoracic fluids. Continuous dependable monitoring of pulmonary edema for hospital patients can improve management and reduce duration of hospitalization. KYMA's solution is based on a matchbox-sized monitoring device, which monitors thoracic fluid content and trends. The µCor monitor transmits and receives electromagnetic signals that are propagated through tissue layers. Conduction is highly related to the amount of accumulated fluids in tissues. This trial investigated the correlation between KYMA's lung water index (LWI) and directly assessed extravascular lung water (EVLW) in the scenario of acute pulmonary edema induced in seven sheep.
Methods Acute pulmonary edema was induced by intravenous infusion of noradrenaline and dextrane, with stepwise increased dosage. KYMA measurements of LWI were compared with PiCCO extravascular lung volume as the reference gold standard. The experiment continued until maximum increase of EVLW and complete heart failure were reached.
Results All seven sheep developed pulmonary edema, which was validated by increased LVEDP and EVLW. A linear correlation was found between invasive measurements of EVLW (PiCCO) and non-invasive KLWI.
Conclusion KYMA's fluid index demonstrated excellent correlation with invasive lung water measurement (R^2 = 0.96; P <0.0001) and was able to detect dynamic accumulation of EVLW in a range of 40 to 50 cm³ increments (Figure 1). Since the change in fluid content between a normal and congested lung ranges between 250 and 500 cm³, the demonstrated sensitivity as reflected in this study, supports its use for high-resolution and accurate thoracic fluid monitoring.

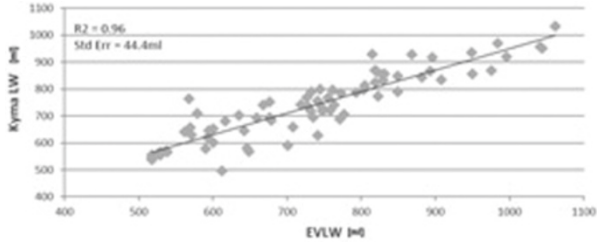

Figure 1 (abstract P137). Pooled correlation between EVLW and KYMA LWI.

P138

Adherence to the nurse-driven hemodynamic protocol during postoperative care

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Critical Care 2014, **18(Suppl 1):**P138 (doi: 10.1186/cc13328)

Introduction The aim of this work is to verify that low incidence of hemodynamic interventions in hemodynamically monitored patients in our postoperative ICU is not caused by insufficient attention being paid to the drop of noncalibrated cardiac index (nCI). In the last 2 years there was a need for hemodynamic intervention in 92% of patients with perioperative cardiac output monitoring, while only 31% of these patients needed at least one hemodynamic intervention postoperatively in the ICU.
Methods High-risk patients planned to undergo elective major abdominal surgery were routinely monitored with LiDCOrapid; the monitoring continues overnight after surgery. The target nCI for the postoperative monitoring, as well as hemodynamic interventions in case of its drop, were prescribed by the anesthetist in the protocol upon handover of the patient to the postoperative ICU. The hemodynamic protocol in the ICU was then nurse driven with compulsory recording of patient's hemodynamic data into the patient's documentation every 2 hours and at the time of each intervention. Data from the memory of the LiDCOrapid monitor were analyzed using LiDCOview software and compared with patients' documentation.
Results A total 649 hours of hemodynamic record were analyzed in 40 patients chosen at random from 121 patients monitored in the last 2 years. We found 22 drops in nCI that were noticed by the nursing staff and led to volume challenge in accordance with the protocol. One-half of these interventions was carried out outside the 2-hour interval of protocol-required monitoring and documentation entry. We identified nine drops in nCI that were not reacted to. None of them happened within the first 4 hours postoperatively and all of them were outside the 2-hour interval of protocol-required monitoring. In five of these episodes the pulse pressure also dropped, suggesting impairment of the reading of the waveform from the arterial line.
Conclusion The need for hemodynamic intervention in postoperative care was quite rare in our patients. The drop in nCI was noticed in most of the cases and the patient was treated according to the protocol. However, isolated episodes of nCI drop were missed during the night after the operation. The results were pointed out to the nursing staff and a comparative survey will be conducted. As with any monitoring modality, (non)adherence to the protocol may become the limiting issue to the benefit for the patient.

P139

Pulse wave transit time technique for perioperative non-invasive hemodynamic monitoring

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Critical Care 2014, **18(Suppl 1):**P139 (doi: 10.1186/cc13329)

Introduction The aim of this work is to evaluate perioperative hemodynamic monitoring for major abdominal surgery using the estimated continuous cardiac output (esCCO) technique available with the NIHON KOHDEN Vismo monitor as compared with the LiDCOrapid hemodynamic monitoring system.
Methods The esCCO technique is a novel noncalibrated non-invasive method of cardiac output monitoring. It is based on the estimation of pulse pressure from the speed of pulse wave propagation, which is measured as a time delay between the ECG R-wave and the corresponding peripheral pulse wave detected by pulse oximetry – the delay being called the pulse wave transit time (PWTT) [1]. LiDCOrapid estimates noncalibrated cardiac output (nCO) by pulse wave contour analysis from an arterial line and is a well-established monitoring modality in our department. The patients planned for elective major abdominal surgery with ASA score of III and expected operation duration over 90 minutes are routinely monitored by LiDCOrapid with a perioperative hemodynamic optimalization protocol. In accordance with the protocol, an arterial line was inserted and LiDCOrapid monitoring was started before the induction of anesthesia. At the same time, non-invasive esCCO monitoring was started.
Results Ten patients were monitored with a total of 141 esCCO–nCO measurement pairs. The correlation coefficient between esCCO and nCO was 0.65 and in the Bland–Altman difference analysis bias was +1.2 l/minute and 95% limits of agreement were ± 2.6 l/minute. The change of cardiac output between two consecutive measurements detected by LiDCOrapid was detected by esCCO in 80% of cases.
Conclusion Hemodynamic monitoring with esCCO yields cardiac output values different from those measured by LiDCOrapid. The reliability of PWTT is questionable when systemic vascular resistance

changes (as with any other noncalibrated cardiac output monitor), but it can still trace the trends of CO changes. Due to its non-invasiveness, esCCO might be the monitoring of choice for high-risk patients undergoing low-risk surgery.

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P140

Validation of cardiac output from Mostcare compared with a pulmonary artery catheter in septic patients

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Critical Care 2014, **18(Suppl 1):**P140 (doi: 10.1186/cc13330)

Introduction The Mostcare monitor is a non-invasive cardiac output monitor. It has been well validated in cardiac surgical patients but there is limited evidence on its use in patients with severe sepsis and septic shock [1].

Methods The first 22 consecutive patients with severe sepsis and septic shock in whom the floatation of a pulmonary artery catheter was deemed necessary to guide clinical management were included. Cardiac output measurements were simultaneously calculated and recorded from a thermodilution pulmonary artery catheter and from the Mostcare monitor respectively. The two methods of measuring cardiac output were compared by Bland–Altman statistics and linear regression analysis. A percentage error less than 30% was defined as acceptable for this study.

Results Bland–Altman analysis for cardiac output showed a bias of 0.31 l/minute, precision (=SD) of 1.97 l/minute and a percentage error of 62.54%. Linear regression produced a correlation coefficient r^2 for cardiac output of 0.403. See Figure 1.

Conclusion Compared with thermodilution cardiac output, cardiac output studies obtained from the Mostcare monitor have an unacceptably high error rate. The Mostcare monitor is not a reliable monitoring device to measure cardiac output in patients with severe sepsis and septic shock on an ICU.

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P141

Novel non-invasive technology for cardiac output determination

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Critical Care 2014, **18(Suppl 1):**P141 (doi: 10.1186/cc13331)

Introduction The aim of this animal study was to determine the feasibility and accuracy of a new non-invasive system for determination of cardiac output (CO) compared with a known device (PiCCO; Pulsion Medical). In ICUs and ORs, hemodynamic management using goal-directed therapy has been shown to improve patient outcomes [1,2]. The invasiveness of current technology may prevent clinicians from obtaining hemodynamic information. We developed a non-invasive system for detection of hemodynamic variables utilizing a photo-acoustic sensor (PA-S) and indicator dilution. The PA-S utilizes a combination of a miniature ultrasound sensor, a laser diode and an optical detector to accomplish the measurement.

Methods Five pigs weighing 25 to 29 kg were used in the study approved by the local animal use and care committee. The animals were anesthetized, medically paralyzed, intubated and mechanically ventilated. Central venous and arterial catheters were placed for injection of the indicator and connection to the PiCCO system. The PA-S was placed in contact with the skin over the saphenous artery on the animal and adjusted to receive the maximum acoustic signal. The adjustment included the depth of ultrasonic penetration and the exact location on top of the blood vessel. Each indicator dilution was accomplished using three central venous injections of 15 ml normal saline at room temperature. Variation in CO was accomplished by removing up to 50% of the blood volume after splenectomy. The PA-S results were obtained using the empirical regression method. The resulting cardiac output readings from the PA-S were compared with the PiCCO readings.

Results The correlation between the PA-S and the PiCCO system was (R^2 = 0.746) over a range of CO from 1 to 6 l/minute. The Bland–Altman analysis demonstrated a bias of –0.05 l/minute and precision of 0.50 l/minute.

Conclusion This animal study demonstrated the feasibility of the new PA-S for determination of indicator dilution CO in a limited range. The system showed good correlation with the PiCCO system even in the case of vasoconstriction as a result of blood loss. Since the PA-S utilizes transpulmonary indicator dilution, other variables such as intrathoracic blood volume, global end-diastolic volume and extravascular lung water can be calculated. Additionally, continuous CO can be obtained from the optical sensor signal utilizing arterial waveform analysis.

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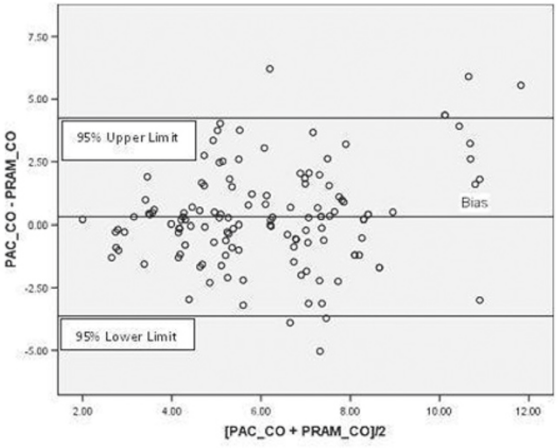

Figure1: Bland Altman plot for CO measurements
PAC_CO= Pulmonary artery catheter thermodilution derived cardiac output measurements
PRAM_CO= Mostcare derived cardiac output measurements
Mean Cardiac Output: 6.297L.min^{-1}
Bias: 0.306l.min^{-1}
Limits of agreement: 4.251L.min^{-1} to -3.634L.min^{-1}
Percentage error: 62.54%

Figure 1 (abstract P140). Cardiac output Bland–Altman analysis.

P142

Performance of pulse contour and pulse wave transit time-based continuous cardiac output analyses: clinical validation of two methods in Thai patients undergoing cardiac surgery

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Critical Care 2014, **18(Suppl 1):**P142 (doi: 10.1186/cc13332)

Introduction The aim was to evaluate the performance of arterial pressure-based cardiac output (APCO) [1] and pulse wave transit time-based cardiac output (esCCO) [2] monitors in Thai patients undergoing coronary artery bypass graft surgery (CABG) with cardiopulmonary bypass.
Methods We studied 50 Thai surgical patients undergoing CABG with cardiopulmonary bypass and requiring pulmonary artery catheter and radial artery catheter placement as a standard of clinical care. All patients were measured for APCO using the Vigileo/FloTrac and for esCCO using the esCCO monitoring system. The data were compared with thermodilution cardiac output (TDCO) monitoring as a reference method, simultaneously at pre-induction, post-induction, and every 30 minutes thereafter until the completion of the surgery. The bias and precision were assessed using Bland–Altman analysis.
Results In total, 310 pairs of simultaneous measurements of APCO versus TDCO and 303 pairs of esCCO versus TDCO were obtained from 50 patients. Both APCO ($R = 0.53$, $P < 0.0001$) and esCCO values ($R = 0.56$, $P < 0.0001$) were correlated with TDCO values. Either of the changes in APCO ($R = 0.63$, $P < 0.0001$) or any changes in esCCO ($R = 0.60$, $P < 0.0001$) were correlated with changes in TDCO. For APCO relative to TDCO, the bias, precision, and the limits of agreement were 0.70, 1.63, and −2.5 to 3.9 l/minute, while those of esCCO were 1.20, 1.59, and −1.9 to 4.3 l/minute, respectively. Comparisons of the bias of APCO and esCCO revealed a level of significance of $P < 0.001$.
Conclusion Despite the overestimation of cardiac output measurements, APCO and esCCO calibrated with patient information has shown an acceptable trend as compared with TDCO in Thai patients undergoing CABG with cardiopulmonary bypass. Compared with esCCO, APCO demonstrated no significant differences of precision; however, a lower mean bias was exhibited.

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P143

Comparison of PiCCO and VolumeView: simultaneous measurement in sepsis pig models

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Critical Care 2014, **18(Suppl 1):**P143 (doi: 10.1186/cc13333)

Introduction Transpulmonary thermodilution is useful in the critical care. Following PiCCO, VolumeView is now available. Although previous studies concluded that significant correlation was found between VolumeView and PiCCO [1,2], all experiments and data analysis were done by Edwards Lifescience. The aim of the present study was to compare the new VolumeView with PiCCO to clarify their compatibility and to give a neutral answer.
Methods Six pigs (about 10 kg) were used and we made sepsis models by LPS administration. All pigs were instrumented with a right (PulsioCath) and a left (VolumeView) thermomistor-tipped femoral arterial catheter. The central venous catheter was inserted through the right jugular vein. CO, GEDV and EVLW were measured by the two systems.
Results We performed measurements at 57 points. There was a good correlation between the two devices regarding CO and GEDV, but VolumeView showed higher GEDV than PiCCO. Regarding EVLW, there was no significant correlation between two systems. VolumeView showed significantly higher EVLW than PiCCO (Figure 1 and Table 1).

Table 1 (abstract P143). Explanation of abbreviations

	CO	GEDV	EVLW
PiCCO	PCO	PGEDV	PEVLW
VolumeView	ECO	EGEDV	EEVLW

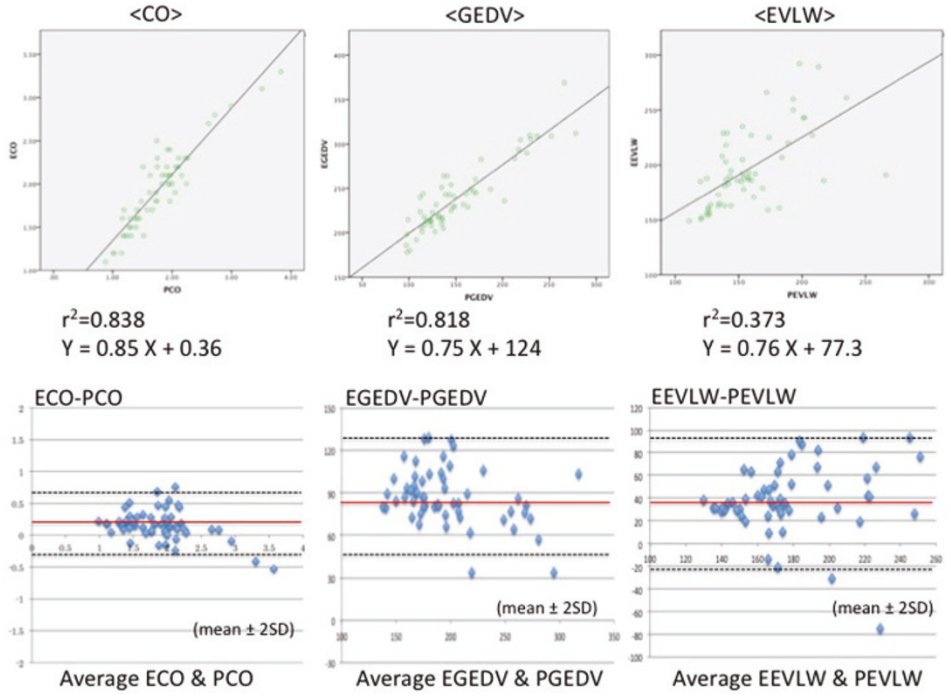

Figure 1 (abstract P143). CO, GEDV, EVLW correlation and Bland–Altman analysis.

Conclusion Our data analysis showed that PiCCO and VolumeView were not the same. Neither the normal values of two devices nor the rates of change were same. Careful attention should be paid to interpret the data obtained from two systems.

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P144

Effects of the restrictive fluid strategy on postoperative pulmonary and renal function following pulmonary resection surgery

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Critical Care 2014, **18(Suppl 1):**P144 (doi: 10.1186/cc13334)

Introduction Goal-directed therapy used in the perioperative period of patients undergoing cardiac surgery shortens the length of ICU stay [1]. We aimed to compare the postoperative results of the liberal and restrictive fluid strategy used in patients undergoing pulmonary resection surgery (PRC).

Methods We have been using the restrictive fluid strategy since March 2013 in our institute. Patients who were on the liberal fluid regime were analyzed retrospectively. From March 2013 until today, patients who were on restrictive fluid strategy were analyzed prospectively. A total of 125 patients were included in the study. Age, duration of anesthesia, type of fluids given intraoperatively, fluid index (ml/kg/hour), fluid intake/output balance, creatinine and lactate levels were compared with pulmonary and renal morbidity, and length of stay in ICU, using multivariate analysis.

Results A significant correlation (P <0.05) was established between the amount of crystalloid given intraoperatively, fluid index and fluid balance with pulmonary morbidity (n = 52). The fluid index and inotropes usage were correlated with the postoperative creatinine levels (P <0.05). There was no correlation between perioperative lactate levels with fluid balance and fluid index. Intraoperative blood loss, the amount of given crystalloid, colloid, blood and FFP, fluid balance, duration of anesthesia and postoperative blood transfusion were found to be related (P <0.05) with the length of ICU stay. Four percent of the patients required renal replacement therapy and the overall mortality was 0.8%.

Conclusion To reduce the morbidity of patients undergoing major surgery, the protocols of using the restrictive fluid strategy in the perioperative period and simultaneous protection of end organs, especially the kidneys, is currently the subject of this discussion. We observed that the restrictive fluid strategy did not lead to global organ hypoperfusion, which was monitored by lactate. Even though there was a negative correlation between the fluid index with creatinine levels and renal failure, the need for renal replacement therapy was observed only in one case. As a conclusion, the postoperative pulmonary morbidity and length of ICU stay can be reduced in patients who undergo PRC by using the restrictive fluid strategy (4.2 ± 0.3 ml/kg/hour), without causing any vital organ dysfunction.

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P145

Perioperative fluid balance and postoperative changes in serum creatinine in patients admitted to critical care after elective major surgery

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Introduction The rationale for perioperative fluid therapy has been to preserve organ perfusion. However, conservative postoperative fluid balance (FB) is now encouraged to avoid the effects of iatrogenic fluid overload. In addition, fluid expansion has been described as a confounder of acute kidney injury (AKI) diagnosis by dilution serum creatinine (SCr).

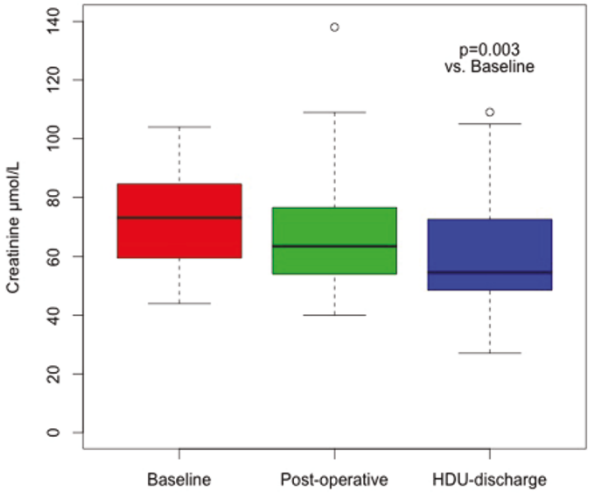

Figure 1 (abstract P145). Serum creatinine changes after major surgery.

Methods We conducted a prospective audit of FB and renal function in patients undergoing major elective surgery admitted to critical care over a 28-day period. Fluid overload was defined as: (positive FB) / (weight × 0.6) × 100%.

Results Thirty-two patients (56% female, median age 64) were studied over a median of 3 critical care days (range 1 to 7). Total FB was +3.9 l at discharge; however, 75% of this occurred intraoperatively so that positive FB in critical care was only +390 ml/day. Patients had median 9% fluid overload at discharge. Two patients had transient AKI stage 1. Overall SCr decreased significantly from preoperatively to discharge (P = 0.003), median 73 to 55 µmol/l, with decreases occurring both postoperatively and during critical care stay (Figure 1).

Conclusion We achieved near-neutral fluid balances after admission, but did not resolve intraoperative fluid accumulation. SCr fell significantly, even after there was no further net fluid accumulation. This suggests a decrease in creatinine generation after major surgery, rather than fluid expansion, may largely account for sCr decreases in these patients.

P146

Very limited usefulness of pulse pressure variation as a predictor of volume responsiveness in critically ill septic patients

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Critical Care 2014, **18(Suppl 1):**P146 (doi: 10.1186/cc13336)

Introduction The aims of the study are to assess the usefulness of pulse pressure variation (PPV) as a predictive marker of fluid responsiveness and to estimate the value of central venous–arterial difference of carbon dioxide (PCO_2cv-a) to predict the outcome of critically ill septic patients. The question of whether a septic patient needs fluids or not is crucial. Although PPV is a very reliable predictor of volume responsiveness, there are many limitations for its application. Cardiac arrhythmia, spontaneous breathing and low tidal volume ventilation prevent the extended use of this index.

Methods This is a *post-hoc* analysis of data from a prospective observational study [1], which included a population of patients with severe sepsis or septic shock as the main reason for ICU admittance. After an echo for the assessment of the cardiac systolic performance, we measured PPV, central venous oxygen saturation, blood gases from arterial and central venous lines, central venous pressure, systolic, diastolic, mean and pulse pressures, before and after volume challenge. We calculated changes in pulse pressure before and after volume challenge, and an increase of 9% was used as criterion to define volume responsiveness [2].

Results Among 72 patients (71% men, APACHE II score 23.2) included in this study, 41 (57%) were responders. Due to spontaneous breathing and cardiac arrhythmia we were able to calculate PPV only in 18 patients (25%). Moreover, only eight (11%) calculations of PPV proved useful because of the application of low tidal ventilation (4 to 6 ml/kg ideal body weight) in the remaining 10 patients. We did not find any value of the PCO_2cv-a to predict the outcome of the patients (mortality 26.3%), since the difference between survivors and nonsurvivors was not statistically significant (7.7 vs. 7.9, $P > 0.05$).
Conclusion The usefulness of PPV, the marker with the best performance in the prediction of volume responsiveness, due to its limitations, is very limited.
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P147

Effects of central hypovolemia induced by tilt table on the Doppler-based renal resistive index in healthy volunteers

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Critical Care 2014, **18(Suppl 1):**P147 (doi: 10.1186/cc13337)

Introduction The renal resistive index (RI) determined by Doppler ultrasonography allows a semiquantitative evaluation of kidney vasculature at the bedside. Interpretation of the RI in clinical practice is difficult due to interaction with cardiac output, heart rate (HR) and blood pressure [1,2]. The impact of global hemodynamics on the RI remains to be evaluated. This study aims to investigate the relationship between the RI and changes in central hemodynamic during a central hypovolemia model in healthy volunteers (HV).
Methods Eleven healthy volunteers (27 ± 8 years; eight male) participated in this study. Two different models were performed: the first model was performed by applying the head-up tilt (HUT) test. The complete maneuver was done by a 10-minute step that consisted of tilting the table from a supine position (Sup) to an angle of 70° (HUT) and back to supine (Sup'). The second model was performed by applying three consecutive valsalva maneuvers. Global hemodynamics included stroke volume (SV), HR, and mean arterial pressure, which were continuously measured non-invasively with a Finometer. At least three RI readings were obtained and averaged from the right and left kidneys in all HV.
Results All HV had a significant decrease of SV from 83 ± 17 ml to 63 ± 14 ml and an increase in HR from 67 ± 10 bpm to 88 ± 13 bpm during the HUT. Figure 1 shows the temporal changes of mean RI in both kidneys. A significant decrease in the RI in both kidneys was seen during HUT. After the move back to supine, RI returned to baseline values, with a significant variation of RI in the early measurements on the right kidney compared with late measurements on the left kidney (0.67 ± 0.05 vs. 0.61 ± 0.05, $P < 0.05$). Valsalva maneuvers significantly increased the RI in the right and left kidneys, from 0.6 ± 0.04 and 0.6 ± 0.05 to 0.7 ± 0.1 and 0.68 ± 0.15 ($P < 0.05$), respectively.
Conclusion These preliminary results showed that Doppler renal RI was affected equally in both kidneys during HUT, suggesting an effect of hemodynamic alterations during our model of central hypovolemia.
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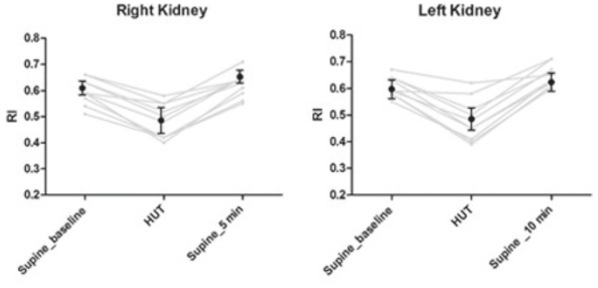

Figure 1 (abstract P147). Doppler-based renal resistive index in both kidneys during HUT.

P148

Tissue oxygenation as a target for goal-directed therapy in high-risk surgery

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Critical Care 2014, **18(Suppl 1):**P148 (doi: 10.1186/cc13338)

Introduction Tissue hypoxia occurs frequently during surgery and may contribute to postoperative organ dysfunction [1]. We hypothesised that intraoperative optimisation of tissue oxygenation reduces postoperative complications and evaluated the feasibility of the optimisation protocol used.
Methods We randomised 50 high-risk patients who underwent major abdominal surgery. Tissue oxygenation was monitored at the thenar eminence using near-infrared spectroscopy. All patients were treated according to a standard care algorithm. In addition, patients in the intervention group received dobutamine if necessary to keep tissue oxygenation ≥80%. Data were recorded continuously and complications were recorded during the hospital stay with a maximum of 28 days.
Results The number of complications tended to be lower in the intervention group (11 vs. 20). Eleven patients in the intervention group had no complication, versus seven in the control group. There was no significant difference between groups in length of stay in ICU or in hospital. Administration resulted in a 5% increase of tissue oxygenation. The cardiac index increased 0.3 (0.0 to 0.6) l/minute/m^2 (Figure 1). The overall protocol adherence was 94%.
Conclusion Intraoperative optimisation of tissue oxygenation will potentially result in better outcome after high-risk abdominal surgery. The protocol used may be considered feasible for clinical practice.
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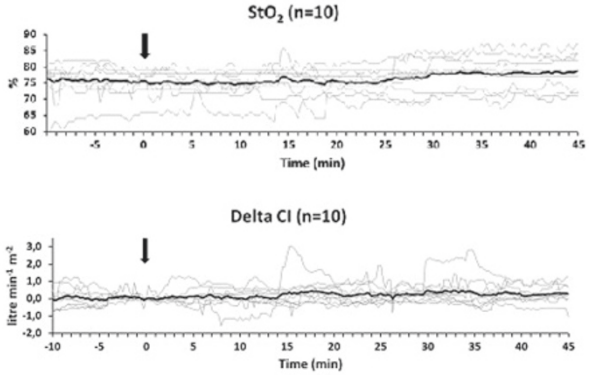

Figure 1 (abstract P148). Evolution of individual patient values (thin lines) and the average values (thick lines) of the tissue oxygenation (StO_2) and the relative change of cardiac index (CI), delta CI. All graphs are synchronised at the moment of the first dobutamine administration (time = 0; arrow). Values are shown from 10 minutes before dobutamine administration until 45 minutes after.

P149

Why measurements do (not) work: the human factor

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Critical Care 2014, **18(Suppl 1):**P149 (doi: 10.1186/cc13339)

Introduction Passive leg raising (PLR) has been suggested as a simple diagnostic tool to guide fluid administration in critically ill patients [1]. Although the basic principles of PLR have been well studied, little is known about the impact of the introduction of this technique in daily clinical practice. The aim of the study was to describe the changes in fluid balance of ICU patients before and after the introduction of PLR, and to determine the compliance of medical personnel with a PLR-driven protocol of fluid administration.
Methods In this single-centre prospective study, mixed ICU patients equipped with a PiCCO system received fluid therapy on the basis of PLR test results in the first 48 hours of treatment, after careful introduction of a new PLR-driven protocol. Exclusion criteria were increased abdominal pressure, fracture of leg or pelvis, deep vein thrombosis, head trauma and pregnancy. The control group existed of patients admitted to the ICU 1 year prior to the introduction of the protocol.
Results We included 21 patients in each group. There was no significant differences in the fluid balance between the control and study group after 24 hours (5.0 ± 2.9 l vs. 3.6 ± 2.7 l, $P = 0.11$) and 48 hours (5.7 ± 3.5 l vs. 4.8 ± 3.7 l, $P = 0.39$). However, compliance with the protocol was poor (56%). After 2/11 positive tests, fluid was not administered; and after 21/39 tests, fluid was administered despite a negative test result (Figure 1).

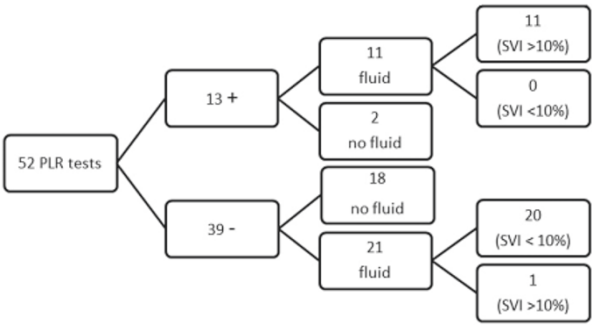

Figure 1 (abstract P149). SVI, stroke volume index; –, negative PLR; +, positive PLR; fluid 250 cm^3 RL solution.

Conclusion The implementation of a PLR-driven protocol of fluid administration did not change mean fluid balances after the first 48 hours. Noncompliance with the protocol was an important confounder.
Reference

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P150

Fluid responsiveness in septic shock

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Critical Care 2014, **18(Suppl 1):**P150 (doi: 10.1186/cc13340)

Introduction The correct assessment of volume status and prediction of response to filling fluid challenge is of crucial importance in the patient with septic shock. A patient is a fluid responder if there is an increase in cardiac index (CI) >15% in response to the fluid challenge. Identifying which patient will be a fluid responder is crucial. The aim of this prospective study is to evaluate which patient is a fluid responder in septic shock using dynamics echocardiography with the distensibility index of the inferior vena cava (DIIVC), which has been shown to be predictive of an increase in CI [1].
Methods In a period of 1 year, 42 adult patients were admitted to the ICU in septic shock. All patients were treated according to the guidelines of the Surviving Sepsis Campaign International Guidelines for Management of Severe Sepsis and Septic Shock 2012 [2]. All patients were mechanically ventilated and subjected to transesophageal echocardiography in bicavale projection, calculating the DIIVC through the M-mode by measuring the change in diameter with the acts of positive pressure ventilation and using the formula: (100 × (maximum diameter – minimum diameter)) / minimum diameter. A value >18% was considered a predictor of an increase in CI >15%. The CI was measured continuously through use of the pressure recording analytical method on a Mostcare Vytech monitor. All patients were subjected to a bolus of 500 ml crystalloid through a central venous catheter only after reaching central venous pressure (CVP) ≥10 mmHg during treatment. The results were expressed as the mean with standard deviation and percentage.
Results Sixteen patients (38%) had a change in DIIVC <18%, on average 11 ± 5%, and when subjected to fluid challenge did not have an increase in CI >15%, average 8 ± 3%, not proving to be a fluid responder. Twenty-six patients (62%) had a change in DIIVC >18%, on average 45 ± 22%, and when subjected to fluid challenge had an increase of the CI >15%, on average 31 ± 8%, proving to be a fluid responder.
Conclusion We have shown that the DIIVC can predict the response of patients to fluid challenge regardless of the values of CVP and then distinguish fluid responders from nonresponder patients. This can help us in the choice of treatment for patients in septic shock.
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P151

Use of pulse pressure variation and stroke volume variation in spontaneously breathing patients to assess dynamic arterial elastance and to predict arterial pressure response to fluid administration

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Introduction Dynamic arterial elastance (Eadyn), defined as the pulse pressure variation (PPV) to stroke volume variation (SVV) ratio, has been suggested as a predictor of the arterial pressure response to fluid administration. Rather than a steady-state assessment, Eadyn depicts the actual slope of the pressure–volume relationship providing a dynamic evaluation of the arterial load. So the higher the Eadyn value, the more likely arterial blood pressure is to improve after fluid challenge (FC). The aim of this study was to assess the effectiveness of Eadyn, measured non-invasively in preload-dependent, spontaneously breathing patients.
Methods Patients admitted postoperatively and monitored with the Nexfin monitor were enrolled in the study. Patients were included if they were spontaneously breathing and had an increase in cardiac output ≥10% after a FC. They were classified according to the increase in mean arterial pressure (MAP) after FC into MAP-responders (MAP increase ≥10%) and MAP-nonresponders (MAP increase <10%). Eadyn was calculated from the PPV and SVV values obtained from the monitor.
Results A total of 34 FCs from 26 patients were studied. Seventeen FCs (50%) induced a positive MAP response. Preinfusion Eadyn was significantly higher in MAP-responders (1.39 ± 0.41 vs. 0.85 ± 0.23; $P = 0.0001$) (Figure 1). Preinfusion Eadyn predicted a positive MAP response to FC with an area under the ROC curve of 0.92 ± 0.04 of SE (95% CI: 0.78 to 0.99; $P < 0.0001$). A preinfusion Eadyn value ≥1.06 (grey zone: 0.9 to 1.15) discriminated MAP-responders with a sensitivity and specificity of 88.2% (95% CI: 64 to 99%).
Conclusion Non-invasive dynamic arterial elastance, defined as the PPV to SVV ratio, predicted the arterial pressure increase to fluid administration in spontaneously, preload-dependent patients.

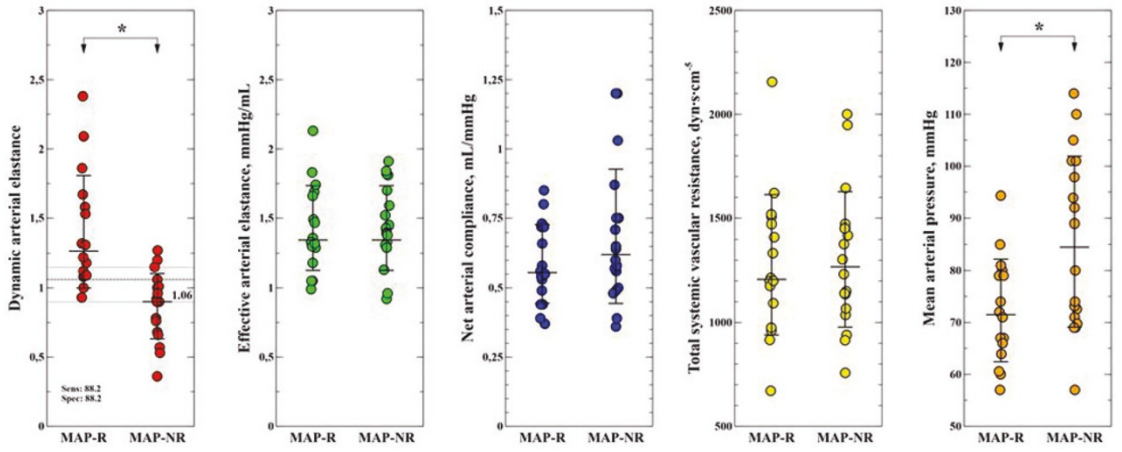

Figure 1 (abstract P151). Distribution of individual arterial load parameters at preinfusion time.

P152

Accuracy of the plethysmographic variation index as a predictor of fluid responsiveness after cardiac surgery

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Critical Care 2014, **18(Suppl 1):**P152 (doi: 10.1186/cc13342)

Introduction Recent studies showed that the plethysmographic variability index (PVI), a dynamic index resulting from cardiopulmonary interactions, could predict fluid responsiveness (FR) in mechanically ventilated patients during general anesthesia and in the ICU [1,2]. In this study, we aimed to compare, in patients after cardiac surgery, the clinical utility of the PVI versus traditional statics and dynamics indices to predict FR.
Methods We prospectively enrolled 52 consecutive adult patients in sinus rhythm and mechanically ventilated (tidal volume of 8 (7.5 to 8.5) ml/kg ideal body weight) admitted to the ICU of CHU de Charleroi (Belgium) after scheduled cardiac surgery. Before and after fluid challenge (FC), we measured: heart rate (HR), BP, PVI (Masimo Corporation, Irvine, CA, USA) and PPV. PAOP and cardiac index (CI) were estimated by Swan–Ganz catheter (Edwards Lifesciences LLC, Irvine, CA, USA). Patients with an increase in CI of at least 15% after FC and subsequently were considered responders (R). Continuous variables were analyzed with Mann–Whitney *U* tests. Categoric variables were analyzed with the Fisher's exact test. Correlations were assessed by Spearman's correlation. The discriminatory ability of each haemodynamic parameter to determine FR was assessed by area under the receiver operating characteristic curve (AUC), between R and nonresponders (NR). $P < 0.05$ was considered statistically significant.
Results Twenty-five (48%) patients were classified as R. Before FC, R and NR patients were comparable except for HR (91 (83 to 108) for R vs. 80 beats/minute (72 to 89) for NR; $P = 0.009$), PVI (18 (12 to 26) for R vs. 12% (9 to 15) for NR; $P = 0.003$), PAOP (8 (6 to 9) for R vs. 11 mmHg (8 to 12) for NR; $P = 0.001$), and PPV (13 (8 to 19) for R vs. 10% (4 to 13) for NR; $P = 0.086$). PVI and delta PP before FC were correlated ($r = 0.53$, $P < 0.0001$). AUC showed a better prediction of FR for PVI (AUC = 0.74, $P < 0.001$) than for PPV (AUC = 0.64, $P = 0.05$). Nevertheless, the sensitivity (Se) and specificity (Sp) of both indices were low: for a PPV over 13%, Se = 48% (0.301 to 0.665),and Sp = 82% (0.627 to 0.921); for a PVI over 12%, Se = 68% (0.482 to 0.828) and Sp = 69% (0.498 to 0.835). As for PAOP, increasing values are associated with NR (AUC = 0.22, $P < 0.0001$).
Conclusion The PVI appears to be useful to predict FR in mechanically ventilated patients after cardiac surgery. However, Se and Sp remain low in the type of patients with relative euvolemia and cardiac dysfunction.
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P153

Kinetics of volume expansion during a fluid challenge

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Critical Care 2014, **18(Suppl 1):**P153 (doi: 10.1186/cc13343)

Introduction According to Guyton and colleagues [1], expansion of blood volume can increase cardiac output (CO) in so far as the change in volume affects the mean systemic filling pressure (Pmsf). However, rapid stress relaxation occurs after acute intravascular volume expansion so that the effect of volume on Pmsf and CO may disappear after a few minutes. The objective of the present study is to describe the extent of the haemodynamic changes generated by a fluid challenge during 10 minutes on critically ill patients.
Methods Patients admitted to the ICU were monitored with a calibrated LiDCOplus (LiDCO, UK) and Navigator (Applied Physiology, Australia) to estimate Pmsf analogue (Pmsa). Then 250 ml Hartmann's solution or Volplex was infused over 5 minutes. Data were recorded automatically from baseline to 10 minutes after the end of fluid infusion. The time to maximum response and percentage change between baseline and last value of different haemodynamic parameters are also reported.
Results Sixty fluid challenges were studied in 34 patients, with a mean duration of 5.3 minutes (± 2.5). In 22 events (37%), CO increased more than 10% (responders). The change between baseline and last value was greater in nonresponders for heart efficiency (Eh) (–9.2% ± 9.7 vs. –3.1% ± 13.9, $P = 0.05$) but not in other haemodynamic variables. Time to maximal response on CO was 2 minutes after the end of the infusion (Figure 1).
Conclusion Stress relaxation damps down the effect of a fluid challenge after 10 minutes except in terms of heart efficiency. The effect of a fluid challenge should be assessed up to 2 minutes after the end of fluid infusion. Failure to do so may mislead clinicians about the patient's fluid responsiveness.

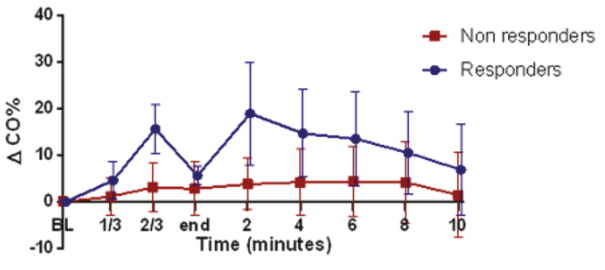

Figure 1 (abstract P153). Change of CO during and after a fluid challenge. BL, baseline; end, end of fluid infusion.

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P154

Fluid challenge with shock

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Critical Care 2014, **18(Suppl 1):**P154 (doi: 10.1186/cc13344)

Introduction The latest sepsis guideline has emphasized early resuscitative fluid management [1]. Early goal-directed therapy (EGDT) has been shown to improve 28-day mortality in recent studies [2,3]. This strategy was based on improving tissue perfusion and oxygenation in spite of other supportive and therapeutic measures. Technically and historically, central venous pressure (CVP) measurement is one of the most dependent methods to estimate fluid responsiveness and intravascular volume status on resuscitation. The Surviving Sepsis Campaign (SSC) guidelines recommended goal levels of CVP 8 to 12 mmHg in order to obtain appropriate tissue perfusion [1]. In this study, we objected to re-evaluate effectiveness of a fluid resuscitation strategy in sepsis, comparing the effect of patients' daily fluid balances (DFB) and CVP on patients' survival.
Methods Patient records (APACHE II, length of stay (LOS), CVP, DFB, vasopressor and ventilator needs) were retrospectively collaborated, and a randomly-assigned 100 (63 men and 37 women, age 64.2 ± 15.5 years) were statistically analyzed for survival function.
Results The mean APACHE II score was 23.6 ± 7.7, LOS was 9.7 ± 10.0 days, intubated period was 6.4 ± 8.6 days, vasopressor period was 4.7 ± 5.5 days, CVP was 10.5 ± 5.5 mmHg, DFB was 1,147.9 ± 1,157.6 ml, and 42 survived. Kaplan–Meier survival and COX regression analysis showed that CVP levels of 6 to 9 mmHg and DFB +800 to +900 ml, but not above, significantly predicted survival, and also shorter LOS, intubated days and lower vasopressor needs with earlier discharge possibility. On the other hand, over-increased DFB and CVP levels strictly correlated with longer LOS and higher mortality rates, and the first 24-hour mean fluid balance alone was surprisingly not predictive.
Conclusion Fluid resuscitation therapy is a double-edge-sword. (1) Despite lower volumes, higher volumes also increase mortality. (2) Overall, DFB seemed more important than the first 24-hour DFB.
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P155

In vivo effect of hydroxyethyl starch solution (HES 130/0.4) on different fibrinogen assays

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Introduction Previous *in vitro* studies have shown that photometric assays may overestimate fibrinogen levels after hemodilution with HES. The *in vivo* effect of HES on fibrinogen assays was therefore studied.
Methods Forty patients with intracranial tumor gave their consent to participate in this ethical approved study. Plasma fibrinogen levels were analyzed with ELISA, two photometric assays (Dade and Multifibren) and one mechanical (Hook). In addition, ROTEM FibTEM-MCF was analyzed.
Results Twenty-five of the 40 patients received 1 l HES. Mean reduction of hematocrit was 17%. ELISA was lower than Hook and Multifibren. The FibTEM relative decrease of 43% differed significantly from the other assays. See Figure 1.
Conclusion After *in vivo* hemodilution with HES, some assays overestimated fibrinogen levels. An overestimation of around 0.3 g/l may lead to undercorrection of fibrinogen in critical bleeding situations. The aggravated response on the FibTEM-MCF may better reflect HES effects on clot structure.

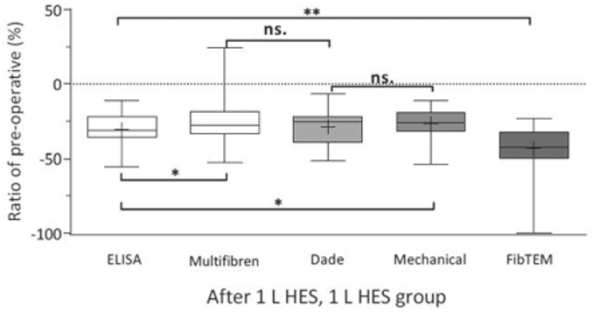

Figure 1 (abstract P155). Relative change of P-fibrinogen compared with preoperative values.

P156

BXL 628 ameliorates toxicity of lactated Ringer in HK-2 human renal proximal tubule cells in a hypovolemia mimicking model

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Introduction Lactated Ringer (L/R) for resuscitation of hemorrhagic shock is suggested by the ATLS program. However, prior studies showed that resuscitation with L/R was associated with more kidney damage in rats with severe hemorrhagic shock. The direct effects of L/R on human renal tubule cells have not been reported.
Methods Human proximal renal tubular cell line HK-2 was used. Viability was examined by MTT assay. An additional equal volume of phosphate-buffered saline (PBS) served as control. Addition of 200 nM dipyridyl and 1 mM H_2O_2 served as conditions of hypoxia and oxidative stress, respectively. Patterns of cell death were observed by flow cytometry.
Results To imitate early resuscitation in hypovolemic shock, medium was replaced with 40% v/v of L/R with dipyridyl plus H_2O_2 for 4 hours, followed by replacing with complete medium for 44 hours. In such

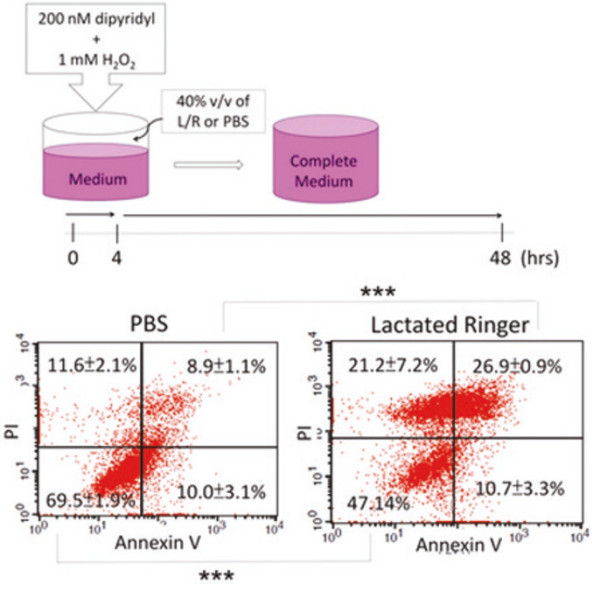

Figure 1 (abstract P156). Cell death of HK-2 cells after lactated Ringer administration in a hypovolemia mimic model.

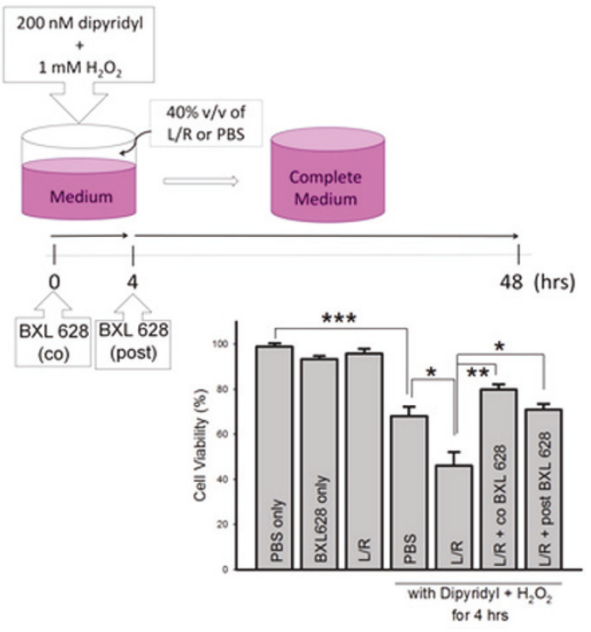

Figure 2 (abstract P156). Elocalcitol (BXL 628) ameliorates toxicity of lactated Ringer in HK-2 human renal tubule cells.

conditions, L/R augmented cytotoxicity, and more annexin V (+) cells were observed. Co-treatment or post-treatment with BXL 628, a novel VDR agonist, reversed L/R-induced cytotoxicity. See Figures 1 and 2.
Conclusion BXL 628 rescued L/R-induced apoptosis in human renal proximal tubule cells in a hypovolemia mimicking model.

P157

Hypotonic fluids after liver transplantation may be associated with prolonged ICU stay

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Critical Care 2014, **18(Suppl 1):**P157 (doi: 10.1186/cc13347)

Introduction Morbidity after liver transplantation has been linked with preoperative MELD scores and transfusion volumes [1]. We hypothesized that in the immediate post-transplant period there may be modifiable risk factors associated with prolonged ICU stays.
Methods In a retrospective, case–control study, we reviewed all liver transplant adult recipients over a 33-month period, January 2010 to September 2013. Recipients were divided into two groups based on *a priori* determined cutoff value of 8 days after transplantation. Significant associations for prolonged ICU admission were identified using chi-square analysis for categorical and ANOVA for continuous variables. P <0.05 was considered significant. SPSS version 22.0 was used for all analyses.
Results Total numbers of transplants performed were 162. Mean pre-transplant MELD score was 19.5 ± 7.7; viral hepatitis was the most common indication for transplant, 44 (27%). Living-related donor transplants were carried out in 87 (54%) cases. Median ICU length of stay was 4 ± 11.9 days and ICU mortality was 15 (9%). Acute kidney injury developed in 30 (19%) with 5% needing renal replacement therapy. Early complications developed in 33%. Prolonged ICU stay was related to: a higher pre-transplant INR (P = 0.000), larger volumes of RBC (2,064 ± 1,701 vs. 1,176 ± 1,454 ml, P = 0.000), platelets (453 ± 271 vs. 365 ± 276 ml, P = 0.046) and cryoprecipitate transfusions (47 ± 98 vs. 23 ± 85 ml, P = 0.037) received in the OR and mean volumes of hypotonic crystalloids administered in the first 24 hours (P = 0.002), 48 hours (P = 0.010) and 72 hours (P = 0.007) of ICU admission. Serum sodium, chloride, lactate or creatinine levels were not significantly different between the two groups.
Conclusion The administration of hypotonic fluids in the first 72 hours of liver transplantation may be a risk factor for prolonged ICU admission. This effect appears independent of serum electrolyte levels or renal dysfunction.
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P158

Early Vasopressin Application in Shock study

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Introduction Vasopressin is frequently used to maintain blood pressure in refractory septic shock [1]. This study is looking into the hypothesis that vasopressin compared with norepinephrine would decrease the severity of septic status, evolution to multiple organ dysfunction, length of hospitalization, and mortality among patients with septic shock.
Methods In this randomized, double-blind study, we assigned patients who still needed vasopressor to restore tissue perfusion after fluid resuscitation to receive norepinephrine (0.05 to 2.0 µg/kg/minute) or vasopressin (0.01 to 0.03 U/minute) with low doses of norepinephrine. Both groups had the vasoactive drug infusions titrated and tapered to maintain a target mean blood pressure. The analysis included the total time of use and dosage of vasopressors every 6 hours, the move to single organ dysfunction and multiple organ failure, length of ICU stay and hospitalization, and mortality 7, 14 and 28 days after the start of infusions.
Results A total of 407 patients underwent randomization but 387 patients were included in this study (191 patients received vasopressin, and 196 received norepinephrine only). The total time for vasopressors was 37 hours and 68 hours in the vasopressin and norepinephrine groups with P = 0.02. Single organ dysfunction and multiple organ dysfunction using vasopressin and norepinephrine were respectively: 37.7% vs. 49.2%, P = 0.02; and 17.8% vs. 26%; P = 0.05. Length of stay in the ICU was 14 and 17 days (P = 0.29) and the time of hospitalization was 23 and 28 days (P = 0.11) respectively. There was a significant difference between the vasopressin and norepinephrine groups in the mortality rate at 14 and 28 days (29.3% vs. 36.7%, P = 0.05; 34% and 42.3%, P = 0.03), but there were no significant differences in the overall rates for 7-day mortality (21.2% vs. 23.9%, respectively; P = 1.1).
Conclusion Early application of vasopressin reduced the time of vasopressor use, progression to multiple organ dysfunction, length of stay in the ICU, and mortality rates at 14 and 28 days as compared with norepinephrine only. This observed difference can be attributed to early restoration of tissue perfusion in the control group making the state of septic shock shorter and reducing the potential for multiple organ dysfunction, which directly influenced patient survival.
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P159

Terlipressin-induced hyponatraemia

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Critical Care 2014, **18(Suppl 1):**P159 (doi: 10.1186/cc13349)

Introduction Terlipressin is a vasopressin (V1 receptor) agonist that causes splanchnic constriction and is used in the management of variceal bleeding. This case report demonstrates the profound hyponatraemia, sufficient to cause a fall in conscious level, developing following terlipressin administration for variceal gastrointestinal bleeding.

Methods A 28-year-old man was admitted to the ICU following intubation and sedation for seizures due to acute alcohol withdrawal. A CT scan of the brain was normal. In the ICU the patient became haemodynamically unstable and fresh blood was aspirated from the nasogastric tube. Gastroscopy showed bleeding oesphageal varicies and hypertensive portal gastropathy. The patient was treated with variceal banding, tazobactam/pipacillin (4.5 g three times daily) and terlipressin (2 g four times daily) as per protocol for variceal bleeding. He was successfully extubated 48 hours later.
Results On admission the patient's serum sodium was 139 mmol/l. The patient received terlipressin for 4 days in the following regimen: 2 g four times daily for 48 hours, then 1 mg four times daily for 24 hours and then 0.5 mg four times daily for a further 24 hours before stopping. On the last day of his terlipressin therapy, the patient's GCS dropped from 15 to 11. Serum sodium had fallen acutely to 116 mmol/l. The last two doses of terlipressin were cancelled and no other treatment for hyponatraemia was administered. His serum sodium and GCS returned to normal limits within 13 hours of terlipressin cessation with no neurological consequences.
Conclusion There are few case reports of terlipressin-induced hyponatraemia [1]. Hyponatraemia is considered a rare side effect brought about by the partial agonist effect of terlipressin on renal vasopressin V2 receptors. Sola and colleagues monitored serum sodium concentrations in patients with acute variceal bleeding. They found that rapid reduction in serum sodium was common (up to 36%) and one patient developed osmotic demyelination syndrome. Hyponatraemia resolved on cessation of terlipressin [2]. Close monitoring of serum sodium levels is essential in patients on terlipressin therapy so rapid drops in sodium can be identified and managed to stop associated neurological complications.
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P160

Angiotensin II may be useful for the treatment of hypotension in distributive shock, but a safe and efficacious dose is unknown

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Critical Care 2014, **18(Suppl 1):**P160 (doi: 10.1186/cc13350)

Introduction Patients with distributive shock who require high-dose vasopressors have a high mortality. Vasopressors belong to two classes: catecholamines and vasopressin analogs. Each class has limitations. Patients receiving catecholamines often develop tachyphylaxis and metabolic complications (for example, lactic acidosis). Vasopressin analogs can cause mesenteric or myocardial ischemia and oliguria. Angiotensin II (ATII) is an endogenous peptide that increases blood pressure and aldosterone production. Preclinical data suggest a role for ATII in the treatment of sepsis-associated acute kidney injury. ATII may prove useful in patients who remain hypotensive despite catecholamine and vasopressin therapy. This is the first randomized clinical trial to date which seeks to evaluate ATII for use in distributive shock.
Methods Twenty patients with distributive shock and a cardiovascular Sequential Organ Failure Assessment score ≥4 were randomized to either ATII infusion (n = 10) or placebo (n = 10) plus standard of care. ATII was started at a dose of 20 ng/kg/minute, and titrated per a protocolized schedule for a goal of maintaining a mean arterial pressure (MAP) of 65 mmHg. The infusion (either ATII or placebo) was continued for 6 hours and then titrated off. The primary endpoint was the effect of ATII on the standing dose of norepinephrine required to maintain a MAP of 65 mmHg. Secondary endpoints included the effect of ATII on urine output, serum lactate and creatinine clearance, as well as 30-day mortality.
Results The mean age was 62.9 ± 15.8 years. Of the patients, 75% were male, 45% were Caucasian and 40% were African American. The 30-day mortality for the two groups were similar for the ATII cohort and the placebo cohort (50% vs. 60%, P = 1.00). ATII resulted in marked reduction in norepinephrine dosing in all patients. The mean norepinephrine dose for the placebo cohort was 20.1 ± 16.8 μg/minute vs. 7.3 ± 11.9 μg/minute for the ATII cohort (P = 0.022). The most common adverse event was hypertension, which occurred in 20% of patients receiving ATII.
Conclusion ATII is an effective vasopressor agent in patients with distributive shock requiring multiple vasopressors. The initial dose range of ATII that appears to be appropriate for patients with distributive shock is 2 to 10 ng/kg/minute. Further studies to assess the use of ATII in patients with distributive shock are warranted.

P161

Vasopressin versus norepinephrine for the management of septic shock in cancer patients

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Introduction Patients with septic shock die mainly due to refractory shock. Vasopressin is commonly used as an adjunct to catecholamines to support blood pressure in refractory septic shock, but its effect on mortality is unknown. We hypothesized that vasopressin as compared with norepinephrine would decrease mortality among cancer patients with septic shock.
Methods In this, randomized, double-blind trial, we assigned patients who had cancer and septic shock and needed a vasopressor to receive norepinephrine or vasopressin in addition to open-label vasopressors. All vasopressor infusions were titrated and tapered according to protocols to maintain a target blood pressure. The primary endpoint was the mortality rate 28 days after the start of infusions.
Results A total of 107 patients underwent randomization in this first part of trial, and were infused with the study drug (53 patients received vasopressin, and 54 norepinephrine), and were included in the analysis. There was no significant difference between the vasopressin and norepinephrine groups in the 28-day mortality rate (67.9 and 58.5%, respectively; P = 0.31). There were no significant differences in the overall rates of serious adverse events (5.3% and 5.5%, respectively; P = 1.00).
Conclusion Vasopressin did not reduce mortality rates as compared with norepinephrine among patients with cancer and septic shock who were treated with catecholamine vasopressors.
Acknowledgement Clinical Trials number: NCT 01718613.

P162

Heart rate reduction with esmolol in septic shock: effects on myocardial performance

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Critical Care 2014, **18(Suppl 1):**P162 (doi: 10.1186/cc13352)

Introduction Clinical study suggests that beta-blockers, by decreasing the heart rate (HR) together with an increase in stroke volume (SV), do not negatively affect cardiac output (CO), allowing an economization of cardiac work and oxygen consumption in patients with septic shock [1]. Whether this hemodynamic profile leads to an amelioration of myocardial performance is still unclear. The objective of the present study was therefore to elucidate whether a reduction in HR with esmolol is associated with an improvement of cardiac efficiency in patients with septic shock who remained tachycardic after hemodynamic optimization.
Methods After 24 to 36 hours of initial hemodynamic stabilization, 24 septic shock patients with HR >95 bpm and requiring norepinephrine (NE) to maintain mean arterial pressure (MAP) between 65 and 75 mmHg

despite adequate volume resuscitation received a continuous esmolol infusion to maintain the HR between 94 and 80 bpm. NE was titrated to achieve a MAP between 65 and 75 mmHg. To investigate myocardial performance, we simultaneously assessed LV ejection fraction (LVEF), tricuspidal annular plane solid excursion (TAPSE) by echocardiography, the dP/dt MAX and the cardiac cycle efficiency (CCE) both estimated from the arterial pressure waveform. Data were obtained at baseline and after achieving the predefined HR threshold (T1).

Results For a MAP between 65 and 75 mmHg, esmolol administration significantly decreased HR (115 ± 10 to 91 ± 7 bpm), NE (0.7 ± 0.4 to 0.5 ± 0.3 μg/kg/minute), and dP/dt MAX (1.1 ± 0.3 to 0.8 ± 0.3 ms/mmHg). Conversely, TAPSE (15 ± 3 to 20 ± 3 mm), CCE (–0.2 ± 0.4 to –0.03 ± 0.4 units) and SV (37 ± 8 to 42 ± 10 ml) significantly increased at the end of the study period (all P <0.05). CO (4.1 ± 0.8 to 3.9 ± 0.8 l/minute) and LVEF (46 ± 10 to 48 ± 10%) did not change.

Conclusion In patients with established septic shock who remained tachycardic after hemodynamic optimization, titration of esmolol to reduce the HR to a predefined threshold economized cardiac function, resulting in a maintained CO with a lower HR and a higher stroke volume. Such a hemodynamic profile was characterized by an improved cardiac efficiency, as indicated by the decrease in dP/dt MAX associated with an increase in CCE. Finally, echocardiographic data suggest that reducing HR with esmolol positively affects right ventricular function.

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P163

A new automatic urinometer shows lower bias, no loss of precision due to temporal deviation and higher user evaluation when compared with a manual standard urinometer in an ICU setting

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Critical Care 2014, **18(Suppl 1):**P163 (doi: 10.1186/cc13353)

Introduction In the intensive care setting, most physiologic parameters are monitored automatically. However, urine output (UO) is still monitored hourly by manually handled urinometers. This study evaluated an automatic urinometer (AU) and compared it with a manual urinometer (MU).

Methods This was a prospective study in the ICU of a cardio-thoracic surgical clinic. In postoperative patients (n = 36) with indwelling urinary catheters and an expected stay of 24 hours or more, hourly UO samples were measured with an AU (n = 220, Sippi®; Observe Medical, Gothenburg, Sweden) or a MU (n = 188, UnoMeter™ 500; Unomedical a/s, Birkeroed, Denmark), and thereafter validated by cylinder measurements. Malposition of instrument at reading excluded measurement. Data were analyzed with the Bland–Altman method. The performance of the MU was used as minimum criteria of acceptance when the AU was evaluated. The loss of precision with the MU due to temporal deviation from fixed hourly measurements was recorded (n = 108). A questionnaire, filled out by the ward staff (n = 28), evaluated the ease of use of the AU compared with the MU.

Results Analysis according to Bland–Altman showed a smaller mean bias for the AU, +1.9 ml, compared with the MU, +5.3 ml (P <0.001). There was no statistical difference in measurement precision between the two urinometers, defined by their limits of agreement (±15.2 ml vs. ±16.6 ml, P = 0.11). The mean temporal variation with the MU was ±7.4 minutes (±12.4%), limits of agreement ±23.9 minutes (±39.8%), compared with no temporal variation with the AU (P <0.001). A total 86% of the ward staff considered the AU superior to the MU (P <0.001).

Conclusion The AU had a significantly lower bias than the MU and the loss of precision of hourly UO due to temporal deviations using the MU was avoided with the AU. The AU was also evaluated higher by the ward staff, reflecting perception of higher reliability, easier use, less contact with urine bags and less time usage for measurements. The features of the AU may also indicate a favorable clinical impact in the normal ward, when staffing does not allow hourly measurements with a MU.

P164

Haemodynamic effects of phenylephrine commenced prior to induction of anaesthesia in older patients undergoing high-risk vascular surgery

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Introduction Fall in mean arterial blood pressure (MAP) during anaesthetic induction is common and may result in profound hypotension. Using the LiDCORapid (LiDCO Ltd, UK), we previously demonstrated that the fall in MAP is usually driven by a reduction in stroke volume (SV) that was presumed due to venodilation. Low-dose phenylephrine (PE), a venoconstrictor, commenced immediately prior to induction ameliorated these effects to a significant degree [1]. However, it is important that the pre-induction administration of PE should not cause any marked changes in MAP and CO. We retrospectively studied a group of 40 high-risk patients about to undergo major peripheral vascular surgery where PE was commenced immediately pre-induction. The haemodynamic effects of this dose of PE on MAP, SV and CO were analysed.

Methods A radial artery line was inserted prior to induction of anaesthesia, and baseline MAP, CO and SV were obtained using the LiDCORapid. The PE infusion was commenced at a rate of 1 to 2 mg/hour. Remifentanil was then administered using a target-controlled infusion pump until a 2 ng/ml predicted effect site concentration (Ceff) was reached. Propofol was then administered to induce anaesthesia. Haemodynamic changes from the pre-PE baseline to commencement of propofol were recorded at 5-second intervals. The changes in MAP, SV and CO were assessed as the percent change in values obtained immediately prior to PE and followed for at least 5 minutes until commencement of propofol.

Results Patient demographics, mean (range): age 71 (46 to 89) years, 31 male, weight 80 (55 to 115) kg, ASA 3 (2 to 4). The changes in MAP and CO were not clinically or statistically significant. MAP increased by an average of only 2%, range –25 to +12; CO by 0%, range –23 to +16 (P = 0.35 and P = 0.36 respectively).

Conclusion In a previous study [1], PE administered prospectively prior to induction markedly reduced the haemodynamic changes following induction of anaesthesia in high-risk patients using remifentanil and propofol. This effect was achieved without significant changes in MAP and CO in the 5-minute to 10-minute period between commencement of PE and induction of anaesthesia.

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P165

Acetaminophen-induced hypotension in the surgical ICU

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Introduction Acetaminophen (APAP) is commonly administered in the surgical ICU (SICU) for its analgesic and antipyretic effects. Case reports have described the potential for APAP to cause allergic reactions with and without hypotension. Furthermore, there have been case reports of APAP causing isolated hypotension in the absence of other allergic responses [1]. This has been well described following intravenous administration [2]. However, other routes of administration causing hypotension and associated diagnoses remain to be elucidated. The present case series describes 11 patients with APAP-induced hypotension in the SICU at a Level I trauma center.

Methods Patients admitted to the SICU over a 7-month time frame who were reported by the nursing staff to have experienced hypotension following the oral or rectal administration of APAP were included. Their electronic medical records were retrospectively reviewed to describe the change in systolic blood pressure (SBP) and mean arterial pressure (MAP) within the first hour following all administrations of APAP. Additional data collected consisted of patient age, sex, admission diagnoses and formulation/route of APAP administration.
Results Of the 11 patients included, six had spontaneous intracranial hemorrhage (ICH), four had traumatic ICH and one was free of neurologic injury. Following administration of 393 doses of APAP, the average change in MAP for all patients was –7.52 mmHg and SBP was –12.04 mmHg. When evaluated on an individual basis, patients with ICH had an average change in MAP of –10.64 (–5.2 to –19.08) and SBP of –17.81 (–7.54 to –35.75). The patient without neurologic injury had an average change in MAP and SBP of –3.01 and –2.42. The average change in MAP and SBP following administration of oral APAP solution (n = 357) was –7.84 and –12.39 while the change following rectal administration (n = 3) was –4.22 and –8 and tablet administration (n = 33) was –4.4 and –8.61.
Conclusion It appears from this small case series that patients with ICH may experience more isolated hypotension following administration of APAP when compared with others. These changes seemed to be greater than previously reported for intravenous administration. It may also be possible that APAP solution exudes hypotensive effects more commonly when compared with tablet or rectal formulations.
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P166

Experiences of a tertiary center with use of extracorporeal membrane oxygenation support in patients with cardiogenic shock after cardiac surgery

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Introduction Profound myocardial depression can occur after cardiac surgery. Use of ventricular assist support through venoarterial extracorporeal membrane oxygenation (ECMO) has been positively reported. This study will focus on the outcomes of patients who, upon suffering hemodynamic failure after cardiac surgery, were supported by the use of ECMO during their stay in the surgical ICU of Incor FMUSP.
Methods This was a retrospective, single-center and observational study. The records of 48 patients who underwent cardiac surgery and, subsequently, needed percutaneous or surgical implantation of ventricular assist devices were evaluated. The evaluation considered the following criteria: basal characteristics, indications for ventricular assistance, duration, length of ICU and hospital stay, and hospital mortality, through data collection forms.
Results Of the 48 patients included on the study, 26 (54%) were males, and 31 (64%) were younger than 18 years old. These patients developed cardiogenic shock during 72 hours after cardiac surgery. In all cases, ECMO was inserted after cardiac surgery. Of all patients, 32 (66%) were central ECMO, inserted in the operative room, and 16 were percutaneous, inserted in the ICU. The median duration of ventricular assistance was 6 days (IQR 0 to 41), the length of ICU stay was 16 days (IQR 1 to 111), and hospital stay was 29 days (IQR 1 to 198). Twenty patients survived (41%) and were discharged from our hospital.
Conclusion The use of mechanical circulatory assists devices is an efficient tool to manage seriously ill patients after cardiac surgery. This tool should be considered early in the diagnosis of cardiogenic shock after cardiac surgery.

P167

Potential use of veno-arterial extracorporeal membrane oxygenation for cardiogenic shock refractory to mechanical assist devices: baseline physiology and mortality data

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Introduction Mortality from cardiogenic shock remains high [1] and, despite a physiological rationale, intra-aortic balloon counterpulsation (IABP) has recently been shown to be ineffective in reducing mortality [2,3]. Veno-arterial extracorporeal membrane oxygenation (V-A ECMO) may offer a survival advantage over IABP. The objective of this study was to describe the characteristics and outcomes of patients supported with IABP or Impella and to identify the characteristics of patients who die, despite mechanical assistance, for whom a proposed V-A ECMO programme may be beneficial.
Methods A retrospective cohort study in a 30-bed, medical–surgical ICU. All adult patients supported with IABP or Impella over 2 years to March 2013 were identified and data were extracted by case-note review. Subgroup analysis was carried out for patients aged ≤65 and for those who fulfilled the modified Melbourne criteria for V-A ECMO [4]. Data collected included demographic data, physiology and organ support at baseline and at 6, 12, and 24 hours, ICU and hospital outcomes and cause of death. Comparisons between survivors and nonsurvivors were made with *t* test/chi-squared tests as appropriate.
Results A total of 129 patients were identified: 78% were male, mean age was 70 years (SD ±11.8), mean APACHE II score was 20 (±5) and ICU mortality was 44%. Comparing survivors with nonsurvivors the only statistically significant difference was metabolic acidosis (–6.8 ± 5.3 vs. –10.9 ± 7.0 mEq/l; P <0.05). Heart rate, mean arterial pressure, lactate, central venous oxygen saturation, cardiac index, arterial blood pH and mechanical ventilation failed to show a significant difference. Eleven of these patients would have fulfilled the proposed criteria for V-A ECMO, with an ICU mortality of 36%.
Conclusion Only metabolic acidosis was associated with mortality in patients supported with mechanical assist devices. Our data do not allow discrimination of survivors from nonsurvivors. Patients who fulfilled the proposed criteria for V-A ECMO showed a similar mortality to a recent series treated with V-A ECMO [4]. The proposed criteria do not identify a cohort, in this population, that would expect a mortality benefit from V-A ECMO.
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P168

Normobaric oxygen paradox and the microcirculation in the critically ill patient: a prospective observational study

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Introduction The normobaric oxygen paradox (NOP) is a recent concept that postulates the use of intermittent hyperoxia to stimulate erythropoietin (EPO) production [1]. Hyperoxia increases oxygen free radicals and may lead to endothelial damage and vasoconstriction [2]. We evaluated the microvascular response to transient hyperoxia and its effects on EPO production.
Methods Six patients with hemodynamic stability and mechanically ventilated with FiO_2 <50% were included in this prospective observational study. Patients underwent a 2-hour period of hyperoxia (FiO_2 100%). The sublingual microcirculation (sidestream dark-field imaging (SDF)) was evaluated at baseline (t0), 2 hours after hyperoxia (t1), and 2 hours after return to basal FiO_2 (t2). SDF monitoring was continuously performed also during the variation of FiO_2 for 2 minutes. EPO levels were assayed at baseline and for 2 days.

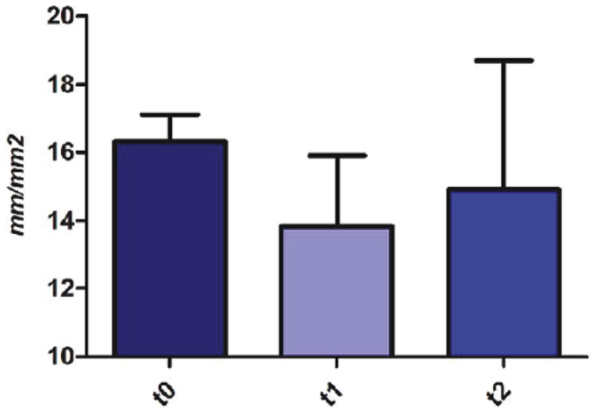

Figure 1 (abstract P168). TVD and NOP.

Results An early vasoconstriction and a trend towards total vessel density (TVD) reduction were observed at t1 (Figure 1). The TVD tended to increase without returning to baseline levels at t2. EPO increased in four patients out of 6 (P = NS). A negative correlation was found between the change in TVD after hyperoxia (t1 – t0) and the change in EPO (r = –0.88, P = 0.03).
Conclusion Hyperoxia leads to vasoconstriction that seems to be reversible at hyperoxia cessation. Further data are needed to verify the efficacy of the NOP in stimulating erythropoiesis in the critically ill. There might be a relation between hyperoxia-induced reduction in vessel density and the EPO increase.
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P169

Predictive criteria for the development of intra-abdominal hypertension and abdominal compartment syndrome

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Introduction This study aims to develop predictive criteria to identify which patients are at risk of developing intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) upon admission to the ICU.
Methods This is a prospective, observational study of 403 consecutively admitted ICU patients in a 3-month period, requiring the insertion of an indwelling urinary catheter. Intra-abdominal pressure was measured at least twice daily in all patients.
Results Thirty-nine and 2% of patients developed IAH and ACS as per consensus definitions. Upon ICU admission, patients that would go on to develop IAH had a significantly higher APACHE III score (62 (44 to 81) vs. 50 (37 to 68); P <0.001), abbreviated SOFA score (6 (4 to 8) vs. 4 (2 to 6); P <0.001), CVP (17 (13 to 20) vs. 15 (12 to 17) mmHg; P <0.001), lactate (2.2 (1.4 to 3.8) vs. 1.5 (1.1 to 2.4) mmol/l; P <0.001), INR (1.3 (1.1 to 1.5) vs. 1.2 (1.1 to 1.3); P <0.001), bilirubin (11 (7 to 19) vs. 10 (6 to 15) µmol/l; P = 0.027), creatinine (108 (76.8 to 175) vs. 84.0 (66.0 to 118) µmol/l; P <0.001), 24-hour fluid balance (2.47 (0.95 to 4.05) vs. 1.23 (0.29 to 2.27) l; P <0.001), vasopressor requirement (60 vs. 39%; P <0.001), mechanical ventilation requirement (71 vs. 58%; P = 0.011), PEEP (8.00 (5.00 to 10.00) vs. 5.50 (5.00 to 8.00) cmH_2O; P <0.001), and peak airway pressure (24 (21 to 30) vs. 22 (19 to 24) cmH_2O; P <0.001). These patients also had a significantly lower abdominal perfusion pressure (61 (55 to 71) vs. 69 (60 to 77) mmHg; P <0.001), pH (7.29 (7.22 to 7.35) vs. 7.33 (7.28 to 7.37); P <0.001) and PaO_2:FiO_2 ratio (182 (100 to 263) vs. (264 (168 to 371); P <0.001) upon ICU admission. Abdominal distension (odds ratio, 4.95; 95% CI, 1.19 to 7.24; P <0.001), hemoperitoneum/pneumoperitoneum/intraperitoneal fluid collection (odds ratio, 3.61; 95% CI, 1.29 to 10.12; P = 0.014), obesity (odds ratio, 3.41; 95% CI 1.97 to 5.90; P <0.001), fluid received >2.3 l (odds ratio, 2.68; 95% CI, 1.48 to 4.84; P = 0.001), abbreviated SOFA score >4 points (odds ratio, 2.49; 95% CI, 1.49 to 4.15; P <0.001) and lactate >1.4 mmol/l (odds ratio, 2.28; 95% CI, 1.33 to 3.91; P <0.001) were identified as independent predictors of IAH upon admission to ICU. The presence of three or more of these risk factors at admission predicted the onset of IAH with sensitivity of 75% and a specificity of 76%, and the onset of grade II, III and IV IAH with a sensitivity of 91% and a specificity of 62%.
Conclusion IAH is a common clinical entity in the intensive care setting. Predictive criteria, based on data readily available upon a patient's admission to ICU, were developed and effectively predicted the risk of developing IAH.

P170

Early lactate-guided therapy in cardiac surgery patients: a randomized controlled trial

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Introduction It is unknown whether lactate monitoring aimed to decrease levels during the first hours in patients undergoing cardiac surgery improves outcome. The aim of this study was to evaluate the effect of lactate monitoring and resuscitation directed at decreasing lactate levels in patients admitted to the ICU in the first 8 hours with lactate level ≥3.0 mEq/l.
Methods Patients were randomly allocated to two groups. In the lactate group, treatment was guided by lactate levels with the objective to decrease lactate by 20% or more per 2 hours for the initial 8 hours of ICU stay. In the control group, the treatment team had no knowledge of lactate levels (except for the admission value) during this period. The primary outcome measure was the incidence of complications in 28 days.
Results The lactate group received more fluids and dobutamine. However, there were no significant differences in lactate levels between the groups. The rate of complications was similar between groups (11% vs. 7%, P = 0.087). Length of ICU stay was higher in the lactate group (3.5 vs. 2.4 days, P = 0.047) when compared with the control group.
Conclusion In patients with hyperlactatemia on ICU admission, lactate-guided therapy did not reduce complications and was related to a longer ICU length of stay. This study suggests that goal-directed therapy aiming to decrease initial lactate levels does not result in clinical benefit.

P171

Lactate as a predictor of deterioration in emergency department patients with and without infection

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Introduction The use of serum lactate level to risk-stratify emergency department (ED) patients with sepsis is widely used. Studies in nonsepsis populations also suggest its utility in predicting adverse outcomes. Whether lactate prognosticates equally across disease states is not clearly defined. This study compares the ability of lactate to identify patients at risk for deterioration (intubation, acute renal dysfunction, vasopressor use, or death) and mortality during hospitalization in infected and non-infected populations.
Methods A prospective, observational cohort study of ED adult patients presenting from 11 November 2012 to 1 February 2013 who had lactate measured and abnormal vital signs (hearth rate ≥130, respiratory rate ≥24, shock index ≥1, systolic blood pressure <90 mmHg). Patients with isolated atrial tachycardia, seizure, intoxication, or psychiatric agitation

were excluded. Patients were stratified into three groups by lactate <2.5 (low), 2.5 to 4 (intermediate), and >4 mmol/l (high). Chi-square test for trend was used to compare outcome rates between lactate levels for each diagnostic category.
Results Of 1,152 patients identified, 366 were excluded and 298 did not have lactate measurements, leaving 488 for the analysis: 289 sepsis patients and 202 nonsepsis patients. Of these, 168 (34.4%) met the deterioration outcome, and there were 61 (12.5%) deaths. For infected patients, 46/342 (13.5%; 95% CI 10.2 to 17.5) low, 34/100 (34.0%; 95% CI 25.4 to 43.7) intermediate, and 20/46 (43.5%; 95% CI 30.2 to 57.8) high lactate patients suffered deterioration (P <0.01). Likewise, 6/342 (1.6%; 95% CI 0.7 to 3.9) low, 19/100 (19.0%; 95% CI 12.4 to 27.9) intermediate, and 11/46 (23.9%; 95% CI 13.8 to 38.0) high lactate patients died during hospitalization (P <0.01). For non-infected patients, 42/342 (12.3%; 95% CI 9.2 to 16.2) low, 13/100 (15.1%; 95% CI 7.6 to 21.1) intermediate, and 13/46 (28.2%; 95% CI 17.2 to 42.7) high lactate patients suffered deterioration (P = 0.01). In the regression models, lactate was strongly associated with deterioration for both infected (odds ratio (OR) = 1.94; 95% CI 1.4 to 2.3) and non-infected (OR = 1.48; 95% CI 1.14 to 1.91) groups. In regression models for mortality, lactate had better discrimination ability in infected (OR = 1.8; 95% CI 1.4 to 2.3) patients than in the non-infected (OR = 1.11; 95% CI 0.85 to 1.47) patients.
Conclusion Lactate levels can be used to identify patients who are at increased risk of deterioration regardless of infection status. Lactate identifies high-risk patients for mortality in infected patients more strongly than in non-infected patients.

P172

Adipose tissue lactate clearance but not blood lactate clearance is associated with clinical outcome in severe sepsis or septic shock during the post-resuscitation period

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Introduction Blood lactate clearance, a surrogate of tissue hypoxia, is associated with increased mortality in septic patients. However, no study has directly measured lactate clearance at the tissue level in the post-resuscitation period of sepsis. This study aimed to examine the relative kinetics of blood and tissue lactate clearances and to investigate whether these are associated with outcome in ICU patients having severe sepsis or septic shock during the post-resuscitation phase.
Methods A microdialysis catheter was inserted in the subcutaneous adipose tissue of the upper thigh and interstitial fluid samples were collected. Serial measurements of blood and interstitial fluid lactate levels were performed over a 48-hour period. Lactate clearance was calculated according to the formula: (lactate (initial) – lactate (delayed) / lactate (initial)) × 100%. Lactate (initial) is blood or tissue lactate within the first 24 hours after ICU admission (H0). Lactate (delayed) is blood or tissue lactate at H4, H8, H12, H16, H20, H24 and H48 (H = hours).
Results A total of 112 patients having septic shock (n = 79) or severe sepsis (n = 33) were examined. Tissue lactate clearance was higher compared with blood lactate clearance at H0 to H8 (P = 0.02), H0 to H12 (P = 008), H0 to H16 (P = 0.01), H0 to H20 (P = 0.01), and H0 to H24 (P = 0.02). Tissue lactate clearance was higher in survivors compared with nonsurvivors at H0 to H12, H0 to H20 and H0 to H24 (P = 0.02, for all). Multivariate analysis showed that ARACHE II along with tissue clearances at H0 to H12, H0 to H20 and H0 to H24 <30% were independent outcome predictors. Blood lactate clearance was not related to survival.
Conclusion In critically ill septic patients, after the initial resuscitation phase, adipose tissue clears lactate earlier than blood. High tissue lactate clearance, but not blood lactate clearance, is associated with a favorable clinical outcome.

P173

Correlation between conventional and advanced hemodynamic parameters versus serum lactate in patients with severe sepsis

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Introduction The aim of this study was to determine the correlation between levels of serum lactate (SL) and conventional hemodynamic parameters (HPs) (mean arterial pressure (MAP), heart rate (HR), central venous pressure (CVP), urinary output (UP)) in patients with severe sepsis. In a subgroup, advanced HPs (central venous saturation (SvO_2), peripheral temperature (PT), cardiac index (CI), global end-diastolic volume index (GEDI) and extravascular lung water (ELWI)) were compared with levels of SL.
Methods An observational prospective, single-center, pilot study was performed in intensive care (IC) of a medium-sized teaching hospital. Adult patients with severe sepsis were included and received standard goal-directed therapy (Surviving Sepsis Guidelines). Every patient received an arterial line and a central venous line in the upper diaphragm position. A subgroup received pulse contour cardiac output (PiCCO)-guided resuscitation and PT measurements. Pearson correlation coefficients (PCCs) were calculated between HPs and SL, which were measured every 4 hours for the first 48 hours after inclusion. P <0.05 was considered statistically significant.
Results Twenty-five patients (12 men) were included. Mean age was 68 years (30 to 93), mean APACHE II score 31 (20 to 42). The most frequent reasons for IC admission were abdominal sepsis (n = 11) and pneumosepsis (n = 7). Mean HPs (with SD and range) were respectively:

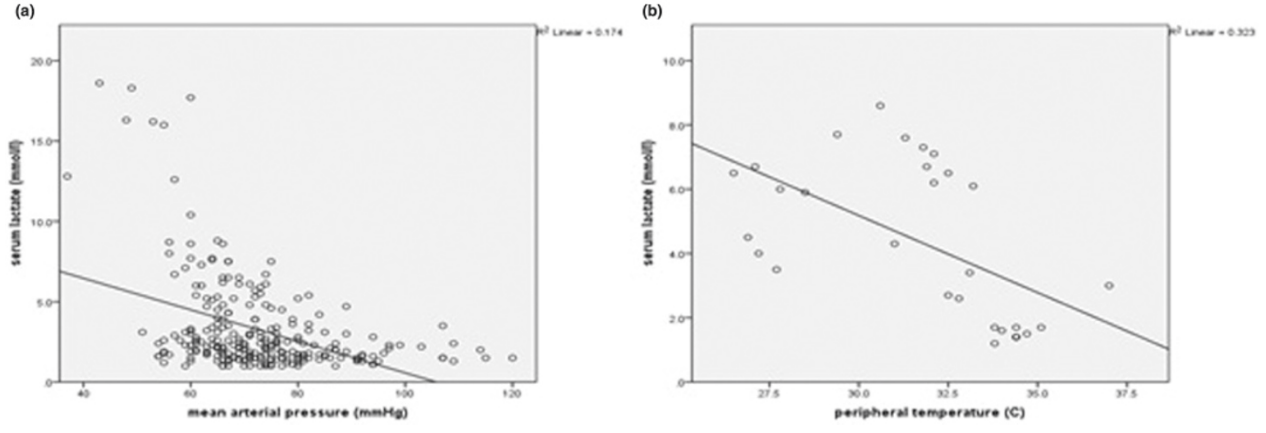

Figure 1 (abstract P173). Scatterplot of **(a)** MAP and SL and **(b)** PT and SL.

MAP 73 mmHg (13, 37 to 120), HR 101 beats/minute (22, 51 to 172), CVP 12 mmHg (5, 1 to 29), UP 55 ml/hour (62, 0 to 500), SL 3.2 mmol/l (3, 1 to 18.6), CI 4.1 ml/kg/minute (1.1, 1.6 to 6.7), GEDI 871 ml/m^2 (210, 500 to 1,691), ELWI 11 ml/kg (5, 4 to 23), PT 32.1 C (2.8, 26.4 to 38), and SvO_2 75% (8, 39 to 93). Relevant and significant (P <0.005) PCCs between HPs and SL were respectively: MAP –0.417, HR 0.195, UP –0.237, SvO_2 –0.204 and PT –0.569. Figure 1 shows the relation between two HPs with the highest correlation with SL.

Conclusion The conventional HPs MAP, HR, UP and SvO_2 are significantly correlated to levels of SL, but clinical value might be limited due to the relatively low correlation coefficients. In a small subgroup, PT is better correlated to the level of SL.

P174

Delayed assessment of serum lactate in sepsis is associated with an increased mortality rate

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Critical Care 2014, **18(Suppl 1):**P174 (doi: 10.1186/cc13364)

Introduction Lactate assessment early in the resuscitation of sepsis has been recommended as a diagnostic biomarker. An abnormal lactate, independent of blood pressure, is an indication for aggressive fluid resuscitation and its normalization is a recommended endpoint of resuscitation. The objective of this study was to evaluate the effect of the timing of lactate assessment on patient outcomes in sepsis.

Methods Data were compiled using the Clinical Vigilance for Sepsis electronic health record (EHR) screening tool, which identified consecutive patients from two hospital systems over 12 months at a 300-bed community hospital and over 24 months from a 500-bed academic tertiary care center. CV Sepsis alert screens the EHR to identify the presence of infection based on a multifactor alert system including labs, vital signs, and treatment team documentation. A physician order for intravenous antibiotics was used as a surrogate for suspected infection. The database identified 37,160 consecutive patients treated for infection from a total of 216,550. Patients with a measured lactate were divided relative to its measurement within 3 hours (eLac) or greater than 3 hours (dLac) of sepsis identification as recommended by the Surviving Sepsis Campaign. The CV Sepsis alert was the reference standard for time zero. Patients were compared in each group for the occurrence of the primary outcome of in-hospital mortality.

Results A total 5,072 of 37,160 consecutive patients (13%) had a measured lactate. Sepsis patients experienced an overall 3% (1,186/37,160) mortality rate. In total, 4,153 (82%) patients had measured lactate within 3 hours, and 919 (18%) were delayed, with a decreased morality rate (eLac 6.8 vs. dLac 24.7, P <0.0001). There was no difference in average lactate levels between the groups (eLac: 2.1 ± 2.6, dLac: 2.3 ± 3.0, P = NS). A larger ratio of delayed-lactate patients had a lactate ≥4 mmol/l (dLac 12.6% vs. eLac 8.7%).

Conclusion The delay in lactate assessment relative to clinical evidence of infection was associated with an increased mortality rate. The average lactate level in each group did not account for this effect. The timing of the assessment, not the lactate level, was prognostic of outcome. The mortality benefit associated with lactate assessment within the 3-hour guideline suggests that an increased clinical awareness may lead to early initiation of time-sensitive interventions known to improve outcomes.

P175

Lactate clearance as a predictor of mortality in colonic perforation

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Introduction The objective of this study was to determine whether lactate clearance (LC) is a significant indicator of mortality in patients with colorectal perforation. LC has been associated with mortality in heterogeneous critically ill patients, but its role as a predictor of mortality in homogeneous patients with colorectal perforation is unclear.

Methods We retrospectively analyzed the clinical data of patients who underwent emergency surgery for colorectal perforation and were admitted to the ICU of our hospital from January 2003 to August 2013. Patients with traumatic, iatrogenic, and appendicitis perforations were excluded. The primary endpoint was survival to hospital discharge. The modified Sequential Organ Failure Assessment (mSOFA) score, a customized SOFA score excluding the central nervous system component [1], was used for prognostic scoring. The mSOFA score and several clinical factors were analyzed by univariate analysis as possible predictors of survival. We collected lactate levels and base excess (BE) measured during surgery and at 6, 12, and 24 hours after the first measurement and calculated the respective LC values. The associations of initial blood lactate level, LC, and BE with mortality were assessed by receiver operating characteristics (ROC) curve and logistic regression analyses.

Results Of the 61 patients identified, five were excluded as their ICU stay was <24 hours. The overall mortality in the remaining 56 patients (mean age of 76.7 ± 10.4 (SD) years) was 21.4%. In univariate analysis, mSOFA and several other variables correlated significantly (P <0.05) with mortality. The area under the ROC curve for LC at 6, 12, and 24 hours was 0.601, 0.719, and 0.731, respectively. LC at 24 hours was the most accurate, and its optimum cutoff value was 37.5%. LC, lactate level, and BE at 24 hours, as well as the significant factors in univariate analysis, were entered into a stepwise logistic regression model, which revealed 24-hour LC ≤37.5% (odds ratio (OR), 23.0) and mSOFA score (OR, 2.1) as independent predictive values of mortality.

Conclusion In patients with colorectal perforation, 24-hour LC is more accurate than LC measured at earlier time points. Patients with 24-hour LC ≤37.5% and a high mSOFA score have a high risk of in-hospital mortality.

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P176

Lactate quartile concentration and prognosis in severe sepsis and septic shock

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Critical Care 2014, **18(Suppl 1):**P176 (doi: 10.1186/cc13366)

Introduction The Surviving Sepsis Campaign (SSC) indicates that a lactate (LT) concentration greater than 4 mmol/l indicates early resuscitation bundles. However, several recent studies have suggested that LT values lower than 4 mmol/l may be a prognostic marker of adverse outcome. The aim of this study was to identify clinical and analytical prognostic parameters in severe sepsis (SS) or septic shock (ShS) according to quartiles of blood LT concentration.

Methods A cohort study was designed in a polyvalent ICU. We studied demographic, clinical and analytical parameters in 148 critically ill adults, within 24 hours from SS or ShS onset according to SSC criteria. We tested for differences in baseline characteristics by lactate interval using a Kruskal–Wallis test for continuous data or a chi-square test for categorical data and reported the median and interquartile ranges; SPSS version 15.0 (SPSS Inc., Chicago, IL, USA).

Results We analyzed 148 consecutive episodes of SS (16%) or ShS (84%). The median age was 64 (interquartile range, 48.7 to 71) years; male: 60%. The main sources of infection were respiratory tract 38% and intra-abdomen 45%; 70.7% had medical pathology. Mortality at 28 days was 22.7%. Quartiles of blood LT concentration were quartile 1 (Q1): 1.87 mmol/l or less, quartile 2 (Q2): 1.88 to 2.69 mmol/l, quartile 3 (Q3): 2.7 to 4.06 mmol/l, and quartile 4 (Q4): 4.07 mmol/l or greater (Table 1). The median LT concentrations of each quartile were 1.43 (Q1), 2.2 (Q2), 3.34 (Q3), and 5.1 (Q4) mmol/l (P <0.001). The differences between these quartiles were that the patients in Q1 had significantly lower APACHE II scores (P = 0.04), SOFA score (P = 0.024), number of organ failures (NOF) (P <0.001) and ICU mortality (P = 0.028), compared with patients in Q2, Q3 and Q4. Patients in Q1 had significantly higher

Table 1 (abstract P176). Baseline characteristics in SS and ShS patients by quartiles of blood LT

value	Lactate <1.87 (*n* = 33)	Lactate 1.88 to 2.69 (*n* = 41)	Lactate 2.7 to 4.06 (*n* = 34)	Lactate>4.07 (*n* = 37)	*P*
Age (years)	57 (45 to 71)	64 (51.5 to 74.5)	65 (48 to 69)	60 (48.5 to 71)	NS
APACHE II	25 (18.5 to 30)	25 (19.5 to 27)	25 (21.5 to 29.5)	27 (22 to 33)	0.04
SOFA	9 (7 to 10.5)	9 (7 to 11)	9 (8 to 11)	11(8 to 13)	0.024
NOF	3 (3 to 4)	3 (3 to 4)	4 (3 to 5)	5 (3.5 to 5)	<0.001
LT (mmol/l)	1.43 (1.16 to 1.56)	2.2 (1.99 to 2.47)	3.34 (3 to 3.72)	5.1 (4.4 to 7.34)	<0.001
Procalcitonin (ng/ml)	2.81 (0.76 to 20.7)	11.5 (2.88 to 37.15)	13.47 (1.91 to 42.1)	21.6 (5.2 to 5.8)	0.05
Cholesterol (mg/dl)	127 (97.5 to 165)	130 (95.5 to 152.5)	100 (72 to 128)	91 (79 to 116.7)	0.06
28-day mortality (%)	10.8	21.2	24.4	35.1	0.029
ShS (%)	83.8	85.4	81.1	87.9	NS

cholesterol ($P = 0.06$) and lower procalcitonin ($P = 0.05$) at enrolment. At the extremes, patients in Q1 had decreased 28-day mortality ($P = 0.023$) and, patients in Q4 had increased 28-day mortality, compared with the other quartiles of patients ($P = 0.009$). Interestingly, patients in Q2 had significant increased mortality compared with patients in Q1 ($P = 0.043$), whereas the patients in Q2 had no significant difference in 28-day mortality compared with patients in Q3.

Conclusion Adverse outcomes and several potential risk factors, including organ failure, are significantly associated with higher quartiles of LT concentrations. It may be useful to revise the cutoff value of lactate according to the SSC (4 mmol/l).

P177

Correlation between arterial lactate and venous lactate in patients with sepsis and septic shock

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Introduction Measurement of arterial lactate (A-LACT) levels has been used to monitor poor tissue perfusion, predicting mortality and guiding resuscitation. Peripheral venous lactate (V-LACT) has been regarded as an unreliable test, but a less invasive approach. We aimed to determine correlation between A-LACT and V-LACT and agreement of both in order to determine the usefulness of V-LACT as a biomarker for assessment in sepsis.

Methods We conduct a prospective, cross-sectional study during June to December 2011 at a university hospital. Septic patients in the ICU were enrolled in this research. Sepsis was defined according to the Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2008. The exclusion criteria were: contraindication for arterial puncture; and denying inform consent. The venous lactate would be sampled at the same point in time as arterial lactate measurement. The correlation and agreement between arterial and venous lactate was the primary outcome.

Results A total of 73 pair-samples in 45 intensive care patients were collected. Mean age was 68.33 ± 14.5 years. Fifty percent of all patients received the vasopressors to stabilize hemodynamics. The mean serum creatinine level was 2.78 mg/dl and the mean anion gap was 13.55 mmol/l. The mean arterial lactate (A-LACT) level was 3.73 ± 4.0 mmol/l, and the mean venous lactate (V-LACT) level was 4.6 ± 4.2 mmol/l. The A-LACT and V-LACT were strongly correlated as shown in Figure 1 ($r = 0.927$, $P < 0.0001$, $r^2 = 0.859$). The mean difference between V-LACT and A-LACT was 0.889 mmol/l. The 95% limits of the V-A difference in the individual patients were between –2.3 and 4.1 mmol/l. However, the agreement looks very good at lactate levels not higher than 4 mmol/l (Figure 2). The regression equation was: A-LACT = (0.877 × V-LACT) – 0.320.

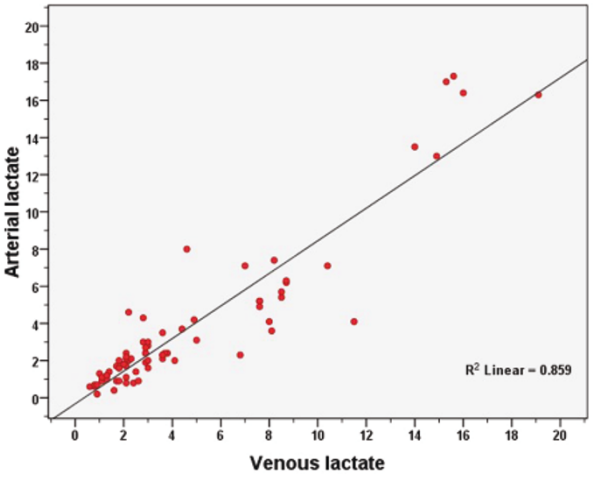

Figure 1 (abstract P177).

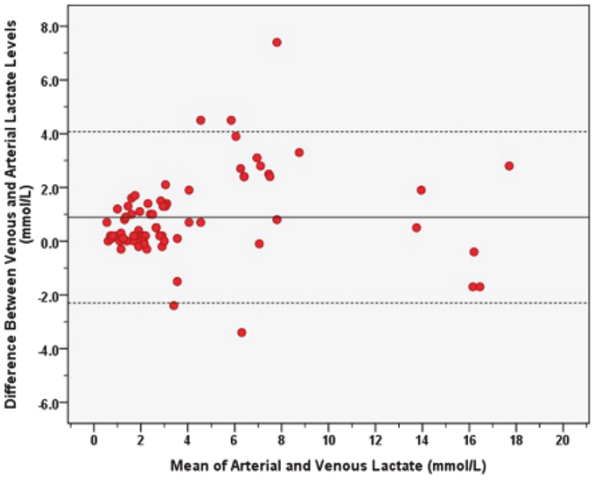

Figure 2 (abstract P177).

Conclusion The arterial lactate and venous lactate levels were strongly correlated in the condition of sepsis or septic shock. Consequently, V-LACT may be used in substitution for A-LACT particularly in lactate levels not higher than 4 mmol/l. However, trending should be generally applied instead of the absolute value.

P178

Comparison of the effects of histidine–triptophan–ketoglutarate solution and crystalloid cardioplegia on myocardial protection during pediatric cardiac surgery

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Critical Care 2014, **18(Suppl 1):**P178 (doi: 10.1186/cc13368)

Introduction The major components of myocardial protection during cardiac surgery are the combination of cardioplegia solutions with hypothermia. The primary endpoint of this study is to compare the effects of histidine–triptophan–ketoglutarate (HTK) solution and crystalloid cardioplegia on release of cardiac troponin-I (cTn-I) and creatine kinase-myocardial band (CK-MB), which are perioperative determinants of myocardial protection; the secondary endpoint is to evaluate the intraoperative and postoperative hemodynamic variables and clinical outcome parameters.
Methods A total of 66 children aged 1 month to 6 years undergoing elective congenital heart surgery were randomly allocated to HTK solution (Group H, $n = 32$) or crystalloid cardioplegia (Group C, $n = 34$) after aortic cross-clamping. Blood samples for cTn-I and CK-MB levels were measured before the surgical incision, at the end of surgery and at 4, 16, 24 and 48 hours postoperatively.
Results Demographic features were similar in both groups. Duration of surgery, aortic clamp and cardiopulmonary bypass times, amounts of intraoperative fluids used and urine outputs were similar between the groups. The groups were not significantly different in terms of cTn-I and CK-MB levels at the intraoperative and postoperative period ($P > 0.05$ for all). The dose of positive inotropic drug at the end of surgery was significantly high in Group H ($P = 0.01$). The requirements for defibrillation were similar in both groups. There were no significant differences between the groups regarding postoperative hemodynamic parameters, positive inotropic requirements, amounts of fluids and blood given and pacemaker requirements ($P > 0.05$ for all). Duration of mechanical ventilation, lengths of ICU and hospital stay were similar in both groups.
Conclusion The present study demonstrated that there is no superiority of HTK solution and crystalloid cardioplegia to each other for myocardial protection during pediatric cardiac surgery.

P179

Hyperdynamic ejection fraction in the critically ill patient

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Introduction The hyperdynamic left ventricular ejection fraction (HDLVEF) in the ICU is a common finding thought to be associated with critical illness and possibly sepsis. The exact etiology of hyperdynamic ejection fraction has yet to be determined, and the prognosis of these patients has not been well defined.
Methods The cohort consisted of 2,632 adults admitted to the ICU with echocardiogram reports using the MIMIC-II database, and was divided into those with HDLVEF and those with normal left ventricular ejection fraction (NLVEF). Those with impaired ejection fraction were excluded from the analysis. Baseline comparisons were performed using chi-squared tests for equal proportion with results reported as numbers, percentages, and 95% CIs. Continuous variables were compared using *t* tests and reported as means with 95% CIs, while non-normally distributed data were compared using Wilcoxon rank-sum tests and reported as medians.
Results Patients with HDLVEF had increased mortality in hospital, at 28 days and at 1 year when compared with patients with NLVEF. HDLVEF patients more frequently required renal replacement therapy (RRT), vasopressors and mechanical ventilation. Of the 2,632 patients, 1,220 were septic. There was an increased proportion of HDLVEF in the septic compared with the nonseptic groups (11.2% vs. 8.6%, $P = 0.026$). Interestingly, other statistically significant associated comorbidities were cancer, CHF, arrhythmias, and hypertension, which were more commonly seen in the HDLVEF group. See Table 1.

Table 1 (abstract P179)

	Normal ($n = 2,373$, 90%)	Hyperdynamic ($n = 259$, 10%)	*P* value
Male	1,159 (49)	98 (38)	**<0.001**
Service type			
MICU	1,234 (52)	138 (53)	0.695
CCU	364 (15)	28 (11)	0.052
SICU	572 (24)	69 (27)	0.367
CSRU	188 (8)	23 (9)	0.590
Primary outcome			
Twenty-eight-day mortality	458 (19)	79 (31)	**<0.001**
One-year mortality	892 (38)	129 (50)	**<0.001**
ICU mortality	296 (12)	60 (23)	**<0.001**
Hospital mortality	433 (18)	80 (31)	**<0.001**
Treatment			
RRT	363 (15)	55 (21)	**0.013**
Vasopressor	1,063 (45)	139 (54)	**0.006**
Ventilated	1,453 (61)	186 (72)	**<0.001**

Conclusion Patients with hyperdynamic LVEF in the ICU clearly have increased mortality. Hyperdynamic LVEF may be a result of increased catecholamines during cytokine storm. It is unclear whether hyperdynamic LVEF itself worsens outcomes. Further investigation is needed.

P180

Impact of nitric oxide on pulmonary regurgitation and cardiac function in the acute stage after right ventricular outflow surgery

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Introduction Pulmonary regurgitation (PR) that develops after right ventricular (RV) outflow reconstruction including the Rastelli and Norwood procedure may often result in serious cardiac events early after surgery. We hypothesized that PR may be associated with pulmonary vascular resistance (PVR) and RV contraction. Accordingly, we assessed the impact of PVR on PR and RV function using a swine model.
Methods Eight pigs (14 ± 2 kg) underwent total resection of the pulmonary valve cusps under cardiopulmonary bypass (PR group). This was compared with a control group ($n = 6$) that underwent only bypass. In both groups, the pulmonary regurgitant fraction (PRF) and cardiac output were measured by a pulsed Doppler flow meter, and the percent segmental shortening of RV (%RVSS) and RV end-diastolic dimension (RVDd) were measured by sonomicrometry. We also performed dobutamine stress evaluation as well as changing the PVR by carbon dioxide ($PaCO_2$) and inhaled nitric oxide (NO).
Results All bypass time was 18 ± 3 minutes. In the PR group, the PRF was 40 ± 4% and the RVDd was 53 ± 9 mm* (vs. control 34 ± 6 mm). *$P < 0.05$. A significant reduction in the %RVSS (18 ± 1%* vs. control 22 ± 1%) and the cardiac output (2.1 ± 0.2 l/minute* vs. control 2.5 ± 0.3 l/minute) were observed. The PRFs were 60 ± 5% ($PaCO_2$ >80 mmHg), 37 ± 2% ($PaCO_2$ <20 mmHg), 24 ± 2% (NO 20 ppm; $PaCO_2$ 40 mmHg), and were positively correlated with the PVR (Figure 1A). During the dobutamine stress, the %RVSS was increased (baseline 18 ± 1%, 5γ 21 ± 2%, 10γ 26 ± 3%), and was negatively correlated with the PRFs (Figure 1B).
Conclusion These results indicated that massive PR resulted in marked deterioration of RV performance; however, low PVR and high RV contractility may contribute to reduce the severity of PR and improve cardiac function. Nitric oxide may be a useful treatment modality the

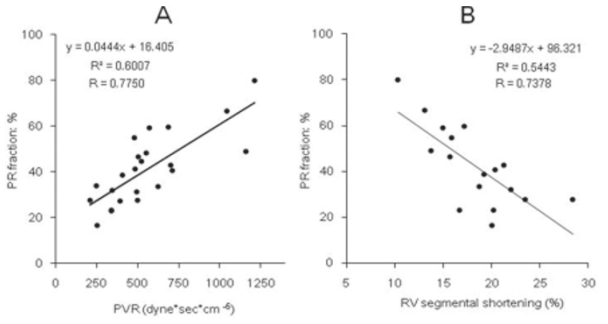

Figure 1 (abstract P180).

same as catecholamine during the acute stage after RV outflow surgery with PR.

P181

Cardiogenic oscillation in pediatric patients after cardiac surgery

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Introduction Cardiogenic oscillation is the fluctuation in flow tracing in mechanically ventilated patients. Large cardiogenic oscillation may cause autotriggering in adult patients after cardiac surgery [1] and inaccurate volume monitoring [2]. However, it is unknown how cardiogenic oscillation is problematic in pediatric patients. Therefore, we prospectively surveyed cardiogenic oscillation in pediatric patients after cardiac surgery.
Methods We enrolled 17 pediatric patients who underwent cardiac surgery using cardiopulmonary bypass. They were mechanically ventilated with pressure-controlled ventilation. We measured the amplitude in cardiogenic oscillation and compared them between their admission to the ICU and before extubation. We performed statistical analysis with the *t* test and considered $P < 0.05$ significant.
Results Cardiogenic oscillation was 2.1 ± 0.6 l/minute just after the surgery (Figure 1). Autotriggering occurred in seven of 17 patients when triggering sensitivity was set at 1 l/minute. Before the extubation, cardiogenic oscillation significantly decreased to 1.4 ± 0.4 l/minute when autotriggering disappeared. Intensive care including adjustment of inotropes and intravascular volume might have contributed to the decrease in cardiogenic oscillation.
Conclusion In pediatric patients after cardiac surgery, cardiogenic oscillation was initially large but was decreasing at the extubation.
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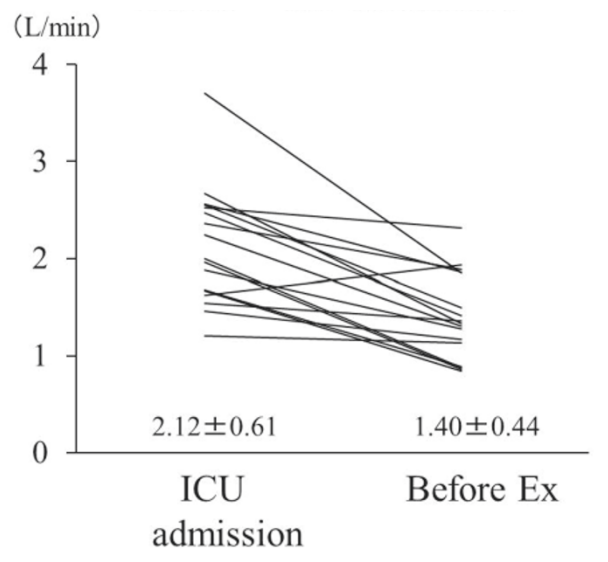

Figure 1 (abstract P181). Cardiogenic oscillation.

P182

Intraoperative dexamethasone on left atrial function and postoperative atrial fibrillation in cardiac surgical patients

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Introduction Postoperative new-onset atrial fibrillation (PNAF) is very common after cardiac surgery. The inflammatory response due to surgery and cardiopulmonary bypass (CPB) may contribute to PNAF by inducing atrial dysfunction [1]. Corticosteroids reduce the inflammatory response and may thus reduce atrial dysfunction and PNAF [2]. The aim of this study was to determine whether dexamethasone protects from left atrial dysfunction and PNAF in cardiac surgical patients.
Methods Patients undergoing cardiac surgery were randomized to a single dose of dexamethasone (1 mg/kg) or placebo after inducing anesthesia. Transesophageal echocardiography was performed in patients after CPB. The primary outcome was left atrial total ejection fraction (LA-TEF) after sternal closure; secondary outcomes included left atrial diameter and PNAF, detected by Holter monitoring.
Results Sixty-two patients were included. Baseline characteristics were well balanced. Postoperative LA-TEF was 36.4% in the dexamethasone group and 40.2% in the placebo group ($P = 0.15$) (Figure 1). Secondary echocardiographic outcomes were also insignificant (Table 1). The incidence of PNAF was 30% in the dexamethasone group and 39% in the placebo group ($P = 0.47$).

Table 1 (abstract P182). Secondary postoperative echocardiographic parameters in both groups

Parameter	Dexamethasone	Placebo	*P* value
LA-TEF	36.4	40.2	0.15
LA diameter	4.6	4.3	0.19
LA area	16.0	16.4	0.81

Conclusion Intraoperative high-dose dexamethasone did not have any protective effect on postoperative LA-TEF or dimension and did not reduce the risk of PNAF in cardiac surgical patients.

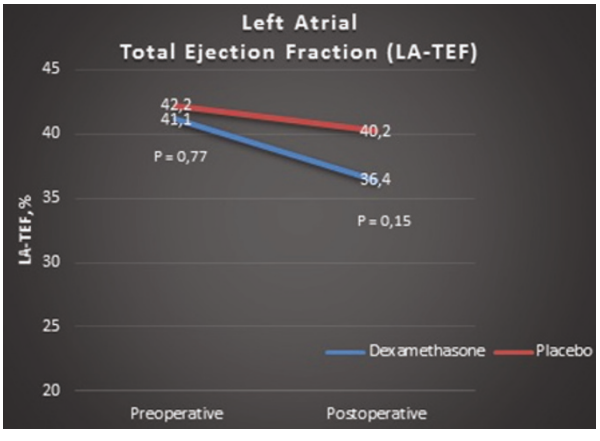

Figure 1 (abstract P182). Primary outcome preoperatively and postoperatively in dexamethasone and placebo groups.

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P183

White blood cell count and new-onset atrial fibrillation after cardiac surgery

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Critical Care 2014, **18(Suppl 1):**P183 (doi: 10.1186/cc13373)

Introduction Postoperative new-onset atrial fibrillation (PNAF) is the most common complication after cardiac surgery. Inflammation as an underlying mechanism has been studied by various inflammatory markers, and white blood cell count (WBC) is the only present consequent inflammatory marker predicting PNAF [1]. This study aimed to determine the association between perioperative WBC and PNAF.
Methods Patients >18 years undergoing elective cardiac surgery with a sinus rhythm preoperatively were recruited from the Dexamethasone for Cardiac Surgery-PNAF trial for this *post-hoc* cohort study. The WBC was prospectively measured preoperatively and once during each of the first four postoperative days. Development of PNAF was evaluated with continuous 12-lead ECG monitoring the first 5 days postoperatively.
Results A total of 657 patients were included in this trial, 277 developed PNAF. The WBC was significantly higher in the PNAF group on day 2 and day 4 (Figure 1). However, multivariate analysis showed that preoperative and postoperative WBC, days 1 to 3, were not associated with PNAF (Table 1). Older age (OR: 1.05; CI: 1.03 to 1.07; P <0.001), CABG plus valve surgery (OR: 2.95; CI: 1.78 to 4.88), single valve surgery (OR: 3.09; CI: 2.03 to 4.69; P <0.001) and other surgery (OR: 2.21; CI: 1.23 to 3.97; P <0.001) were correlated with the occurrence of PNAF.

Table 1 (abstract P183). Multiple regression analysis of association between high WBC and developing PNAF

Time point	OR	95% CI
Baseline	1.04	0.96 to 1.13
Day 1	1.03	0.98 to 1.08
Day 2	1.03	0.99 to 1.08
Day 3	1.03	0.96 to 1.11
Day 4	1.09	1.01 to 1.16

Conclusion Preoperative and postoperative WBC were not associated with development of PNAF.
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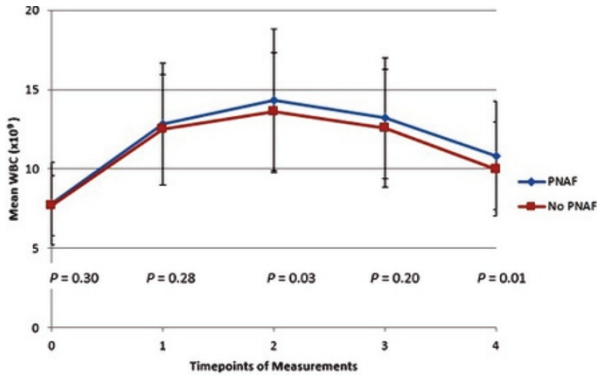

Figure 1 (abstract P183). WBC at baseline (t = 0) and in the four postoperative days (t = 1 to 4), PNAF versus no PNAF.

P184

Anti-adrenergic effects of ranolazine in isolated rat aorta

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Critical Care 2014, **18(Suppl 1):**P184 (doi: 10.1186/cc13374)

Introduction Ranolazine, a piperazine derivative, is used as an anti-anginal drug to treat patients with chronic angina in clinical practice [1] and may improve coronary blood flow by reducing compression effects of ischemic contracture, and by improving endothelial function [2,3]. In the present study we investigate the vascular effects of ranolazine on the endothelium, adrenergic system and Ca^{2+} in isolated rat aorta.
Methods Rat aortic segments (3 mm long) with and without endothelium were mounted for isometric tension recording in organ baths containing Krebs–Henseleit solution. Electrical field stimulation (2, 4 and 8 Hz, 20 V, 0.25 ms duration for 30 seconds) was provided by a Grass S88 stimulator via two platinum electrodes positioned on each side and parallel to the axis of the aortic segment. Concentration–response curves of ranolazine (10^{-7} to 10^{-4} M) were obtained in a cumulative manner using endothelin-1, noradrenaline, thromboxane A2 and KCl as constrictor agents.
Results The contractile responses to electrical field stimulation were abolished by tetrodotoxin, guanethidine and prazosin, indicating that the contractile effect is due to the action of noradrenaline on alpha adrenoreceptors. Ranolazine diminished (P <0.05) neurogenic adrenergic contractions induced by electrical field stimulation in aortic rings with and without endothelium. Ranolazine produced concentration-dependent relaxation in rings precontracted with noradrenaline (Emax 86 ± 6%, n = 10; P <0.05) but not in rings precontracted with endothelin-1, thromboxane A2 and KCl. Neither L-NAME (10^{-4} M), an inhibitor of nitric oxide synthase, nor indomethacin (10^{-5} M), an inhibitor of cyclooxygenase, modified the relaxation induced by ranolazine. The calcium antagonist nifedipine (10^{-6} M) reduced the relaxation induced by ranolazine.
Conclusion These results indicate that ranolazine diminished the contractile response induced by adrenergic stimulation, suggesting an effect as an adrenergic blocker. The relaxant effects of ranolazine on rat aortic vessels is not dependent on the endothelium-derived factors (nitric oxide or dilator prostanoids) but involves an interference with the entry of calcium through dihydropyridine calcium channels.
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P185

Delays in extubation following elective adult cardiac surgery

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Critical Care 2014, **18(Suppl 1):**P185 (doi: 10.1186/cc13375)

Introduction Early extubation post coronary artery bypass grafting does not increase perioperative morbidity and reduces the length of stay (LOS) in the ICU and in hospital [1]. Use of low-dose opioid-based general anaesthesia and time-directed protocols for fast-track interventions does not increase mortality or postoperative complications in low–moderate-risk patients and has been found to have a reduced time to extubation and shortened ICU stay [2]. Our mean time to extubation is 6 hours, although patients are assessed to be safe to be weaned from mechanical ventilation at 2 hours following arrival in the ICU. This study aims to identify factors that delay extubation in patients undergoing routine cardiac surgery at our institution.
Methods A prospective analysis was performed on all patients post adult cardiac surgery from 14 May 2013 to 10 July 2013. Emergency surgical patients and those with intraoperative complications were excluded.
Results A two-sample t test was used to analyse the data. Patient demographics are presented in Table 1. There were significant delays in time of extubation in those who received morphine prior to extubation compared with those that did not (P = 0.0184) (Table 2). There were no

Table 1 (abstract P185). Patient demographics

Age (years)	66 (10.1)
EUROSCORE (%)	2.90 (1.84)

Table 2 (abstract P185). Morphine versus no morphine

	Morphine	No morphine
Patient number	51	20
Time to extubation (hours)	7:48 (4:42)	4:48 (2:19)
LOS ICU (hours)	51:21 (55:16)	40:06 (28:47)
LOS hospital (days)	9.83 (5.01)	10.8 (13.5)

significant differences in LOS in ICU or hospital. Factors such as age, EUROSCORE and type of operation did not have an influence on time to extubation.

Conclusion Administering morphine prior to extubation causes significant delays in weaning from mechanical ventilation. We plan to introduce intraoperative and postoperative protocols to facilitate rapid weaning from mechanical ventilation for elective cardiac surgical patients.

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P186

Effects of perfusion pressure on the splanchnic circulation after cardiopulmonary bypass: a randomized double cross-over study

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Introduction No randomized trial has assessed the effects of different mean arterial pressure (MAP) targets in postcardiac surgery intensive care. We investigated the short-term effects of MAP of 65 or 85 mmHg on splanchnic oxygen flux, metabolic function, mucosal perfusion and cytokine regulation.

Methods A single-center, randomized controlled, double cross-over trial was performed. Patients were randomized to: HLH (high–low–high) where MAP targets were 85–65–85 mmHg in sequence, with each lasting 2 hours, or LHL (low–high–low) where MAP targets were 65–85–65 mmHg. Blood pressure was adjusted with noradrenalin infusion.

Results Six + six patients were included in the study. MAP targets were achieved in all patients at all time points (64 ± 3, 84 ± 4; 65 ± 5 mmHg in the LHL group and 84 ± 3; 66 ± 2; 85 ± 5 mmHg in the HLH group at the first, second and third time points), with corresponding changes in filling pressures. Cardiac output did not change over time. Hepatic venous saturation was 41 ± 15; 58 ± 24; 56 ± 21% in the LHL group and 50 ± 19; 43 ± 20; 41 ± 18% in the HLH group at the first, second and third time points, with a significant time group interaction (P <0.05). No changes were observed in global or trans-splanchnic lactate levels and cytokine levels or in gastric tonometry CO_2.

Conclusion Increasing MAP with norepinephrine has some effects splanchnic oxygenation, but has no impact on metabolic or biochemical function and key cytokine removal or release. MAP targets of 60 to 65 mmHg or 80 to 85 mmHg appear physiologically equivalent for the splanchnic circulation.

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Isoflurane attenuates left ventricular akinesia and preserves cardiac output in the Tako-tsubo rat model

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Introduction Tako-tsubo cardiomyopathy (TCM) is an acute cardiac syndrome with regional hypokinesia in the left ventricle (LV), often affecting the apex causing apical ballooning. TCM is frequent in patients with adrenergic overstimulation and is probably common in ICU patients [1]. In a TCM rat model we evaluated whether different anesthetic agents could attenuate LV akinesia in TCM.

Methods Isoprenaline was intraperitoneal (i.p.) injected, which induces LV akinesia and apical ballooning within 90 minutes [2]. We performed the study in two different settings. In the first setting, spontaneously breathing rats (n = 12 in each group) were sedated with either pentobarbital, ketamine, isoflurane or no anesthetic before i.p. isoprenaline. One additional group received the K-ATP blocker glyburide before sedation with isoflurane. In the second setting, rats were anaesthetized with ketamine + midazolam, mechanically ventilated and the carotid artery was cannulated. Before i.p. isoprenaline, animals were randomized to either no isoflurane (0 MAC), isoflurane 0.5 MAC or isoflurane 1.0 MAC (n = 12 in each group). Arterial blood gas was obtained before isoprenaline and 60 minutes after isoprenaline. The heart rate (HR), systolic blood pressure (SBP) and body temperature (BT) were recorded continuously. After 90 minutes, echocardiography was performed. Extent of akinesia was expressed as the percentage of total LV endocardial length. End-diastolic and end-systolic LV volumes were measured, and stroke volume (SV) and cardiac output (CO) were calculated.

Results In spontaneously breathing rats, the degree of akinesia was significantly lower with pentobarbital and isoflurane (± glyburide) but not with ketamine compared with controls. The degree of akinesia was lowest with isoflurane. In ventilated rats, the degree of apical akinesia (%) was significantly lower at 0.5 MAC (8.7 ± 7.3) and 1 MAC (5.7 ± 7.4) versus 0 MAC (17.7 ± 8.0). This was accompanied by a higher CO and SV. HR was lower at 1 MAC (6%) and SBP was lower at 0.5 MAC (106 ± 7) and 1 MAC (98 ± 7) versus 0 MAC (126 ± 8). BT and pH was lower in both isoflurane groups. In a multivariate model, isoflurane was the only variable that was independently associated with the degree of LV akinesia.

Conclusion Isoflurane prevents experimental TCM and preserves LV function, an effect not mediated via opening of K-ATP channels. The effect cannot be explained entirely by attenuation of myocardial stress. Isoflurane sedation in the ICU might be an interesting approach for patients suffering from hyperadrenergic conditions at risk of developing TCM.

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P188

Preoperative therapy with angiotensin-converting enzyme inhibitors in cardiac surgery patients: is there any impact on postoperative renal function?

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Introduction Preoperative therapy with angiotensin-converting enzyme inhibitors (ACEI) is common in patients undergoing cardiac surgery. The aim of this study was to evaluate the still-debated impact of preoperative use of ACEI on postoperative renal function in cardiac surgery patients [1,2].

Methods A total of 624 consecutive patients, who underwent cardiac surgery from July 2012 to October 2013, were evaluated. Data were prospectively collected in our clinic's electronic database and were retrospectively analyzed as to preoperative ACEI therapy. The chi-square test was used for correlations. Endpoints of the study were the development of postoperative acute kidney injury (AKI) and the difference between hospital admission and discharge glomerular filtration rate (GFR). The AKI definition was based on modified RIFLE classification. GFR values were estimated by the MDRD formula.

Results A total of 354 patients (56.7%) were treated with ACEI preoperatively. Overall, 95 patients (15.3%) developed postoperative AKI. Preoperative use of ACEI was not associated with the development

Table 1 (abstract P188). AKI and GFR difference

	ACEI users (n = 354)	ACEI nonusers (n = 270)	P value
AKI	54 (15.3%)	41 (15.2%)	0.981
GFR difference (mean)	+1.43	+2.3	0.511

of postoperative AKI (P = 0.981). Mean GFR values on admission day were 65.23 ± 16.89 for ACEI users, and 65.06 ± 19.62 for the rest of the cohort. Mean GFR values on discharge day were 66.77 ± 21.25 and 67.35 ± 25.64 respectively. The difference in GFR at the time of hospital admission and on discharge day had no statistical difference, P = 0.511 (Table 1). Overall, 25 patients (4%) needed dialysis.

Conclusion The impact of preoperative ACEI treatment on postoperative renal function after cardiac surgery is still debated. We found no association, neither protective nor harmful, between preoperative ACEI therapy and renal function impairment.

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P189

Characterization of the profile and clinical variables associated with mortality in a Brazilian coronary ICU

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Introduction Cardiovascular disease is the leading cause of death worldwide and the outlook for 2020 data is even more alarming [1,2]. In this context, the coronary ICUs (CICUs) have become increasingly numerous. However, data concerning this are still very limited in the literature. This study aims to characterize the profile of CICU admissions in Brazil and the main clinical variables associated with increased mortality.

Methods To conduct the study we analyzed the database of a CICU of a medium-sized hospital in the city of Presidente Prudente, Brazil. Admissions that occurred during the period 1 September 2010 to 31 August 2013 were analyzed. The information was collected from the EPIMED MONITOR system and statistically analyzed using EPI INFO, version 3.5.2 software. P <0.05 two-tailed was considered significant, and confidence intervals at 95% (95% CI) were used for the logistic regression multivariate estimated in the sample.

Results A total of 2,098 admissions were recorded, of which 42.1% were female and 57.9% male. The average age was 66.99 ± 13.30 years. The prognosis for SAPS 3 admission score averaged 40.8 ± 15.48 points and the mean unit length of stay was 3.5 ± 5.01 days. The main admission diagnoses were unstable angina (13.06%), non-ST-segment elevation myocardial infarction (8.29%), ST-segment elevation myocardial infarction (8.10%) and supraventricular cardiac tachyarrhythmia (6.91%). We observed a higher risk of death among patients who had, at admission, congestive heart failure NYHA 2, 3 or 4 (odds ratio (OR) = 2.81, 95% CI: 2.07 to 3.83, P = 0.001), chronic renal failure (OR = 2.48, 95% CI: 1.68 to 3.67, P = 0.001), peripheral artery disease (OR = 1.93, 95% CI: 1.04 to 3.58, P = 0.033), severe chronic obstructive pulmonary disease (OR = 3.17, 95% CI: 1.82 to 5.51, P = 0.002), and infection at admission (OR = 7.88, 95% CI: 5.27 to 11.78, P = 0.001).

Conclusion The results reported may direct healthcare professionals to profile the patient hospitalized in a CICU, paying attention to the most disturbing and lethal comorbidities present on admission.

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P190

Hospital visit pattern and its effect on reperfusion time and clinical outcomes in ST-segment elevation acute myocardial infarction

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Introduction The reperfusion time is critical in ST-segment elevation myocardial infarction (STEMI), and it makes a difference to clinical outcomes. This study was designed to investigate the hospital visit pattern and its effect on reperfusion time and clinical outcomes of STEMI patients.

Methods A total of 199 STEMI patients were registered in this study from three university hospitals in Kyungsang-do area, Korea, and were divided into two groups; group 1 (n = 69) who directly visited the hospitals capable of percutaneous coronary intervention (PCI), and group 2 (n = 130) who first visited local hospitals and then transferred to PCI-capable hospitals. We analyzed the estimated distance and time to the hospitals using a driving navigation system, elapsed time from chest pain to primary PCI hospitals, chest pain to reperfusion time, and in-hospital outcomes.

Results There was no difference in first medical contact time between groups 1 and 2. But the time from chest pain to PCI hospital was shorter in group 1 (206.2 ± 268.5 vs. 370.3 ± 415.2 minutes, P = 0.001). Sixty patients in group 1 and 108 patients in group 2 underwent reperfusion therapy (P = 0.473). The chest pain to reperfusion time was shorter in group 1 (294.6 ± 255 vs. 397.2 ± 341.9 minutes, P = 0.045). The difference in estimated time by navigator and actual hospital visit time was also shorter in group 1 (194.2 ± 269.9 vs. 321.6 ± 411.0 minutes, P = 0.009). In-hospital mortality was higher in group 2 (0 vs. 4.6%, P = 0.094).

Conclusion A primary visit to a local hospital was associated with longer reperfusion time and was associated with higher mortality. Therefore, the reperfusion time could be reduced by patient education and management of the community healthcare system.

P191

Tissue-aggressive inflammatory response defines the tissue aggressiveness of the post-infarction milieu

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Introduction A potential measure of post-ischemic milieu in myocardium subject to acute ischemic injury is to assess the so-called myocardial salvage index (SI) by relating the final infarct size to the initial myocardium at risk (MaR). Cardiac magnetic resonance (CMR) has previously been shown to enable determination of both infarct size using late gadolinium enhancement and MaR using T2-weighted imaging. This technique could thus potentially be used to identify inflammatory responses that could be targeted to accomplish cardioprotection. The aim of this study was to relate SI, as determined by CMR, to the inflammatory response in patients with acute myocardial infarction.

Methods Fifteen patients with first-time ST-elevation myocardial infarction were included in the study. All patients underwent primary PCI due to an acute occlusion in one branch of the left coronary artery. Final infarct size and MaR was determined by CMR performed 1 week after the acute event. The ischemic time was defined as the time from pain onset to opening of the occluded vessel. Blood samples were taken for assessment of inflammatory response. Inflammatory cells were analyzed by flow cytometry in a BD FACS Aria. Parameters were gated against control antibody and fluorescence minus one strategy. Cytokine patterns were analyzed by BioRad BioPlex multiplex protein analysis technology.

Results The SI did not correlate with MaR (P = 0.2720, R^2 = 0.09191). The population was divided into the lowest half of the SI (representing the most hostile milieu; SI: 23 to 57%) and the upper half of the SI (representing the friendliest post-infarction milieu; SI: 71 to 95%). The patients' profile of adaptive inflammatory response was characterized by flow cytometry. The two groups did not differ with regard to their T-regulatory response ($CD25^+FoxP3^+$, P = 0.7203) or NK-cell ($CD3^-CD56^+$,

$P = 0.5742$) response. However, the proportion of TH1 ($CD4^+$ $IFN\gamma^+$) cells was higher in the group with the lowest SI (57.47 ± 4.805 vs. 38.10 ± 6.514, $P = 0.0349$).
Conclusion This is the first study that identifies inflammatory cell patterns which influence the hostility of the infarction milieu *in vivo*. The study indicates that SI can be used as an evaluator of post-ischemic milieu and that TH1 response is associated with unfavorable post-infarction injury and could therefore be a possible target for future studies to limit infarction size. The current study is, by its size and observational character, important; an argument for rather than a substitute for future interventional studies in this area.

P192

Impact of positive end-expiratory pressure application on ventriculo-arterial coupling in decompensated left ventricles after cardiac surgery: a non-invasive echocardiographic study

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Introduction The management of ICU patients following heart surgery can be hustling when coping with severe left ventricular (LV) dysfunction. Single beat (Sb) measurements of ventriculo-arterial coupling (VAc) can be used by the intensivist when dealing with altered hemodynamic states [1]. LV elastance (Ees) and arterial elastance (Ea) can be measured by trasthoracic echocardiography (TTE) in a Sb fashion [2], so allowing quick assessment of VAc. PEEP application is common practice in the ICU but can have hemodynamic consequences and lead to instability. Speckle tracking analysis by TTE has been recently reported to help titrating PEEP in critically ill patients [3]. However, this can be demanding and require specific ultrasound tools. In this study we aimed to assess whether standard TTE can be useful in evaluating the effect of respiratory treatment with PEEP on cardiovascular efficiency by measuring VAc after coronary artery bypass surgery (CABG).
Methods TTE was performed before anesthesia induction and upon ICU arrival in 15 patients with preoperative diagnosis of LV dysfunction defined as an EF <35%. In-ICU measurements of Ees, Ea and VAc were taken at different steps of PEEP application lasting 3 minutes as follows: 0 cmH_2O PEEP (ZEEP), 5 cmH_2O PEEP, 10 cmH_2O PEEP and 15 cmH_2O PEEP. TTE and hemodynamic parameters were recorded and analyzed.
Results All patients were uncoupled preoperatively (VAc >1.31, average VAc (AVAc) = 1.56) before anesthesia induction and showed worsened uncoupling postoperatively at ZEEP. PEEP application altered VAc by modifying both Ees and Ea at all steps and all patients showed further uncoupling at any level of PEEP application (AVAc at ZEEP = 1.97, at 5 cmH_2O PEEP = 1.61, at 10 cmH_2O PEEP = 1.87, at 15 cmH_2O PEEP = 2.23) A PEEP of 5 cmH_2O provided the more favorable VAc.
Conclusion Sb evaluation of Ea/Ees shows that following CABG the patients with depressed LV remain uncoupled, and that in such patients the application of PEEP leads to further decoupling. In this preliminary experience, 5 cmH_2O PEEP seems to be the most appropriate in preventing further worsening of the VAc. A large RCT is needed to draw conclusions on the PEEP effect on VAc following CABG in a depressed heart.
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P193

Prevalence of elevated cardiac troponin T in ICU patients using the high-sensitivity assay and the relationship with mortality

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Introduction Elevated cardiac troponin levels are common in ICU patients even in the absence of acute coronary syndromes and may be predictive of mortality. The recently introduced high-sensitivity cardiac troponin T (HS cTnT) assay has resulted in an increased detection of elevated cTnT in ICU patients [1]. The aim of this study was to determine the prevalence of elevated cTnT using the HS assay and its relationship with mortality.
Methods A retrospective observational study was performed on all ICU admissions over a 12-month period. Data were obtained from the clinical information system (ICIP; Philips) and the ICU audit databases (AcuBase). Data collected included patient demographics, peak cTnT value, APACHE II score, requirement for organ support and mortality. The primary outcome measure was hospital mortality. Data were analysed using SPSS v.17.0. cTnT levels were divided into categories for analysis: normal (<14 ng/l) and elevated. The elevated category was further subdivided into quartiles. Univariate analysis was performed between potential risk factors and mortality followed by multivariate regression analysis to ascertain independent predictors of mortality.
Results There were 417 admissions to the ICU during the study period, 89 of whom were excluded because of an absent cTnT value, leaving 328 patients included in the analysis. cTnT was elevated in 85% of patients. ICU mortality was 19% and hospital mortality was 28%. Hospital mortality (%) per cTnT category was: <14 ng/l = 2%; 14 to 38 ng/l = 19%; 39 to 90 ng/l = 26%; 91 to 252 ng/l = 39%; >252 ng/l = 43%. On univariate analysis, cTnT levels, age, ventilation and APACHE II score were significantly associated with mortality. cTnT levels were significant in multivariate regression independent of age and ventilation but did not reach significance ($P = 0.06$) in a multivariate analysis that included the APACHE II score.
Conclusion In 85% of general ICU patients, troponin measured by HS cTnT assay was elevated. cTnT levels were significantly associated with mortality and are predictive of mortality independent of age and mechanical ventilation, but not independently of APACHE II score. There was a high correlation between troponin levels and APACHE II scores.
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P194

Rhabdomyolysis following cardiac surgery: from prevalence to prevention

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Introduction In the view of robust consequences following cardiac surgery, acute kidney injury (AKI) remains a major concern. Rhabdomyolysis (RML) following cardiac surgery and its relation to AKI need to be investigated. We aim to study the prevalence of RML development following cardiac surgery and the perioperative risk factors that may expedite the occurrence of RML.
Methods All patients undergoing cardiac surgeries in our hospital were enrolled in the study during the period of 1 year in a prospective descriptive study measuring the occurrence of RML and its association with AKI, where all patients in the study underwent serial assessment of serum creatinine kinase (CK) and serum myoglobin. Serial renal function, prior statin treatment, cardiac injury, lengths of ventilation, and lengths of stay in the ICU and hospital were monitored.
Results We recruited 202 patients in our study, 185 males and 17 females with mean age 52 ± 12.4 years. According to the existence of RML (CK 2,500 U/ml or more) [1], patients were divided into group 1 where RML was identified in 17 patients (8.4%), which was associated with AKI in seven patients (41%), and group 2 without RML (185 patients), where AKI occurred in 34 patients (18.4%) ($P = 0.025$). We observed a significantly longer duration of ventilation and lengths of stay in the ICU and in hospital in the RML group (P <0.01 for all observations).
Conclusion Early increase in the serum CK and myoglobin in postoperative high-risk cardiac surgeries may predict the concomitance of early AKI, where proper intervention may prevent the sequelae of logistic organ dysfunction.
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P195

Open cavity abdominal surgery in octogenarians and nonagenarians admitted to a university teaching hospital ICU: a retrospective review

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Introduction This review was undertaken to establish the ICU and hospital mortality rates in patients aged 80 and over admitted to our ICU following abdominal cavity surgery. Intensive care mortality increases progressively with age [1] and as the population changes we are likely to see increasing numbers of patients over the age of 80 admitted to critical care units.
Methods We searched the ICNARC database from 2006 to 2013 for patients aged 80 years or over, admitted from theatre or after surgery. Data were referenced against the electronic theatre management system, and patients not undergoing abdominal cavity surgery were excluded. The data were analysed using an Excel spreadsheet (Microsoft) and Medcalc software.
Results Eighty-five patients were included, with ages ranging from 80 to 99 years. Fifty-one (60%) patients were male and 79 (93%) patients were categorized as having an emergency operation. ICU mortality was 34/85 (40%) and hospital mortality was 48/85 (56%). Variables assessed for association with hospital mortality can be seen in Table 1. Only invasive ventilation and time (days) from hospital admission to ICU admission were significant predictors of hospital mortality.

Table 1 (abstract P195). Survivors versus nonsurvivors

	Survivors	Nonsurvivors	*P* value
Age	83	83	0.82
Time	1, 1 to 8	4.5, 1 to 8	0.004
APACHE II	17, 14 to 20	17, 14 to 21	0.96
Sex (%)	M57, F43	M63, F37	0.65
Ventilation (*n*, %)	31, 83	48, 100	0.005
RRT (*n*, %)	6, 16	11, 23	0.58

Data presented as median, IQR or *n*, %.

Conclusion ICU and hospital mortality rates were high at 40% and 56% respectively. Increasing age did not correlate with mortality. However, invasive ventilation and time between hospital and ICU admission were associated with a higher mortality. This may be due to a delay in diagnosis or surgical intervention. We suggest that one considers early intervention in patients aged over 80. A functional outcome measure at discharge may be a more clinically relevant endpoint.
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P196

Risk factors for acute renal impairment in patients with severe acute pancreatitis

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Introduction The aim of this study was to clarify the risk factors for acute renal impairment (ARI) in patients with severe acute pancreatitis (SAP).
Methods We conducted a retrospective observational case–control study. The data of all patients admitted to the ICU at a university hospital with the diagnosis of SAP from January 2008 to December 2012 were abstracted from the hospital database. ARI was defined according to RIFLE criteria. Patients with any signs of renal impairment (serum creatinine value ≥1.5-fold from the estimated baseline) on admission or history of kidney disease were excluded. A control group was composed of randomly selected patients with SAP who did not develop ARI.
Results Of 145 patients, 24 patients who developed ARI at any time during hospitalization (ARI group) were contrasted with 24 patients without ARI (control group). The patients were older in the ARI group: age 57 ± 13 versus 49 ± 16, $P = 0.046$. Although none of the patients in the ARI group had creatinine values ≥1.5-fold from the estimated baseline, the creatinine values on admission were higher in this group: 100 ± 38 versus 68 ± 16, $P = 0.001$. The severity of pancreatitis was similar. On admission, the APACHE II and SOFA scores were higher in the ARI group (12.7 ± 3.7 vs. 8.6 ± 3.4, $P = 0.001$ and 5.6 ± 3.4 vs. 2.8 ± 1.9, $P = 0.002$, respectively). The patients in the ARI group had higher intra-abdominal pressure and SOFA respiratory score on admission and after 72 hours ($P < 0.01$). Although on admission the cardiovascular SOFA score was similar in both groups, it increased significantly after 72 hours in the ARI group from 1.1 ± 1.7 to 2.1 ± 1.8, $P = 0.012$ and became higher compared with the control group: 2.1 ± 1.8 versus 0.6 ± 1.2, $P = 0.001$. Lactate was higher in the ARI group on admission and after 72 hours ($P < 0.05$). The percentage of patients requiring vasopressors over 72 hours was greater in the ARI group: 66.7% versus 29.2%, $P = 0.01$. Positive fluid balance after 72 hours in ICU was higher in the ARI group: 8,594 ± 7,044 ml versus 4,192 ± 4,467 ml, $P = 0.004$; however, the infused volume of crystalloids did not differ between groups. Central venous pressure was higher on admission ($P = 0.036$) and after 72 hours ($P = 0.001$) in the ARI group. Multivariable logistic regression analysis revealed that development of ARI was independently associated with cardiovascular SOFA score after 72 hours: odds ratio = 1.475, 95% CI 1.049 to 2.073, $P = 0.025$.
Conclusion The development of ARI in SAP was associated with hemodynamic instability, whereas excessive volume expansion does not prevent ARI.

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Severe acute pancreatitis in ICU: a 5-year audit

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Introduction Severe acute pancreatitis (SAP) is associated with significant mortality and morbidity. The objective of this study is to examine the profile, outcome and resource utilization for patients with SAP admitted to the ICU in a university teaching hospital over a 5-year period.
Methods A retrospective observational study was carried out of all patients admitted to the ICU from 1 January 2008 to 31 December 2012 with SAP. Data were collected from the ICU database (AcuBase), the medical records and the ICU clinical information system. Data collected included patient demographics, etiology of SAP, data for APACHE II, Imrie, Ranson and Acute Kidney Injury Network (AKIN) scores, and requirement for organ support. Outcomes recorded were length of stay, ICU mortality and hospital mortality. Cost of ICU care was calculated based on previously reported methodology.
Results Thirty-eight eligible patients were identified. Mean age was 51.4 years (range 24 to 86), 68% were male. The commonest etiologies were alcohol (53%) and gallstone pancreatitis (24%). The mean APACHE II score was 18.5 (IQR 14 to 23). Twenty-eight patients (74%) required mechanical ventilation, three of whom required high-frequency oscillation (all three survived). Twenty-two patients (58%) had evidence of an acute kidney injury on admission (AKIN criteria). Eighteen (47%) required renal replacement therapy and 60% required inotropes. The ICU mortality and the hospital mortality were 26%. There was no significant difference in age, APACHE II, Imrie, or Ranson scores between survivors and nonsurvivors. The median length of stay in the ICU was 11 days (IQR 5.25 to 28.5) and the median hospital stay was 45.4 days (IQR 22.25 to 104.5). Nine patients (24%) required multiple ICU admissions and the mortality was significantly higher in this group ($P < 0.05$, chi-square test). In total, 834 ICU bed-days were taken up by 38 patients. Based on a median cost for an ICU bed-day of €2,205 [1], the total cost of ICU care for these patients is estimated at €1,838,970 or almost €50,000 per patient.

Conclusion A hospital mortality rate of 26% is similar to that reported recently from a specialist unit in the UK [2] but less than the 42% reported in the UK in 2007 [1], suggesting some improvement in recent years. SAP is associated with prolonged ICU and hospital stay and significant resource utilization.

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Bacterial infection in severe acute pancreatitis patients admitted to the ICU

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Introduction Controversy surrounds the empirical use of antibiotics in severe acute pancreatitis (SAP). There are concerns that the widespread use of antibiotic therapy in the absence of documented infection may lead to selection of drug-resistant organisms [1]. The aim of this study was to review the profile of pancreatic fluid isolates in patients with SAP admitted to the ICU.
Methods Data were reviewed for 38 patients admitted to the ICU over a 5-year period. We evaluated organisms cultured from pancreatic specimens, as well as the prevalence of drug-resistant organisms in this group of patients.
Results Aspirate of pancreatic material for culture was obtained in 55% of patients (n = 21). The mean time to acquisition of samples for culture from admission to ICU was 15.5 days. Fluid was sterile in 67% (n = 14) of initial samples. Gram-positive organisms were cultured from 43% (n = 9) of samples, Gram-negative organisms from 5% (n = 1) and yeasts from 5% (n = 1). Antibiotic therapy was administered in 95% of patients prior to samples being obtained for culture. On review of all samples received from patients (including nonpancreatic specimens), vancomycin-resistant enterococci (VRE) were isolated in 13 patients. Linezolid-resistant enterococci (LRE) were isolated in six patients, five of whom had VRE isolated prior to the culture of LRE. Extended-spectrum beta-lactamase organisms were isolated in two patients, and carbapenem nonsusceptible Gram-negative organisms in three patients. The mean APACHE II score was 18.5 and overall hospital mortality was 26%.
Conclusion In the majority of patients, initial aspirates of pancreatic material were sterile. This may be a result of prior antibiotic usage. Where organisms were cultured from initial aspirates, Gram-positive organisms predominated, possibly as a result of prior anti-Gram-negative antibiotic use. Therefore, in patients with ongoing sepsis who are receiving broad-spectrum antibiotic therapy, consideration needs to be given to the empiric treatment of Gram-positive infection, and in particular drug-resistant organisms such as VRE. Local epidemiology should be taken into account. Rationale use of antibiotics, in accordance with best-practice guidelines, may limit development of drug resistance; however, other risk factors for resistance may exist in this group and this would need to be further evaluated.

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P199

Determining late predictors of outcome for acetaminophen-induced acute liver failure using classification and regression tree modeling analysis

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Introduction Liver transplantation (LT) in acetaminophen-induced acute liver failure (APAP-ALF) patients often presents significant challenges. The King's College Criteria (KCC) have been validated on admission but not in later phases of illness. The aim was to improve determinations of prognosis on and after admission in APAP-ALF patients using the classification and regression tree (CART) methodology to construct optimal binary splits on independent variables to predict outcome.
Methods CART models were applied to US ALFSG registry data for prediction of 21-day spontaneous survival on admission and late stage (days 3 to 7). Analyses were carried out using R software (package rpart) for all (n = 803) APAP-ALF patients enrolled between January 1998 and September 2013 with complete outcome data. Training data were used to build CART trees and test data were used to evaluate prediction accuracy (AC), sensitivity (Sn) and specificity (Sp).
Results Of the 803 APAP-ALF patients, the median age was 37 (29 to 47) years and 76% were female. A total of 238 (30%) patients were listed for and 87 (11%) received LT. A total of 531 (66%) patients recovered without LT at 21 days. Using standard logistic regression methods for all patients with complete data (n = 679), KCC (INR, creatinine, coma grade 3/4, pH) yielded an AC of 69% (Sn 90%, Sp 27%) at admission. For late-stage data (n = 341), KCC provided similar AC (70%) and Sn (97%), but suffered poor Sp (15%). CART analysis using the KCC variables on admission offered predictive AC (66%) and Sn (65%), with increased Sp (67%). Using day 3 to 7 data, the KCC-CART model had increased AC (82%) and Sn (86%), with improved Sp (46%) compared with logistic KCC. New CART models were developed with 18 variables based on previous literature. A new CART model on admission (MELD, lactate and MV: test AC 72%, Sn 71%, Sp 77%) performed better than KCC-CART. For days 3 to 7, a CART model (MELD, lactate, coma grade) offered superior prediction (test AC 86%, Sn 91%, Sp 46%) compared with days 3 to 7 KCC-CART.
Conclusion CART analysis increased predictive performance compared with traditional KCC. KCC-CART trees have higher Sp and similar predictive AC compared with traditional KCC, with newer CART trees providing marginal improvement over KCC-CART models.
Acknowledgment Supported in part by a U-01 58369-014 from NIDDK to the US Acute Liver Failure Study Group.

P200

A multicenter retrospective cohort analysis of therapeutic hypothermia in acute liver failure

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Introduction Cerebral edema is a severe and life-threatening complication in acute liver failure (ALF). Concerns exist that therapeutic hypothermia (TH) may increase the risk of infection, worsen coagulopathy and inhibit hepatic regeneration. We therefore reviewed the experience in use of TH in participating US Acute Liver Failure Study Group (ALFSG) centers. The aims were to determine utilization of TH in ALF patients at high risk for cerebral edema (grade III or IV hepatic encephalopathy (HE)) and to determine its effect on survival and complication rates.
Methods A retrospective cohort study of all ALF patients enrolled in the US ALFSG registry between January 1998 and September 2013 with grade III or IV HE. TH using an external cooling device was used in 97 (8%) patients while in 1,135 (92%) patients it was not (controls).
Results TH ALF patients were younger (36 vs. 40, P = 0.03) and had acetaminophen etiology (63 vs. 47%, P = 0.04). Admission MELD (32 vs. 34) and lactate (5.4 vs. 5.0 mmol/l, P >0.2 for all) were similar. More TH ALF patients received renal replacement therapy (63 vs. 40%), vasopressors (61 vs. 43%) and ICP monitoring (40 vs. 22%, P <0.0002 for all). Overall (38% vs. 40%, P = 0.7) and 21-day transplant survival (45 vs. 49%, P = 0.5) were similar. There were no differences in bleeding (12% vs. 12%) or bloodstream infections (17 vs. 18%, P >0.7 for both). More TH ALF patients had arrhythmias (38 vs. 27%, P = 0.03). There were no differences in listing (43 vs. 40%, P = 0.5) or receipt of transplant (18 vs. 25%, P = 0.1). After controlling for MELD, requirement for organ support on multivariable analysis, hypothermia was not independently

associated with 21-day spontaneous survival (P = 0.93) while MELD (P <0.0001) and vasopressors (P <0.02) were.
Conclusion TH was not associated with increased bleeding/infection rates nor differences in survival in ALF patients with high-grade HE. ICP monitoring was not universally used in TH ALF patients (~40%). There is a need for a prospective trial to clarify the use of TH in patients with ALF.
Acknowledgement Supported in part by a U-01 58369-014 from NIDDK to the US ALFSG.

P201

Postoperative resource utilization and survival among liver transplant recipients with Model for End-stage Liver Disease score ≥40: a retrospective cohort study

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Critical Care 2014, **18(Suppl 1):**P201 (doi: 10.1186/cc13391)

Introduction Cirrhotic patients with Model for End-stage Liver Disease (MELD) score ≥40 have high risk of death without liver transplant (LT) [1]. This study aimed to evaluate these patients' outcomes after transplant.
Methods The retrospective cohort included 519 adult cirrhotic patients who underwent LT at one Canadian center between 2002 and 2012. Primary exposure was severity of end-stage liver disease measured by MELD score at transplant (≥40 vs. <40) [2]. The primary outcome was duration of first ICU stay after LT [3]. Secondary outcomes were duration of first hospital stay after LT, rate of ICU readmission, re-transplant rate, and survival rates.
Results On the day of LT, 5% (28/519) of patients had a MELD score ≥40. These patients had longer first ICU stay after LT (14 vs. 2 days; P <0.001). MELD score ≥40 at transplant was independently associated with first ICU stay after transplant ≥10 days (OR, 3.21). These patients had longer first hospital stay after LT (45 vs. 18 days; P <0.001); however, there was no significant difference in the rate of ICU readmission (18% vs. 22%; P = 0.58) or re-transplant rate (4% vs. 4%; P = 1.00). Cumulative survival at 1 month, 3 months, 1 year, 3 years, and 5 years was 98%, 96%, 90%, 79%, and 72%, respectively. There was no significant difference in cumulative survival stratified by MELD score ≥40 versus <40 at transplant (P = 0.59).
Conclusion Cirrhotic patients with MELD score ≥40 at transplant utilize greater postoperative health resources; however, they derive similar long-term survival benefit with LT.
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P202

Causes and consequences of infections in patients after liver transplantation: 2-year study in the only ICU that hospitalizes these cases in Greece

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Introduction Patients with liver transplantation suffer a major risk of infections immediately after the surgery due to heavy immunosuppression, severe stress and underlying pathology. The aim of this study is to find their causes and consequences in our ICU.
Methods We studied 72 cirrhotic patients who were transplanted in our hospital during the years 2011 and 2012. The cases that developed intrahospital infection, its source and microbiology, the surgical complications, the function of the transplant, the duration of mechanical ventilation and their outcome were fully examined.
Results Twenty patients (27.1%) developed 33 episodes of infection. Among them 35% suffered from liver dysfunction, 40% took large doses of immunosuppression and 50% were re-operated. Five out of them showed signs of infection promptly after transplantation. Medium duration of mechanical ventilation was 16.5 ± 12.75 days (vs. 3.24 ± 5.5 of those without an infection) and medium length of stay was 22.14 ± 18.35 days (vs. 6.79 ± 8.86). The medium APACHE II score was 17.8 ± 5.5 (vs. 16.4 ± 4.37, P = 0.256) and medium SOFA was 11.32 ± 2.62 (vs. 9.9 ± 2.62, P = 0.054). The majority of patients was transfused with many blood units, FFP and cryoprecipitates and was hemodynamically unstable (56.3%). MELD score and MELD-Na were higher (22.57 and 27.5 relatively vs. 19.02 and 22.5). Eight cases had VAP from Gram-negative bacteria, 15 had bacteraemia (mainly Gram-negative, but also fungaemia), 10 had intraabdominal infection (most of them with two or three re-operations) and urine infection. The majority of pathogens were multidrug resistant. Regarding *Klebsiella pneumoniae* Carbapenemase, 60% was sensitive to colimycine, 20% to tobramycin, 70% to gentamycin and 40% to tygecycline. In four cases the donors had an infection that was transmitted to the recipient as much as 75%. Fourteen patients died (10 in ICU and four in the transplantation clinic) soon after with multiorgan failure.
Conclusion Patients after liver transplantation with organ dysfunction and multiple transfusions, due to surgical complications, have a major risk of developing an infection inside the ICU that affects their survival.

P203

Extracorporeal membrane oxygenation before and after adult liver transplantation: worth the effort?

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Introduction Extracorporeal membrane oxygenation (ECMO) is increasingly used for the treatment of refractory but potentially reversible respiratory and/or cardiac failure. Data on perioperative support with veno-arterial (V-A) and veno-venous (V-V) ECMO for adult liver transplant recipients are scarce [1,2]. We report our experience of ECMO support in patients with acute liver failure (ALF) as a bridge to transplant and postoperative ECMO use following complications after surgery.
Methods A retrospective study in a specialist tertiary referral ICU. Patients supported with V-V or V-A ECMO before, during, or after orthotopic liver transplant (OLT) were identified.
Results In total, four patients were supported during a 12-month period. Two patients required V-V and two patients V-A support. Two patients with ALF were bridged to OLT, one patient V-V ECMO for refractory respiratory failure and the other patient required emergency V-A support for treatment of intraoperative arrest. Both patients were successfully transplanted but died subsequently on ECMO: disseminated aspergillosis and haemophagocytic syndrome, and anoxic brain injury respectively. Two patients received postoperative ECMO support. The first was treated with V-V ECMO for refractory persistent hypoxaemia following OLT for hepato-pulmonary syndrome, the second received emergency V-A support (eCPR) following cardiac tamponade and arrest on postoperative day 2. Both patients made a full recovery.
Conclusion Emergency ECMO support before and after liver transplant is feasible. Despite the poor outcome in patients with ALF, we consider ECMO a valuable option to bridge selected patients to transplant.
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P204

Is cirrhotic cardiomyopathy a risk factor for post-reperfusion syndrome during liver transplantation?

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Critical Care 2014, **18(Suppl 1):**P204 (doi: 10.1186/cc13394)

Introduction A period of hemodynamic instability following revascularization of the liver graft during liver transplantation is

frequently observed and is termed post-reperfusion syndrome. Recent studies showed the existence of a specific heart disease associated with cirrhosis termed cirrhotic cardiomyopathy (CCM). The aim of this study was to investigate whether the CCM has an influence on the development or the severity of post-reperfusion syndrome.

Methods Fifty-two consecutive liver transplant patients were included in a retrospective observational study. The variables recorded were: age, etiology of the liver disease, MELD and MELD Na scores, the associated pathologies, the length of the QT interval, and plasma levels of brain natriuretic peptide (BNP). The patients with known renal or heart disease and the recipients of organs from extended criteria donors were excluded from the study. The QT interval was corrected for the heart rate using Bazett's formula (QTc). Statistical analysis was performed using SPSS Statistics v.19.1.

Results In our study the criteria used to define post-reperfusion syndrome relied on the hemodynamic changes that occurred at reperfusion. Preoperative echocardiography showed normal systolic and diastolic function at rest in all of the patients. For the identification of patients at risk for CCM we used two of the supportive criteria from the recent definition of CCM: prolonged QTc interval and increased BNP levels. The study group included 28 men (53.8%) and 24 women. Mean (± SD) age was 50.5 (± 11.4). Mean MELD and MELD Na scores were respectively 15.51 (± 5.43) and 18.9(± 6.22). The value of BNP correlated well with the length of the QTc interval (P = 0.005), and with MELD and MELD Na scores (P = 0.025 and P = 0.001). In our study, post-reperfusion syndrome occurred in 63.4% of the patients. We could not find a correlation between post-reperfusion syndrome and the BNP levels (P = 0.85) or the prolonged QTc interval (P = 0.38). The post-reperfusion syndrome did not correlate with the severity of the liver disease as assessed by MELD and MELD Na scores. The severity of post-reperfusion syndrome did not correlate with QTc prolongation or BNP levels.

Conclusion Reperfusion is a critical time during liver transplantation. The clinical predictors of post-reperfusion syndrome are still under debate [1]. Our study showed that the post-reperfusion syndrome is not correlated with the severity of the liver disease or with the presence of risk factors indicating CCM.

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P205

Perioperative management of patients undergoing combined heart–liver transplantation

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Introduction Combined heart–liver transplantation (CHLT) is an uncommonly performed procedure for patients with coexisting cardiac and liver disease [1]. The purpose of this study was to examine and describe the perioperative management of patients undergoing CHLT.

Methods A retrospective review was performed of patients undergoing CHLT at our institution from 1999 to 2013.

Results Twenty-seven CHLTs were performed, with 4/27 including simultaneous kidney transplantation. Familial amyloidosis was the indication for 21 CHLTs (78%), and 12 of these explanted livers were used for domino transplantations. Nineteen patients (70%) were receiving inotropic infusions at the time of organ availability. The median preoperative MELD score was 12, and elevations in preoperative international normalized ratio were due to warfarin in all but one patient. Liver transplantation immediately preceded cardiac transplantation in 2/27 cases to reduce high-titer donor-specific antibodies. Venovenous bypass was utilized in 14 operations (52%) performed with the caval interposition liver transplantation approach, cardiopulmonary bypass during liver transplantation in two cases (7%), and no bypass in 11 operations (41%) performed with a caval sparing (piggyback) surgical technique. Postoperatively, the median duration of mechanical ventilation, ICU stay, and hospital stay until discharge were 1 day, 5.5 days, and 15 days, respectively. Transfusions in the first 48 hours following CHLT were not substantial in the majority of patients. One patient died within 30 days of CHLT.

Conclusion CHLT is a life-saving operation that is performed with relatively low mortality and can be successfully performed in select patients with congenital heart disease. Patients undergoing CHLT at our institution had relatively preserved hepatic function but limited cardiac function often requiring inotropic support. Cardiac transplantation typically precedes liver transplantation during CHLT given the decreased ischemic tolerance of the cardiac graft [2]. However, liver transplantation prior to cardiac transplantation may serve to mitigate high-titer donor-specific antibodies. Various aforementioned operative approaches may be successfully utilized for the liver transplantation portion of these procedures. We attribute the favorable outcomes and perioperative courses to the multidisciplinary approach to care that CHLT patients receive at our institution.

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P206

Impaired balance between coagulation and fibrinolysis plays a prominent role in patients with sepsis

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Introduction The balance between coagulation and fibrinolysis was a prominent factor in the pathophysiology of sepsis, but this mechanism has been poorly understood. We aimed to determine whether collapsing this balance during the first day of sepsis correlates with progression of organ dysfunction and subsequent death.

Methods This study included all patients with sepsis admitted to a tertiary referral hospital in Japan. Global coagulation tests and hemostatic molecular markers such as fibrin/fibrinogen degradation products (FDP), D-dimer, thrombin–antithrombin complex (TAT) and plasmin-alpha 2 plasmin inhibitor complex (PIC) were measured within 12 hours after admission, and then SOFA and APACHE II scores and in-hospital mortality were evaluated. Patients were divided into three groups based on the levels of TAT/PIC and FDP/D-dimer and differences of clinical outcome between groups were assessed by chi-square analysis and ANOVA.

Results We enrolled 101 patients; 87 patients survived, and 14 died. Mortality was significantly higher in the high TAT/PIC group (0%, 19% and 24% for low, middle and high TAT/PIC groups, respectively; P = 0.011). In addition, SOFA and APACHE II scores were significantly higher in the low FDP/D-dimer group (APACHE II = 22.3, 18.9 and 15.3; P <0.01, SOFA = 8.6, 6.5 and 5.1; P <0.01, for low, middle and high FDP/D-dimer groups, respectively). See Figure 1.

Conclusion We demonstrated that the balance between coagulation and fibrinolysis, assessed with FDP/D-dimer and TAT/PIC ratios, was correlated with disease severity and clinical outcomes in sepsis, suggesting that impaired balance of the hemostatic system might play a pivotal role in progression of sepsis pathophysiology.

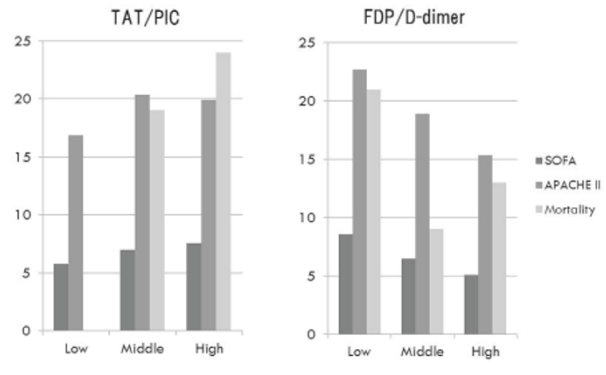

Figure 1 (abstract P206). Comparison of the characteristics between the three groups.

P207

Clinical usefulness of measurement of plasma soluble fibrin levels in critically ill patients

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Critical Care 2014, **18(Suppl 1):**P207 (doi: 10.1186/cc13397)

Introduction The soluble fibrin monomer fibrinogen complex (SF) is a complex coupling fibrin monomer and fibrinogen molecules. As the level of SF reflects the thrombin generation activity in plasma, we may estimate the early-activated state of blood coagulation by the measurement of SF. The aim of this study is to evaluate the clinical usefulness of SF for the hypercoagulated state.
Methods We measured the plasma level of SF in 63 patients within 48 hours after admission and on the 1st, 3rd, 5th and 7th days after admission. Underlying disease mainly includes sepsis, shock, and so on. According to the disseminated intravascular coagulation diagnostic criteria established by the Japanese Association of Acute Medicine, we defined the DIC group as JAAM-DIC score more than 3 within 48 hours after admission, the Subclinical DIC group as score more than 3 within 7 days beyond 48 hours after admission, and the No DIC group as score less than 4 during the entire study period. The SF value of each group was compared with the Mann–Whitney U test.
Results The SF values in the DIC and the Subclinical DIC groups were significantly higher than in the No DIC group. We created the receiver operating characteristic curve of SF value for DIC onset (JAAM-DIC score ≥4) and the SF value of 35 μg/ml was set as the cutoff SF value. The high SF group (SF ≥35 μg/ml) had significantly higher JAAM-DIC score, SOFA score and APACHE II score than the low SF group (SF <35 μg/ml). Mainly in the high SF group except DIC patients on admission, we found that SF increased before the JAAM-DIC score changed. See Figures 1 and 2.
Conclusion We think measurement of the plasma SF level may be clinically useful in evaluating the severity of critically ill patients such as those with sepsis.

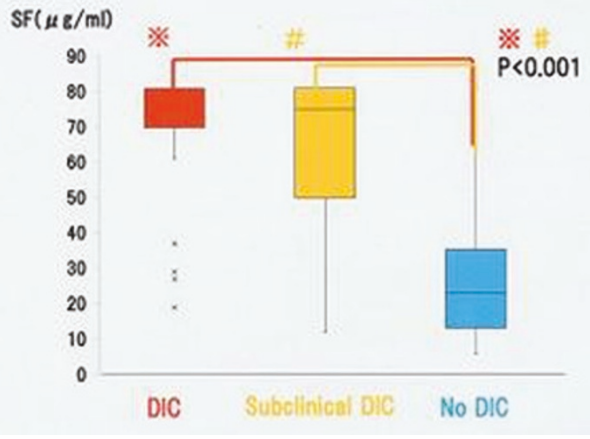

Figure 1 (abstract P207). SF values of the DIC, Subclinical DIC and No DIC groups.

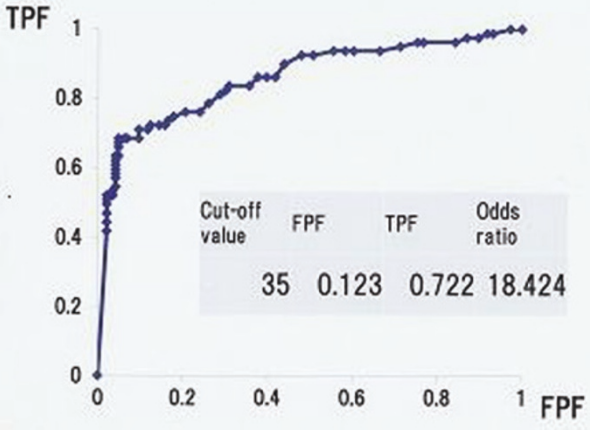

Figure 2 (abstract P207). ROC curve of the SF value for DIC.

P208

Value of microbial metabolites in blood serum as criteria for bacterial load in the pathogenesis of hemodynamic disorders in critically ill patients

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Critical Care 2014, **18(Suppl 1):**P208 (doi: 10.1186/cc13398)

Introduction Hemodynamic disorders in critically ill patients are often connected with bacterial load. Bacterial load is usually associated with bacteremia, LPS, high level of IL-6, PCT and also with aromatic microbial metabolites [1-3], and so forth. In our opinion, microbial metabolites can participate in hemodynamic disorders in critically ill patients, particularly due to their influence on NO production [4] and intestinal permeability.
Methods In a prospective study we observed critically ill patients on the day of admission to a polyvalent ICU, severe cardiac pathology was excluded. The level of phenylpropionic, phenyllactic, p-OH-phenyllactic, p-OH-phenylacetic acids and total phenylcarboxylic acids (PhCAs) were measured in blood serum using gas chromatography (GC-FID). The level of PCT and NT-proBNP were measured using Elecsys 2010. Comparison between patients with hypotension (on vasopressor support) (group A) and without (group B) was performed.
Results We studied 50 ICU patients with different diseases: pneumonia (n = 15), severe kidney failure (n = 13), abdominal surgical pathology (n = 10), alcoholic cirrhosis (n = 5), soft-tissue infection (n = 7). In group A (24/50) the median of PhCAs was 17.8 (IR 11.4 to 30.0) μmol/l, and in group B (26/50) it was 7.2 (IR 3.7 to 13.2) μmol/l, P = 0.003 (t test). In group A, all patients (with or without documented infections) had symptoms of infection manifestation [5], 20/24 (83.3%) of them died. In group B, the symptoms of infection manifestation were revealed in 12/26 (46%) cases, and the mortality was significantly lower, 3/26 (11.5%) (P <0.05). General mortality was 23/50 (46%). The profile of PhCAs differed in groups A versus B.
Conclusion The total level of PhCAs in critically ill patients with hypotension was considerably higher than in hemodynamically stable patients. The participation of microbial factor in pathogenesis of hemodynamic disorders in the presence of systemic inflammation may be validated with the load of microbial metabolites (PhCAs).
Acknowledgement This work was supported by the Russian Foundation for Basic Research (project number 13-04-01758/13).
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P209

Fibrinogen at admission is an independent predictor of mortality in severe sepsis and septic shock

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Introduction Coagulation abnormalities are common in severe sepsis or septic shock [1].
Methods A prospective observational cohort study of 100 patients above 18 years of age diagnosed with severe sepsis or septic shock on admission. The first blood sample collected on admission was analyzed. Data were collected through a predesigned *pro forma*. Those with previous history of any coagulation disorders were excluded.

Results Univariate analysis showed significant correlation of APACHE II, platelet, PT, aPTT, fibrinogen and D-dimer with mortality in patients with severe sepsis or septic shock. Multivariate analysis showed APACHE II >20 ($P = 0.001$), fibrinogen <2 ($P = 0.019$) and D-dimer >1 ($P = 0.06$) are independent predictors of mortality in severe sepsis or septic shock. See Table 1.

Table 1 (abstract P209).

Variable	Died ($n = 65$)	Survived ($n = 35$)	ARR	95% CI of ARR	*P* value
Platelet <150	33 (50.8)	10 (28.6)	1.37	0.03, 1.84	0.03
PT >16	41 (63.1)	14 (40)	1.40	1.02, 1.91	0.027
aPTT >40	41 (63.1)	14 (40)	1.40	1.02, 1.91	0.027
Fibrinogen <2	40 (61.5)	15 (42.9)	1.31	0.96, 1.70	0.07
D-dimer >1	64 (98.5)	31 (88.6)	3.37	0.48, 19.5	0.03
APACHE II >20	53 (81.5)	18 (51.4)	1.80	1.15, 2.84	0.002
Age >65	27 (41.5)	8 (22.9)	1.60	1.04, 2.46	0.02

Conclusion The fibrinogen level at admission is an independent predictor of mortality in patients with sepsis or septic shock. It also confirms correlation of other coagulation abnormalities with the outcome.

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P210

Plasma platelet-derived microparticles to platelet count ratio as a marker of mortality in critically ill patients

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Critical Care 2014, **18(Suppl 1):**P210 (doi: 10.1186/cc13400)

Introduction While the crosstalk between coagulopathy and inflammation plays a key role in the development of multiple organ dysfunction in critically ill patients, the mechanisms governing this crosstalk have yet to be established. Microparticles (MPs) are submicron vesicles shed from a variety of cells that are considered to have proinflammatory and prothrombotic properties. Although platelet-derived MPs (PDMPs) are the main form of MPs, the role of PDMPs in critically ill patients remains unclear [1]. The aims of this study were to investigate serum PDMP levels in critically ill patients and to assess their prognostic value.

Methods This study comprised 119 critically ill patients who were admitted to the ICU. PDMPs were measured by ELISA three times a week, and 372 samples were obtained. We calculated both the mean PDMP value and the mean PDMP/platelet (PDMP/PLT) ratio (converted to plasma PDMP levels per 10^4 platelets) during the course of the ICU stay. Baseline patient data, including APACHE II score, SOFA score, Japanese Association for Acute Medicine DIC score, International Society for Thrombosis and Haemostasis overt DIC score, blood coagulation parameters, C-reactive protein and lactate, were collected at the time of admission to the ICU. The primary outcome was in-hospital mortality. Potential predictors were analyzed for possible association with outcomes.

Results The mean PDMP/PLT ratio was significantly different when comparing hospital survivors ($n = 98$; median, 1.95) and nonsurvivors ($n = 21$; median 8.40; $P = 0.00$). The mean PDMP/PLT ratio was significantly higher in patients with (median, 4.28) than in those without DIC (median, 1.57; $P = 0.00$). In DIC patients, the mean PDMP/PLT ratio was significantly higher in nonsurvivors (median, 9.39) than in survivors (median, 3.65; $P = 0.02$). Multivariate logistic regression analysis revealed that both the mean PDMP/PLT ratio ($P = 0.04$) and APACHE II score ($P = 0.00$) were independently associated with in-hospital mortality. The AUCs were calculated as 0.768 ± 0.073 for the mean PDMP/PLT ratio ($P = 0.00$) and 0.811 ± 0.048 for the APACHE II score ($P = 0.00$).

Conclusion The PDMP/PLT ratio is a good predictor of in-hospital mortality in critically ill patients, especially in patients with DIC.

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P211

Receptor for advanced glycation end products axis in critically ill patients

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Critical Care 2014, **18(Suppl 1):**P211 (doi: 10.1186/cc13401)

Introduction Systemic inflammation caused by infection or trauma often leads to adverse outcome in critically ill patients. Binding of ligands to the receptor for advanced glycation end products (RAGE) activates several pathways, including the nuclear factor-kappa B pathway, which generates inflammatory cytokines, proteases and oxidative stress. RAGE activation has been suggested to link amplification and perpetuation of inflammation to subsequent organ damage and adverse outcome in sepsis, acute lung injury and myocardial dysfunction [1]. The soluble receptor, sRAGE, is thought to act as a decoy, thus protecting against further RAGE activation. High mobility group box 1 (HMGB1) is a nuclear protein that is released during cellular stress and damage. S100A12 is a neutrophil-derived protein that acts as a proinflammatory danger signal. Both are ligands for RAGE. We hypothesized that excessive RAGE activation is linked to adverse outcome in critically ill patients and that a different pattern of RAGE activation and inflammation may be present in patients according to underlying pathology.

Methods We measured sRAGE, HMGB1 and S100A12 serum levels upon admission, day 7 and the last day in the ICU in 405 critically ill surgical patients who needed intensive care for at least 7 days and in 69 matched healthy controls. We assessed the relation of these levels with clinical complications and outcome, in comparison with C-reactive protein (CRP) as a routinely measured clinical parameter of inflammation.

Results Upon ICU admission, levels of sRAGE, HMGB1, S100A12 and CRP were higher as compared with healthy levels. HMGB1, S100A12 and CRP remained elevated throughout the ICU stay but sRAGE decreased to levels lower than in healthy volunteers by day 7. sRAGE and CRP showed distinct time profiles during the ICU stay in patients undergoing cardiac versus other surgery and in patients with versus without sepsis upon admission. Elevated sRAGE upon admission, unlike CRP, was associated with need for renal replacement therapy, liver dysfunction, circulatory failure and mortality. Except for mortality, these associations remained in multivariate logistic regression analysis correcting for baseline risk factors.

Conclusion Critical illness alters several components of the RAGE axis. Elevated sRAGE levels upon admission to the ICU were associated with adverse outcome, independent of baseline pathology.

Reference

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P212

Usefulness of the endotoxin activity assay as a biomarker to assess severity in ICU patients

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Critical Care 2014, **18(Suppl 1):**P212 (doi: 10.1186/cc13402)

Introduction Endotoxin is a component of the membrane of Gram-negative bacteria and plays a key role in the pathogenesis of sepsis [1]. Measurement of endotoxin levels in patient blood is important for the early diagnosis of and appropriate determination of the treatment strategy for sepsis. The aim of this study was to investigate the prevalence of endotoxemia in Japanese critically ill patients using

the endotoxin activity assay (EAA), a newly developed rapid assay of endotoxin. Blood endotoxin levels (EA levels) of 314 patients admitted to our university hospital ICU were measured within 24 hours from admission, and their correlation with disease severity and outcome was examined.

Methods The study is a single-center retrospective analysis of critically ill patients admitted to our university hospital ICU from November 2006 to March 2012. All patients whose EA and procalcitonin levels were measured and severity criteria of disease recorded were enrolled. A total of 314 patients were analyzed.

Results The mean ± SD of all ICU-admitted patients (n = 314) was 0.39 ± 0.25, and that of healthy volunteers (n = 61) was 0.10 ± 0.09. The mean APACHE II score at admission increased in parallel with increased EA levels. The mean (± SD) APACHE II score in the very low group of patients (EA <0.2) was 17.3 ± 8.9, while that in the low group (0.2 ≤EA <0.4) was 20.6 ± 9.2; it was 22.6 ± 8.1 in the intermediate group (0.4 ≤EA <0.6) and 25.3 ± 8.5 in the high group (0.6 ≤EA). The difference between the groups was statistically significant. The difference between the groups was statistically significant. The percentages of patients diagnosed with severe sepsis or septic shock were 19.3%, 34.5%, 50.0% and 81.3% in the very low, low, intermediate and high groups, respectively.

Conclusion Our patients' EA levels were significantly correlated with disease severity criteria and 28-day mortality of the patients. When the EA level and procalcitonin level were used concomitantly, disease severity could be assessed more precisely than when either marker was used alone. These results suggest that the EA level is a useful marker for disease severity assessment and outcome prediction in critically ill patients.

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P213

Usefulness of presepsin and procalcitonin levels in the diagnosis of sepsis in patients with acute kidney injury

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Introduction The presepsin (PSEP) and procalcitonin (PCT) levels are useful biomarkers for differentiating between sepsis and non-infectious systemic inflammatory response syndrome (SIRS). The PSEP and PCT levels have been reported to be abnormally high in patients with chronic renal failure. However, there have been no significant investigations regarding the relationships between these biomarkers and the presence of acute kidney injury (AKI) in the diagnosis of sepsis. The purpose of this study was to clarify the diagnostic accuracy of PSEP and PCT levels in patients with AKI.

Methods This study was conducted as a single-center retrospective study. Blood samples were collected from patients immediately after admission to the Department of Emergency and Critical Care Medicine, Fukuoka University Hospital between June 2010 and August 2013. We enrolled 629 patients in whom both the PSEP and PCT levels were measured on admission. We classified the patients into two groups according to the RIFLE criteria (Risk, Injury, Failure, Loss of kidney function and End-stage kidney disease: Loss and ESKD): the AKI group and the non-AKI group. The patients in the AKI group were further classified into the sepsis group and the nonsepsis group according to each stage of AKI. We subsequently investigated the diagnostic accuracy of the PSEP and PCT levels for detecting sepsis in these groups.

Results We evaluated 254 patients with AKI and 375 patients without AKI. The AKI group included 103 patients who met the Risk criteria, 65 who met the Injury criteria, 66 who met the Failure criteria and 18 who met the Loss and ESKD criteria. The mean PSEP and PCT levels were significantly higher in the sepsis group than in the nonsepsis group among the non-AKI patients and those meeting the Risk, Injury and Failure criteria (P <0.01). The diagnostic accuracy of the PSEP and PCT levels for detecting sepsis was determined according to a ROC analysis; the area under the curve (AUC) for the PSEP and PCT levels was 0.883 and 0.870, respectively, in the non-AKI group. In addition, the AUC values for the PSEP and PCT levels in the Risk, Injury and Failure groups were 0.843 and 0.843, 0.818 and 0.922 and 0.669 and 0.804, respectively. In the Failure group, the AUC for the PSEP and PCT levels was 0.828 and 0.852, respectively, after dividing the PSEP and PCT levels by the creatinine (Cr) level. The optimal cutoff values for the PSEP and PCT levels for diagnosing sepsis were 409 pg/ml/Cr (sensitivity: 66.0%, specificity: 91.7%) and 1.5 ng/ml/Cr (sensitivity: 63.6%, specificity: 95.8%), respectively.

Conclusion The diagnostic accuracy of PSEP and PCT levels for detecting sepsis decreased in the Failure group; however, the value of these parameters for diagnosing sepsis in patients meeting the Failure criteria increased after dividing them by the Cr level.

P214

Differentiating sepsis from non-infective systemic inflammatory response syndrome: comparison between C-reactive protein and leptin

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Critical Care 2014, **18(Suppl 1):**P214 (doi: 10.1186/cc13404)

Introduction Differentiation of sepsis from non-infectious SIRS is important in improving sepsis outcome. We intended in this study to evaluate the role of serum leptin and to compare it with CRP in differentiating sepsis from non-infectious SIRS.

Methods We included 30 patients with SIRS. According to the presence or absence of infection, our patients were classified into the SIRS group and the sepsis group. Leptin and CRP were evaluated in all patients on admission, day 2 and day 4.

Results Our patients had mean age of 52.3 ± 18.6 years, 10 males (33.3%). There were no significant differences regarding baseline demographic and clinical data apart from blood pressures, which were lower in sepsis group. Serum leptin on day 2 only was higher in the sepsis group (44.2 ± 17.7 μg/l vs. 31.1 ± 2.1 μg/l, P = 0.008) with no difference on days 0 and 4 of admission. We detected a serum leptin level of 38.05 μg/l on day 2 to be 93% sensitive and 100% specific to diagnose sepsis. The three serum CRP levels were higher in the sepsis group compared with the SIRS group (61.2 ± 9 mg/l vs. 48.9 ± 7.1 mg/l, P <0.001 on day 0, 71.5 ± 9.6 mg/l and 196.8 ± 39.8 mg/l in the sepsis group vs. 56.9 ± 8 mg/l and 73.7 ± 32.5 mg/l in the SIRS group for days 2 and 4 respectively, P <0.001 for both). We found a CRP of 67.5 mg/l on day 2 having 87% sensitivity and 93% specificity for the diagnosis of sepsis.

Conclusion We concluded that although serum leptin may not be beneficial in early differentiation between sepsis and non-infectious SIRS on admission, it may be highly specific on the second day.

P215

Use of procalcitonin and white blood cells as combined predictors of infection in cardiac surgery patients

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Introduction The aim of this study is to identify a marker able to predict sepsis in cardiac surgery patients and to differentiate SIRS from infectious and non-infectious origin. The occurrence of sepsis after cardiac surgery increases the mortality risk. Sepsis may be mistaken for the cardiac surgery-associated systemic inflammatory response syndrome (SIRS) [1].

Methods A prospective, observational study was carried out to compare procalcitonin (PCT), C-reactive protein (CRP) and white blood cells (WBCs) during the first 10 postoperative days after cardiac surgery with cardiopulmonary bypass (CPB) between 122 patients with infection (Infection group) and 301 without (Control group) to identify predictors of infection.

Results The WBC and PCT median values were significantly (P <0.05) higher in infected than control patients, during 10 postoperative days and on the third and fourth postoperative day, respectively, both variables showing a peak at 3 days in infected patients. The number of times that the WBC count surpassed its second postoperative median value (13,000 cells/mm^3) during the first 3 postoperative days plus the number of times that PCT surpassed its own (1.7 ng/ml) was a parameter (ranging from 1 to 6) with three categories (R1= surpassed zero to one time; R2 = two to three times; R3 = four to six times) significantly associated with risk of infection, which increased with increasing number of times (R2: OR = 2.48 (1.32 to 4.65) and R3: OR = 7.06 (3.17 to 15.71)).
Conclusion Daily assessment of WBC and PCT during the first 3 postoperative days may be of value to diagnose and predict infection in cardiac surgery patients.
Reference

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P216

Single pro-adrenomedullin determination in septic shock and 28-day mortality

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Critical Care 2014, **18(Suppl 1):**P216 (doi: 10.1186/cc13406)

Introduction The early phase of septic shock is dominated by severe alterations of the cardiovascular system. The prognostic value of pro-adrenomedullin (pADM), a vasoactive pro-hormone, measured within 24 hours from septic shock onset was assessed.
Methods A prospective, observational study in 100 patients >18 years with septic shock in a polyvalent ICU of a university hospital. Demographic, clinical parameters and pADM, C-reactive protein (CRP) and procalcitonin (PCT) were studied during the first 24 hours after admission in 2011. Descriptive and comparative statistical analysis was performed using the statistical software packages StatSoft STATISTICA 7.1 and MedCalc 9.2.1.0.
Results We analyzed 100 consecutive episodes of septic shock in the ICU. The median age of the study sample was 64 years, interquartile range 16.8 years, 59% were men; the main sources of infection were respiratory tract (48%) and intra-abdominal (24%). The 28-day mortality was 36%. The profile of dead patients showed significantly higher clinical severity scores, APACHE II (27 vs. 25; P <0.001) and SOFA (12 vs. 10; P <0.001). The area under the curve was 0.72 for pADM, significantly higher than those for CRP (0.62) and PCT (0.65), but similar to those for APACHE II score (0.69) and SOFA score (0.78). Kaplan–Meier survival analysis was significant (P = 0.0012) for patients with pADM <1.2 nmol/l. Cox regression analysis also showed statistical significance (P = 0.0004) and a likelihood ratio =1.26 per each 1 nmol/l increase in pADM.
Conclusion Pro-adrenomedullin is an important prognostic biomarker of survival when measured on admission of septic shock patients to the ICU.

P217

Surfactant protein A: a candidate predictive biomarker of mortality in acute respiratory distress syndrome in sepsis

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Critical Care 2014, **18(Suppl 1):**P217 (doi: 10.1186/cc13407)

Introduction Prediction of mortality in septic acute respiratory distress syndrome (ARDS) is a problem of great significance. The aim of this study was to investigate the role of surfactant protein A (SPA) as a candidate predictive biomarker of mortality in ARDS.
Methods The observational study in ICU ventilated septic patients with peritonitis (65%), pancreonecrosis (20%) and mediastinitis (15%) was performed in 2010 and 2013. ARDS was diagnosed and staged according to the V.A. Negovsky Research Institute criteria [1,2] and the Berlin definition. Plasma SPA was measured on ARDS diagnosis (day 0) and days 3 and 5 by the immunoenzyme essay (BioVendor, USA). Patients were treated according to the international guidelines. Data were statistically analyzed by STATISTICA 7.0, ANOVA method, and presented as median and 25th to 75th percentiles, ng/ml; P <0.05 was considered statistically significant. Areas under the receiver operating curves were calculated.
Results Eighty-five patients (out of 300 screened) were enrolled in the study according to the inclusion/exclusion criteria. Patients were assigned into groups: ARDS (n = 50, 48 ± 5.7 years old, M/F 35/15, mortality 26%) and noARDS (n = 35, 46 ± 8.7 years old, M/F 30/5, mortality 23%). Groups were comparable in APACHE II scores. In the ARDS group SPA was higher at all points than in the noARDS group (day 0: 32.6, 25 to 75 IQR 18.2 to 60.7 vs. 23.4, 25 to 75 IQR 17.8 to 28.6; day 3: 31.5, 25 to 75 IQR 20.9 to 31.5 vs. 24.6, 25 to 75 IQR 19.7 to 24.6; day 5: 32.5, 25 to 75 IQR 17.3 to 66.4 vs. 22.5, 25 to 75 IQR 13.4 to 29.5, P <0.05). The plasma SPA was significantly lower in surviving versus dead patients with ARDS (day 0: 20.9, 25 to 75 IQR 13.0 to 35.7 vs. 45.7, 25 to 75 IQR 23.5 to 67.9; day 3: 25.5, 25 to 75 IQR 11.8 to 35.5 vs. 45.0, 25 to 75 IQR 29.6 to 68.4; day 5: 24.5, 25 to 75 IQR 11.4 to 33.6 vs. 49.6, 25 to 75 IQR 31.3 to 79.0, P <0.05). Plasma SPA on day 0 had a good capacity for prediction of mortality in ARDS patients: SPA on day 0 ≥38.8 ng/ml yielded a sensitivity of 65% and specificity of 80% (AUC 0.74; 95% CI 0.577 to 0.866; P = 0.0026).
Conclusion Plasma SPA level ≥38.8 ng/ml on the day of ARDS diagnosis is a sensitive and specific candidate biomarker of mortality prediction in ARDS septic patients.
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P218

Club Cell protein: a candidate diagnostic biomarker of *Pseudomonas aeruginosa* nosocomial pneumonia

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Critical Care 2014, **18(Suppl 1):**P218 (doi: 10.1186/cc13408)

Introduction Early etiological diagnosis of nosocomial pneumonia (NP) determines prompt targeted treatment. The aim of this study was to investigate the role of Club Cell protein (CCP) as a candidate diagnostic biomarker of *Pseudomonas aeruginosa* (PA) NP.
Methods The observational study in ICU ventilated septic patients with peritonitis (65%), pancreonecrosis (20%) and mediastinitis (15%) was performed in 2010 and 2013. Diagnosis of NP was made according to the standard clinical criteria. Associations of multiresistant Gram-negative bacteria were detected in sputum of all patients. PA was detected in 75% of patients. Plasma CCP was measured on the day of NP diagnosis (day 0) and days 3, 5 and 7 by the immunoenzyme essay (BioVendor, USA). Data were statistically analyzed by STATISTICA 7.0, ANOVA method, and presented as Me and 25 to 75 percentiles, ng/ml; P <0.05 was considered significant. Areas under the receiver operating curves (ROC) were calculated.
Results Ninety patients (out of 350 screened) were enrolled in the study according to the inclusion/exclusion criteria. Patients were assigned to groups: NP (n = 50, 45 ± 4.3 years old, M/F 36/14) and noNP (n = 40, 48 ± 7.2 years old, M/F 30/10). Groups were comparable in APACHE II and CPIS scores. In patients with PA NP (n = 30), plasma CCP was significantly lower at all points than in the patients with no PA detected (n = 20; Figure 1). Plasma CCP on day 0 had a good capacity for the diagnosis of PA NP: CCP on day 0 ≤17.5 ng/ml yielded a sensitivity of 86.5% and specificity of 66.7% (AUC 0.74; 95% CI 0.630 to 0.829; P = 0.0001; Figure 2).
Conclusion Plasma CCP level ≤17.5 ng/ml is a sensitive and specific candidate diagnostic biomarker of PA NP.

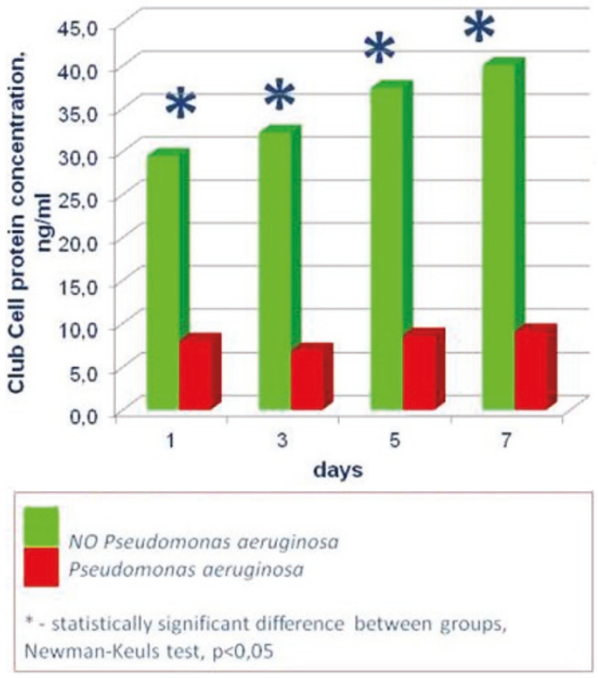

Figure 1 (abstract P218). Club Cell protein concentration in patients with *Pseudomonas aeruginosa* NP.

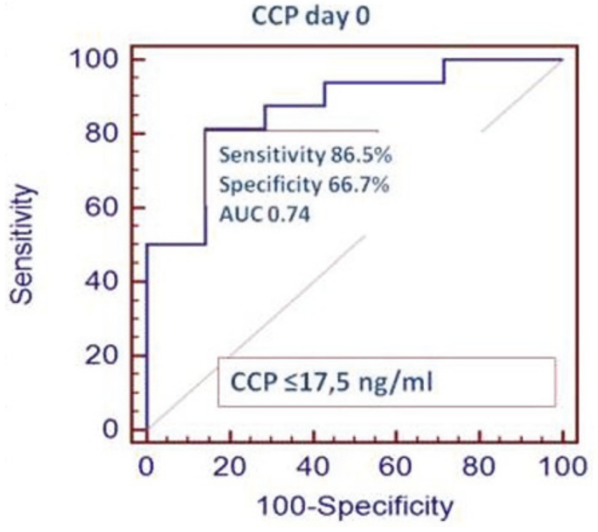

Figure 2 (abstract P218). ROC curve for Club Cell protein (day 0) for the diagnosis of *Pseudomonas aeruginosa* NP.

P219

Plasma cholinesterase activity as diagnostic marker for systemic inflammation

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Critical Care 2014, **18(Suppl 1):**P219 (doi: 10.1186/cc13409)

Introduction Systemic inflammation is a generalized response to internal or external inflammatory stimuli often resulting in multiple organ failure. Therefore, early diagnosis of systemic inflammation would be of great therapeutic and prognostic importance. Various inflammation biomarkers have been used in clinical and experimental practice, but a definitive diagnostic tool for an early detection of systemic inflammation remains to be identified. The neurotransmitter acetylcholine (Ach) has been shown to play an important role in the inflammatory response. Serum cholinesterase (butyrylcholinesterase (BChE)) is synthesized in the liver and acts as the major Ach hydrolyzing enzyme in plasma. Hence, BChE activity has been widely used as a biomarker for liver function. However, the role of this enzyme in the inflammatory pathomechanism has not yet been fully understood. Here, we describe a strong correlation between the BChE activity and the systemic inflammatory response.

Methods In this study we measured BChE activity in healthy subjects and in critically ill patients, clinically diagnosed with systemic inflammation or sepsis. Furthermore, we measured the levels of routine inflammation biomarkers and liver function parameters in blood of critically ill patients. Data were statistically analyzed using unpaired Student *t* test, Pearson correlation or ANOVA followed by Dunnett's *post hoc* analysis. $P < 0.05$ was considered statistically significant.

Results We found that the activity of BChE in patients with systemic inflammation was dramatically reduced in comparison with healthy subjects and negatively correlated with the serum levels of conventional inflammatory biomarkers. BChE synthesis depends on hepatic function. Surprisingly, the observed reduction in the BChE activity during systemic inflammation does not correlate with liver failure.

Conclusion Our results suggest that BchE activity might play an important role in the diagnosis of systemic inflammation independent of overall hepatic function.

P220

Lymphopenia as a predictor of bacteremia in the emergency department

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Critical Care 2014, **18(Suppl 1):**P220 (doi: 10.1186/cc13410)

Introduction Bloodstream infection (BSI) is associated with a reduction in circulating lymphocytes. Lymphopenia has been proposed as an early marker of BSI in pyrexial adults in the emergency department (ED) setting [1]. The aim of this study was to compare lymphocyte

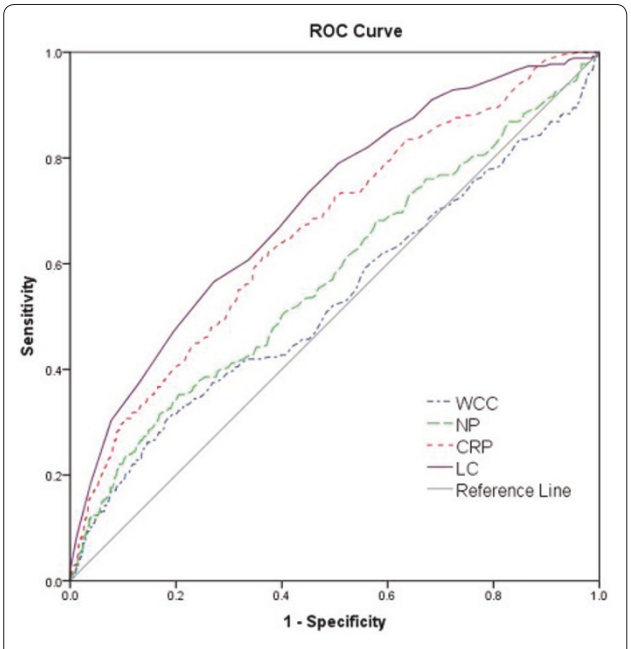

Figure 1 (abstract P220). ROC curve comparing blood test parameters in predicting bacteremia.

count with conventional markers in patients presenting to the ED of a UK hospital with suspected sepsis.
Methods A retrospective review was undertaken of adult patients presenting to the ED (annual census 90,000) with pyrexial illness over a 12-month period, 2011 to 2012. Data included white cell count (WCC), neutrophil count (NC), lymphocyte count (LC) and C-reactive protein (CRP). The results were compared. Sensitivity and specificity were calculated for each parameter and receiver operating characteristic (ROC) curves were constructed.
Results A total of 2,515 patient records were screened. Patients on chemotherapy were excluded, as were those under 18 years old. In total, 1,954 patients (53% female, median age 66 years) were included in the analysis. Blood cultures were positive in 13.7% of cases. There were significant differences between all variables measured, with the exception of WCC, between bacteremic and nonbacteremic patients. The area under the curve of 70.8 was best for lymphocyte count (Figure 1).
Conclusion In adult patients presenting to the ED with pyrexial illness, lymphopenia predicts bacteremia better than the usual markers of infection.
Reference
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P221

Pre-analytic factors and initial biomarker levels in community-acquired pneumonia patients

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Critical Care 2014, **18(Suppl 1):**P221 (doi: 10.1186/cc13411)

Introduction Blood biomarkers are increasingly used to diagnose, guide therapy in, and risk-stratify community-acquired pneumonia (CAP) patients in emergency departments (EDs). How pre-analytic factors affect these markers' initial levels in this population is unknown.
Methods In this secondary analysis of consecutive ED patients with CAP from a large multicentre antibiotic stewardship trial [1], we used adjusted multivariate regression models to determine the magnitude and statistical significance of differences in mean baseline concentrations of five biomarkers (procalcitonin (PCT), C-reactive protein (CRP), white blood cell count, proadrenomedullin (ProADM), copeptin) associated with six pre-analytic factors (antibiotic or corticosteroid pretreatment, age, gender, chronic renal failure or liver insufficiency).
Results Of 925 CAP patients (median age 73 years, 58.8% male), 25.5% had antibiotic pretreatment, 2.4%, corticosteroid pretreatment, 22.3% chronic renal failure, and 2.4% chronic liver insufficiency. Differences associated with pre-analytic factors averaged 6.1 ± 4.6%; the three largest statistically significant changes (95% CI) were: PCT, +14.2% (+2.1 to +26.4%, $P = 0.02$) in patients with liver insufficiency; ProADM, +13.2% (+10.2 to +16.1%, $P < 0.01$) in patients with age above median; and CRP, –12.8% (–25.4 to –0.2%, $P = 0.05$) with steroid pretreatment.
Conclusion The influence of pre-analytic factors on the examined biomarkers is marginal and not clinically relevant. Our observations reinforce the concept of using biomarkers in algorithms with widely-separated cutoff values and overruling criteria considering the entire clinical picture, without adjustment for pre-analytic factors.
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P222

Use of procalcitonin for identification of postoperative complications after coronary artery bypass surgery with cardiopulmonary bypass

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Critical Care 2014, **18(Suppl 1):**P222 (doi: 10.1186/cc13412)

Introduction The values of C-reactive protein (CRP) and procalcitonin (PCT) were investigated to determine their effects on postoperative complications in patients with or without systemic inflammatory response syndrome (SIRS).
Methods In 183 patients, in a prospective observational study, serum CRP and PCT values were collected every day starting on postoperative day 1 through day 5. The definition of SIRS includes two or more of the following: temperature >38 or <36°C; heart rate >90 beats/minute; respiratory rate >20/minute; arterial carbon dioxide pressure <32 mmHg; white blood cell count >12,000/mm^3 and <4.00/mm^3. The ability of PCT to predict sepsis and other postoperative complications were determined by performing receiver operative characteristic curve analysis.
Results All patients were divided *post hoc* into patients with SIRS (Group 1, $n = 83$) and patients without SIRS (Group 2, $n = 100$). A PCT threshold value of 2.79 ng/ml on postoperative day 1 was able to discriminate postoperative complications in patients with or without SIRS with a sensitivity of 82.5% and a specificity of 70% (area under curve: 0.76, $P < 0.01$).
Conclusion (1) Serum PCT values increased significantly after cardiopulmonary bypass in the SIRS group in comparison with patients without SIRS on postoperative day 1 and remain elevated until postoperative day 5. (2) Serum CRP values also follow a similar pattern, but a CRP threshold value was not obtained to differentiate between postoperative complications in patients with or without SIRS. A PCT threshold value of 2.79 ng/ml on postoperative day 1 is a valuable marker to discriminate between patients with or without SIRS.

P223

Altered T-cell repertoire diversity in septic shock patients

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Critical Care 2014, **18(Suppl 1):**P223 (doi: 10.1186/cc13413)

Introduction The occurrence of sepsis-induced immune suppression is associated with multiple organ dysfunctions, although the exact role of T-cell malfunction is obscure. We investigated the impact of sepsis on the adaptive immune system and to monitor T-cell receptor (TCR) diversity.
Methods TCR diversity was analyzed in peripheral blood mononuclear cells (PBMCs) isolated from septic shock patients at three time points (days 1, 3 and 7 after diagnosis of septic shock). TCR diversity was measured in genomic DNA isolated from PBMCs using the Human Immun TraCkeRb test (ImmunID Technologies, Grenoble, France) [1]. Multi-N-plex PCR was performed using a primer specific to a V gene family and several primers specific to J segments. The signal is measured as a function of the fluorescence intensity of the reference marker. Rearrangement validation and map generation were detected and analyzed using the Constel'ID software (ImmunID Technologies). HLA-DR expression on CD14 cells was measured by flow cytometry.
Results TCR diversity was markedly decreased in septic patients at day 1 compared with healthy volunteers. A recovery of TCR diversity was observed at days 3 and 7 except for dead patients. HLA-DR expression was significantly decreased in septic patients at day 1. The total lymphocyte count reduced in septic patients at day 1, but the lymphocyte count recovered at days 3 and 7 except for dead patients.
Conclusion We observed a lower TCR diversity and lymphopenia in the early stages of septic shock. A quick recovery of TCR diversity and lymphocyte count was observed in live patients. On the other hand, dead patients stayed on the lower level over the course of the study. These results suggest that altered TCR diversity and lymphopenia might participate in increased mortality and susceptibility to secondary nosocomial infections.
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P224

Association between DNA haplogroups and severe sepsis in patients who underwent major surgery

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Critical Care 2014, **18(Suppl 1):**P224 (doi: 10.1186/cc13414)

Introduction The aim of this study was to analyze whether mitochondrial DNA haplogroups are associated with severe sepsis and

mortality after major surgery in European populations. Mitochondrial DNA (mtDNA) variants may play an important role for predicting clinical outcome in sepsis [1].
Methods We carried out a case–control study on 240 septic patients (severe sepsis or septic shock; Case group) and 267 patients with systemic inflammatory response syndrome (SIRS; Control group). Furthermore, a longitudinal substudy for analyzing survival was performed in septic patients. mtDNA genotyping was performed by Sequenom's MassARRAY platform.
Results Regarding cardiac surgery, patients with clusters JT and haplogroup J had higher likelihoods of sepsis than patients with clusters HV (OR = 2.76 (95% CI = 1.27; 6.02); $P = 0.010$) and haplogroup H (OR = 3.68 (95% CI = 1.17; 11.54); $P = 0.026$), respectively. No significant association was found for abdominal surgery. When analyzing survival, 45.4% patients died with a survival median of 39 (95% CI = 31.4; 46.62) days. When the clusters were analyzed for all patients, 41% (55/134) of patients within cluster HV died versus 71.4% (10/14) patients within cluster IWX ($P = 0.018$). The adjusted Cox regression showed that patients within cluster IWX had a higher risk of dying than patients within cluster HV (hazard ratio (HR) = 2.24 (95% CI = 1.10; 4.56); $P = 0.027$). No significant association between haplogroups and mortality was found when patients were stratified by the type of surgery.
Conclusion European mitochondrial haplogroups are associated with sepsis development in patients who underwent major cardiac surgery, but not in patients who underwent major abdominal surgery. Besides, mtDNA haplogroups also influence mortality. Haplogroups HV and H were related to low risk of sepsis and death, while JT and J were related to high risk of sepsis, and IWX was associated with death.

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P225

T-cell receptor activation-associated cytokine release is impaired in septic patients with faecal peritonitis

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Critical Care 2014, **18(Suppl 1):**P225 (doi: 10.1186/cc13415)

Introduction Sepsis is associated with immune hyporesponsiveness but the immunological processes behind this are ill defined.
Methods This study quantified differences in plasma concentrations of cytokines between septic patients with faecal peritonitis, age and gender-matched surgical patients (without sepsis) and age and gender-matched healthy participants. In addition, cytokine levels were measured in supernatant from peripheral blood mononuclear cells stimulated with anti-CD3 and anti-CD3+anti-CD28, incubated for 4 days. Cytokine concentrations of IL-1β, IL-5, IL-6, IL-8, IL-10, IL-13, IL-17A, IFNγ and TNFα were determined by multiplex cytometric bead array.
Results Plasma levels of IFNγ and IL-13 were lower in septic patients compared with healthy participants. In contrast, plasma levels of IL-6 (see Figure 1) and IL-8 were increased in septic patients compared with both surgical patients and healthy participants. Plasma levels of IL-10 were significantly higher only in comparison with surgical patients. Following incubation with anti-CD3 and anti-CD3+anti-CD28, concentrations of IL-1β, IL-5, IL-6 (see Figure 1), IL-13, IL-17A, IFNγ and TNFα were markedly decreased in samples from septic patients. In addition, stimulation with anti-CD3+anti-CD28 resulted in lower production of IL-10 in septic patients. Lower concentrations of IL-8 were detected in septic patient samples stimulated with only anti-CD3. We found cytokine levels of IL-12p70 remained unaffected across all groups and stimuli.
Conclusion We demonstrated a proinflammatory cytokine profile in blood from septic patients, preceding a pan downregulation of all assessed cytokines following *in vitro* T-cell stimulation. To our knowledge, this study is the first to perform an immune functional assay across these three groups.

P226

Activated protein C consumption and coagulation parameters in severe sepsis and septic shock

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Critical Care 2014, **18(Suppl 1):**P226 (doi: 10.1186/cc13416)

Introduction Activated protein C (APC) deficiency is prevalent in severe sepsis and septic shock patients. The aim of the study was to relate the anticoagulation activity evaluated by APC with other coagulation parameters adjusted to 28-day mortality.
Methods A cohort study of 150 critically ill adults. Age, sex, sources of infection and coagulation markers within 24 hours from severe sepsis or septic shock onset, defined according to Surviving Sepsis Campaign (SSC) criteria, were studied. We analyzed APC activity using a hemostasis laboratory analyzer (BCS® XP; Siemens). A descriptive and comparative statistical analysis was performed using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA).
Results We analyzed 150 consecutive episodes of severe sepsis (16%) or septic shock (84%) admitted to the UCI. The median age of the study sample was 64 (interquartile range (IQR): 22.3 years; male: 60%). The main sources of infection were: respiratory tract 38%, intra-abdomen

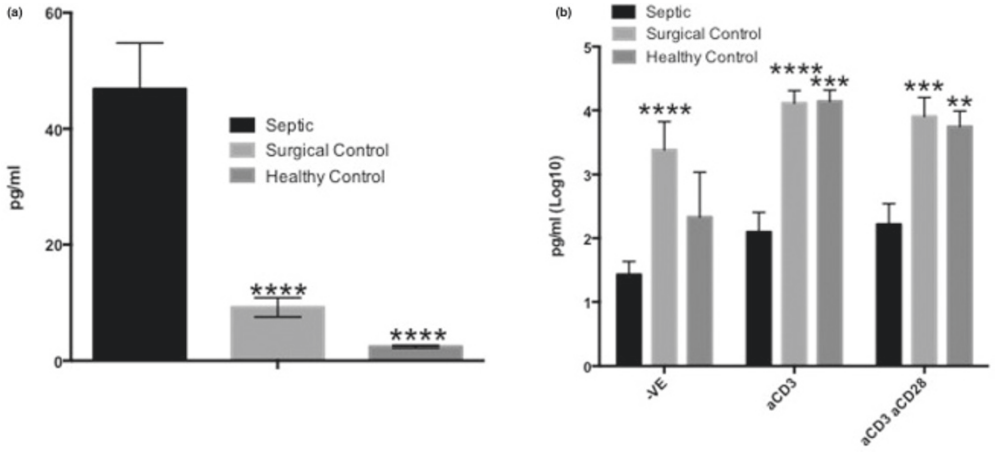

Figure 1 (abstract P225). Concentration of IL-6 in plasma on day 0 **(a)** and supernatant on day 4 **(b)**.

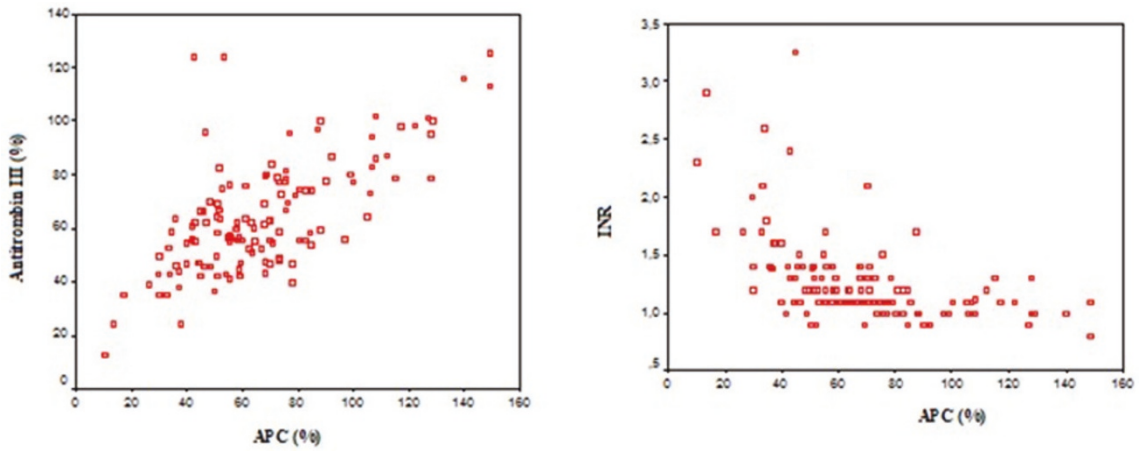

Figure 1 (abstract P226). Relationship between activated protein C and antithrombin III and INR.

45%, and 70.7% had medical pathology. The 28-day mortality was 22.7%. Nonsurvivors had a significantly higher consumption of APC than survivors, 56% (IQR: 38.5) versus 68.6 (IQR: 41.4); $P = 0.023$. The profile of lower levels of APC was a surgery patient with septic shock, neurological focus or catheter-related infection and Gram-negative pathogens from blood cultures. Spearman's showed relationship with antithrombin III, $r = 0.674$ ($P < 0.001$) and International Normalized Ratio (INR), $r = -0.611$ ($P > 0.001$). See Figure 1.

Conclusion Low levels of PC are associated with poor outcome and severity in severe sepsis, and it is well correlated with antithrombin III and INR.

P227

Flow-cytometric analysis in traumatic brain injury to evaluate immunosuppression

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Introduction Flow-cytometric analysis is still restricted to cancer and immunocompromised patients. There are no clinical studies that evaluate the immunological changes in traumatic brain injury (TBI) patients. The objective of this study is to determine whether patients with severe TBI (GCS <9) manifest early (<48 hours after injury) signs of immunosuppression and whether this condition increases the incidence of infection during the ICU stay.

Table 1 (abstract P227). Collected data

Age (years), mean ± SD	55.43 ± 23.12
Sex (M/F)	44/10
Body mass index, mean ± SD	25.51 ± 2.69
ISS, mean ± SD	29.04 ± 26.57
RTS, mean ± SD	5.76 ± 1.53
TRISS, mean ± SD	68.73 ± 28.77
Admission SAPS II, mean ± SD	44.96 ± 14.87
Admission GCS, mean ± SD	7.63 ± 3.88
Flow-cytometric analysis day (days), mean ± SD	1.69 ± 3.34
Discharge GCS, mean ± SD	10.48 ± 3.19
ICU LOS, mean ± SD	10.67 ± 8.08

Table 2 (abstract P227). Flow-cytometric data

		Normal value
WBC ($\times 10^9$/l)	10.67 ± 4.82	4 to 10
Total lymphocytes ($\times 10^6$/l)	1,123.15 ± 547.02	1,200 to 3,000
$CD3^+$ lymphocytes ($\times 10^6$/l)	67.11 ± 11.86	1,100 to 1,700
$CD3^+CD4^+$ lymphocytes ($\times 10^6$/l)	493.07 ± 313.92	600 to 1,400
$CD3^+CD8^+$ lymphocytes ($\times 10^6$/l)	250.65 ± 171.94	300 to 900
$CD4^+DR^+$ lymphocytes ($\times 10^6$/l)	23.19 ± 15.09	
$CD8^+DR^+$ lymphocytes ($\times 10^6$/l)	16.26 ± 20.83	

Methods We retrospectively analyzed data from 54 patients, including 10 patients with isolated brain injury and 44 patients with brain and extracranial injuries. The flow-cytometric analysis was performed within 48 hours of trauma. Collected data are shown in Table 1.

Results Preliminary analysis is limited to descriptive statistics that show an immediate immunosuppression condition after TBI, as established by reduction of $CD4^+$ T lymphocytes and $CD8^+$ T lymphocytes. Significant data are collected in Table 2.

Conclusion In severe TBI patients, an immunosuppression state is early developed. It is relevant to establish whether this condition could affect the course and prognosis of ICU patients.

P228

Polymorphonuclear cell surface expression patterns differ in inflammatory and infectious stages in polytraumatized and septic shock patients

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Critical Care 2014, **18(Suppl 1):**P228 (doi: 10.1186/cc13418)

Introduction Each cell of the immune system shows a characteristic expression of cell surface molecules depending on the grade of activation or suppression. We examined the cell surface profile on polymorphonuclear cells (PMN) of polytraumatized patients and compared them with those of healthy controls and furthermore with patients with severe sepsis or septic shock. Moreover, we wanted to find out in the polytraumatized patients whether there are associations of PMN surface marker patterns with severity of injury, of disease and of organ dysfunctions.

Methods In a prospective observational study, cell surface expression of CD16, CD88, CD64, CD66b, CD11b, CD95, CD33, CD39, IL-17RA, TLR-2, TLR-4 and HLA-DR on PMN was determined using flow cytometry. Thirteen healthy volunteers, eight patients with severe sepsis and

septic shock, and longitudinally, on admission (0 hours), and 4, 12, 24, 48, 120 and 240 hours thereafter, eight polytraumatized patients were monitored. ISS, SAPS3 and SOFA score reflect severity of injury, of disease and of organ dysfunctions.
Results In polytraumatized patients (24 hours measurement), but also in septic patients, $CD88^+$ expression and $CD33^+/CD66b^-$ expression were significantly lower and $CD33^-/CD66b^+$ higher than in healthy controls.
Especially, the lowest values of $CD88^+$ occurred in patients with polytrauma developing septic complications.
Furthermore, the polytraumatized patients revealed higher levels of CD66b, CD11b and CD16, whereas $CD16^+$ was lower. Considering the post-traumatic course, polytraumatized patients with better prognostic evaluation in SOFA and SAPS3 initially expressed higher levels of TLR-2. Polytrauma patients could be divided into two subgroups, one with and the other without septic complications. The septic subgroup presented predominantly higher values in SOFA, SAPS3 and ISS scoring.
Conclusion Cell surface molecules on PMN of polytraumatized patients differ from those of healthy volunteers. Besides, distinct expression patterns resemble those of patients with sepsis. Patents with higher ISS values go along with higher scores in SOFA and SAPS3, and are at risk to develop septic complications.

P229

Lymphocyte surface expression patterns differ in inflammatory and infectious stages in polytraumatized and septic shock patients

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Critical Care 2014, **18(Suppl 1):**P229 (doi: 10.1186/cc13419)

Introduction Lymphocytes show different cell surface molecules depending on the degree of their activation or suppression. We used this surface expression to look at inflammatory or infectious states in patients with polytrauma and patients with sepsis. The present study was performed to clarify: what is the expression profile of lymphocyte surface markers in polytraumatized patients over time; and are there differences in the expression patterns of polytraumatized patients compared with healthy controls and with patients with severe sepsis and septic shock?
Methods In a prospective observational study in a surgical ICU, surface expression of CD3, CD4, CD8, IL7R, CD4/25, CD8/25, CD2/86, CD28, CD3/56, CD2, CD39, CD244, CD11b, and CD56 on lymphocytes was measured by flow cytometry. We collected data from six healthy controls, from eight patients with severe sepsis or septic shock, and, longitudinally from eight polytraumatized patients on admission (0 hours), and at 4, 12, 24, 48, 120, and 240 hours. ISS, SAPS 3 and SOFA score reflect severity of injury, of disease and of organ dysfunctions of the polytraumatized patients.
Results In septic and polytraumatized patients, the expression of CD3, CD28 and CD2 was significantly lower than in controls. In polytraumatized patients, surface expression of CD244, CD39 and CD8/25 was significantly higher than in controls. Within the polytraumatized patients, we found two different subgroups, group A with septic progression and Group B without septic progression of disease. Especially, the septic polytraumatized patients revealed very low levels of CD3, CD2 and CD28. Moreover, their levels of CD39 and CD8/25 were less increased and their ISS higher than those of the nonseptic subgroup.
Conclusion Surface expression molecules of polytraumatized patients differ from those of the healthy controls and within the group. The more heavily injured polytraumatized patients are more likely to develop severe sepsis and septic shock with surface expression profiles on lymphocytes comparable with those of septic patients.

P230

Cl:Na ratio on ICU admission as a prognostic indicator of mortality in sepsis patients

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Critical Care 2014, **18(Suppl 1):**P230 (doi: 10.1186/cc13420)

Introduction The aim of the study is to investigate the relationship between Cl:Na ratio disturbances and mortality in sepsis patients.

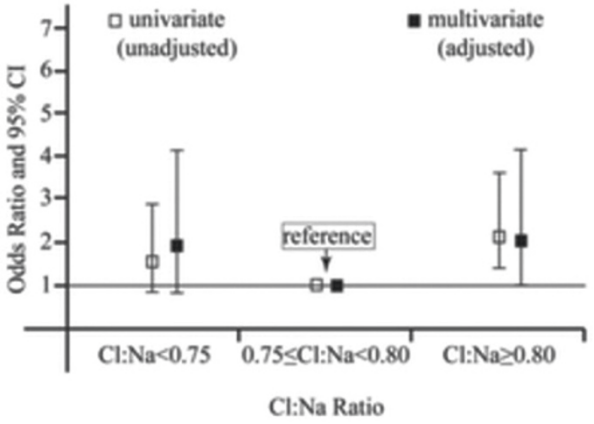

Figure 1 (abstract P230). In the multivariate model, effect of Cl:Na ratio group was adjusted for pH, lactate, anion gap and base excess.

Stewart's strong ion theory can be used in the interpretations of acid–base abnormalities [1]. The Cl:Na ratio is a simple alternative test that obviates the need to solve the complex strong ion gap (SIG) equations [2].
Methods A total of 434 sepsis and severe sepsis patients hospitalized in the ICU of two centers between 2006 and 2012 were included in the study. Three groups were formed as patients having low (<0.75), normal (>0.75 to <0.80) and high (>0.80) Cl:Na ratio within the first 24 hours in the ICU. Patients' age, gender, APACHE II score, SOFA score, pH, $PaCO_2$, HCO_3, base excess, Na, K, Cl, Ca, lactate, strong ion difference, anion gap, length of ICU stay and mortality were recorded. Logistic regression analysis was used to calculate odd ratios and 95% CIs for the association of Cl:Na with mortality. In the fully adjusted model, pH, BE, AG, lactate and Cl:Na ratio were entered into the model. P <0.05 was considered statistically significant.
Results The distribution of the patients was as follows: low Cl:Na (75, 17%), normal Cl:Na (243, 56%), high Cl:Na (116, 27%). Univariate analysis revealed that in low and high Cl:Na ratio patients, mortality was higher by 1.56-fold (0.87 to 2.81) and 2.22-fold (1.36 to 3.61) (P = 0.135 and P <0.01). In multivariate analysis, increased mortality by 1.95-fold (0.92 to 4.12) and 2.02-fold (1.01 to 4.03) was found in low and high Cl:Na ratios (P = 0.081 and P = 0.046) (Figure 1).
Conclusion Stewart's strong ion theory provides assessment for the etiology of acid–base disturbances. This evaluation can be performed easier and faster with the Cl:Na ratio. This study demonstrates that the disturbed Cl:Na ratio is associated with increased mortality in sepsis and severe sepsis patient groups.
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P231

Dysfunction of peroxisomes as one of the possible causes of multiple organ dysfunction syndrome development

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Critical Care 2014, **18(Suppl 1):**P231 (doi: 10.1186/cc13421)

Introduction This study demonstrates that low level of plasmalogens (Pls) is an important marker of peroxisomal dysfunction. The primary-OH group in glycerol Pls was not substituted by the acyl group (fatty acid) as in diacylphospholipids but by the aldehydogenic alkenyl group (fatty aldehyde) found in the form of vinyl ether [1]. It is known that there is disruption of several organ systems in diseases connected with peroxisomal dysfunction, as in the case of multiple organ failure.
Methods The objects of study were 18 people with multiple organ failure (35.6 ± 8.7 years) of various etiologies. The blood of 16 healthy

volunteers aged 37.7 ± 3.2 years served as control. The preanalytical phase was to prepare a solution of ethyl esters of fatty acids (FAc) and diethylacetals of fatty aldehydes (FAl) of blood plasma samples by acidic ethanolysis. Analysis of FAl and FAc in plasma was carried out using capillary gas–liquid chromatography. Quantitative evaluation of the analytes was performed as a mass percentage of the FA and FAl amount. Statistical analysis was performed using the Mann–Whitney U test (P <0.05).

Results In contradistinction to triglycerides, diacylphospholipids and PIs participate in exchange of polyunsaturated fatty acids (PUFA) with a large number of double bonds, such as primarily arachidonic and docosahexaenoic PUFA, acting as an intermediate station, through which these fatty acids are transported to cell membranes [1]. Thus, the ratio of level of FAl to the level of aforementioned blood plasma PUFA may reflect a change in the share of PIs relative to diacylphospholipids. According to our data, at MODS the ratio of fatty aldehydes to amount of arachidonic and docosahexaenoic PUFA is 0.16, while in the control group the figure is 0.27 (P <0.001). Thus, we can conclude that the level of PIs towards diacylphospholipid plasma levels of the experimental group decreased by approximately 40%. Currently, there is evidence that there is a reduction of cholesterol levels in blood plasma of patients with the diseases associated with peroxisome biogenesis disorders [2]. In our study, patients had low levels of plasma total cholesterol (124.6 ± 28.7 mg/dl), which may also indicate peroxisome dysfunction in MODS patients.

Conclusion On the basis of determined deficiency of analyzed compound levels, we concluded the possibility of peroxysomal dysfunction in MODS.

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P232

Differential effect of alcohol on TNFα receptor II production in the presence of LPS challenge *ex vivo*

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Critical Care 2014, **18(Suppl 1):**P232 (doi: 10.1186/cc13422)

Introduction Acute alcohol exposure suppresses proinflammatory response, which may be related to increased susceptibility to infections [1].The purpose of the study was to investigate the effect of acute exposure to alcohol on TNFα production capacity and TNFα receptors (TNFRs) in an *ex vivo* model of whole-blood stimulation with lipopolysaccharide (LPS).

Methods Whole blood was taken from healthy volunteers and was placed in tubes containing EDTA and immediately transferred to the laboratory. Heparinized blood samples were diluted 1:10 in RPMI 1640 culture medium (100 µl whole blood added in 900 µl RPMI 1640). Samples were preincubated with 0, 5, 12.5, 25, 50, 100 and 200 mM alcohol (EtOH) for 10 minutes at room temperature. After incubation, 500 pg LPS was added to each sample for 4 hours at 37°C. At the end of the process, samples were centrifuged (1,800 rpm, 5 minutes, r.t.). Culture supernatants were collected and stored at −70°C until measurements. TNFα and TNFR levels were determined in culture supernatant using the ELISA method [2].

Results We studied 24 healthy males volunteers aged 36.5 ± 1.4 (X ± SEM). TNFα was not detected in samples treated without alcohol in the absence of LPS stimulation (control) or in the presence of alcohol alone (data not shown). TNFα production was significantly decreased at a dose of 25 mM alcohol after LPS stimulation (P <0.0001) compared with LPS-challenged samples (Figure 1A). Alcohol had no effect on TNFR I production when incubated with or without LPS (data not shown). Alcohol at lower doses (<50 mM) seemed to decrease TNFR II levels, but an increase in TNFR II levels was observed at higher doses (>50 mM) of alcohol, which was statistically significant at doses of 100 and 200 mM alcohol after LPS stimulation *ex vivo* (P <0.001) (Figure 1B).

Conclusion Our observations indicate a suppression of proinflammatory response, but also a differential effect of alcohol on TNFR II production of whole blood in the presence of LPS challenge depending on the degree of alcohol intoxication.

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P233

Neutrophil phenotype model for extracorporeal treatment of sepsis

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Critical Care 2014, **18(Suppl 1):**P233 (doi: 10.1186/cc13423)

Introduction Neutrophils play a central role in eliminating bacterial pathogens, but may also contribute to end-organ damage. Interleukin-8 (IL-8), a key modulator of neutrophil function, signals through neutrophil specific surface receptors CXCR-1 and CXCR-2. Expression of these surface receptors can be altered by perfusion through an extracorporeal device. Extracorporeal methods of immune modulation have shown promise for treatment of sepsis; however, achieving an appropriate response is a major challenge [1]. In this study a mechanistic mathematical model was used to evaluate and deploy an extracorporeal sepsis treatment that modulates CXCR-1/2 levels.

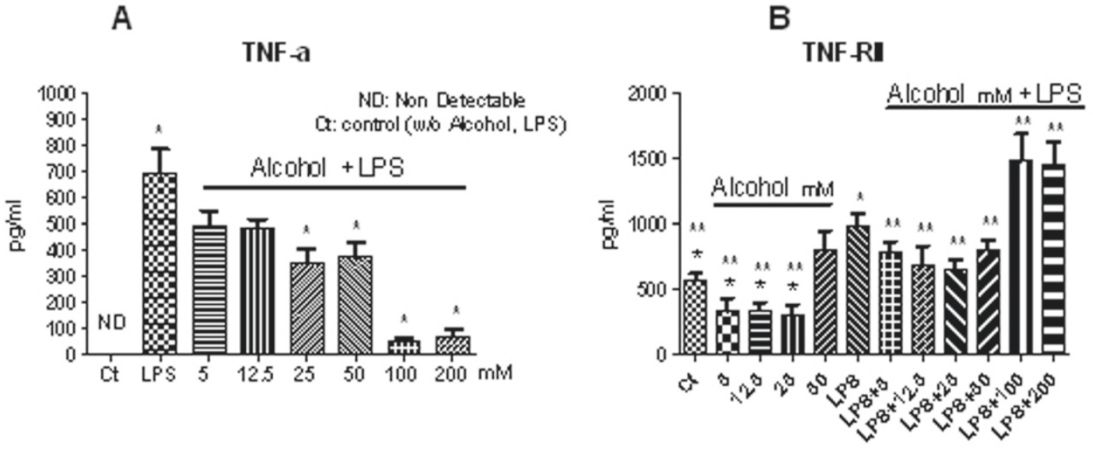

Figure 1 (abstract P232).

Methods A simplified mechanistic mathematical model of IL-8-mediated activation of CXCR-1/2 receptors was developed. Receptor-level dynamics and systemic parameters are coupled with multiple neutrophil phenotypes to generate dynamic populations of activated neutrophils that reduce pathogen load, and/or primed neutrophils that cause adverse tissue damage when misdirected. The mathematical model was calibrated using experimental data from baboons administered a 2-hour infusion of *E. coli* and followed for a maximum of 28 days. An extracorporeal intervention was implemented by introducing a trapped receptor state that limits IL-8 signaling through CXCR-1/2. Time of onset, duration, and capture efficacy of the extracorporeal device were explored to provide probabilistic predictions of the impact on mortality.
Results Of 16 baboons, 11 (69%) died, six (38%) within 1 day of bacterial infusion. The model was well calibrated to the data from survivors and nonsurvivors. Sensitivity analysis identified six model parameters, out of 21, as key determinants of mortality. Predictions indicate best effect with introduction of the proposed extracorporeal intervention within 1 hour of infection for a 72-hour duration, results in the survivor population increasing from 31% to 61%. The treatment can result in harm if initiated <10 hours from infection and continued <24 hours. A delay of 10 hours increases survival by 7% on average. Treatment efficacy quickly diminishes if not introduced within 15 hours of infection.
Conclusion These findings support the continued development of an extracorporeal treatment that modulates CXCR-1/2 levels. Further development of the mathematical model will help guide device development and determine which patient populations should be targeted by treatment.
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P234

Prolactin, cortisol and heat shock proteins in early sepsis: preliminary data

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Critical Care 2014, **18(Suppl 1):**P234 (doi: 10.1186/cc13424)

Introduction Besides cortisol, prolactin might also be important in maintaining normal immune response in stress states. Its role in the hypothalamus–pituitary–adrenal axis hormonal and immune stress response in sepsis has hardly been investigated in a critically ill setting. The aims of the study were to evaluate the early (first 48 hours) ACTH, cortisol and prolactin plasma levels in ICU patients with severe sepsis/septic shock (SS) or systemic inflammatory response syndrome (SIRS) compared with healthy control subjects (C) and to correlate their expression with heat shock proteins (HSPs), interleukins (ILs) and outcome.
Methods Thirty consecutively admitted patients with SS, 22 with SIRS, and 15 C were enrolled in the study. Patients' demographics, laboratory examinations, and APACHE II, SOFA and SAPS III scores were recorded on ICU admission. Blood sampling was performed between 9:00 and 10:00 a.m. Prolactin and cortisol were measured using the ADVIA centaur system, ACTH using the Immulite 2000. Intracellular monocyte HSP (iHSP) was determined after staining with surface antigens $CD33^-$ PE/Cy5 and CD45 PE/Cy7 followed by either HSP72-FITC or HSP90a-PE intracellular staining (four-color flow cytometry). Mean fluorescence intensity values for each HSP were noted and analyzed. ELISA was used to determine extracellular (e) HSP, IL-6 and IL-10 levels.
Results Prolactin (P <0.034), cortisol (P <0.0001), and ACTH (P <0.02) levels differed among groups. Prolactin, cortisol, IL-6, and eHSP90 were higher in SS (P <0.03) and SIRS (P <0.04) compared with C. Cortisol and eHSP90 were higher in SS compared with SIRS (P <0.005; P <0.03); iHSP72 and iHSP90 were higher in SIRS compared with SS (P <0.05; P <0.05) or C (iHSP72, P <0.02). Cortisol related with eHSP90 (r = 0.45, P <0.02), lactate (r = 0.33, P <0.02) and HCO_3 (r = –0.45), and prolactin with SAPS III (r = 0.34, P <0.02), but not with mortality or LOS.
Conclusion Prolactin seems to be a stress hormone, probably related to the severity of illness, increased along with IL-6 and eHSP90 levels in SS. Also in these patients, cortisol correlates to lactate and eHSP90, but in contrast to SIRS the iHSP72 and iHSP90 immune response is depressed.
Acknowledgements This research has been co-financed by the European Union (European Social Fund) and Greek national funds through the Operational Program 'Education and Lifelong Learning' of the National Strategic Reference Framework Research Funding Program: THALES.

P235

AMP-protein kinase may protect against sepsis-induced acute kidney injury through modulation of immune response and endothelial activation

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Introduction Organ injury is a hallmark of sepsis, in particular acute kidney injury (AKI). Yet the mechanisms involved in sepsis-induced AKI are not well understood. Energy prioritization is an important cell defense mechanism, and thus we hypothesized that exogenous activation of AMP-protein kinase (AMPK), a master regulator of cellular energy metabolism, protects against sepsis-induced AKI.
Methods Sixty C57BL/6 male mice, 6 to 8 weeks of age, weighing 20 to 25 g were divided into six groups: 1, cecal ligation and puncture (CLP); 2, CLP+AICAR (AI, AMPK activator, 100 mg/kg 24 hours before CLP); 3, CLP+compound C (AMPK inhibitor, 30 mg/kg; CoC); 4, sham; 5, sham+AI; 6, sham+CoC. Blood/tissue samples were collected 8 hours after CLP. Renal function (creatinine (Cr, mg/dl), BUN (mg/dl) and cystatin C (CysC, ng/ml)), cytokine expression (ELISA), endothelial activation (ICAM-1 expression), neutrophil adhesion (PMN, fluorescence, anti-CD11b mAb-tagged PMNs) and vascular leak (Evan's blue) were assessed. The effect of AI given 4 hours (n = 12) before and 2 hours after (n = 11) CLP was also evaluated. The experiment was reproduced *in vitro* using cell culture (renal epithelial, endothelial cells and macrophages), with similar groups: 1, control; 2, control+AI (1 mM/1 hour pre LPS); 3, LPS (100 ng/ml for 4 hours); 4, LPS+AI; 5, control+CoC (10 μM/1 hour pre LPS); 6, LPS+CoC. Cytokines were measured with ELISA. Data are presented as mean ± SD and as LPS/CLP and LPS/CLP+AI.
Results AI prevented Cr, BUN and CysC from increasing after CLP (0.43 ± 0.18, 0.2 ± 0.02, P = 0.0003; 62.2 ± 10.8, 43.7 ± 17.7, P = 0.01; 103.9 ± 54.8, 49.3 ± 30.8, P = 0.01, respectively). AICAR decreased cytokine release after CLP (IL-6: 1,818 ± 344 vs. 1,374 ± 268, P = 0.04; IL-10: 7,592 ± 5,038 vs. 2,245 ± 2,668, P = 0.05; TNFα: 213 ± 172 vs. 39 ± 16, P = 0.03) and LPS in macrophage culture (IL-6: 241.7 ± 1.5 vs. 7.2 ± 1.5, P = 0.055; TNF: 1,882 ± 583 vs. 82 ± 28, P = 0.04). However, AI lost its protective signal when administered 4 hours pre or 2 hours after CLP (Cr CLP vs. CLP+AI: 0.2 vs. 0.2, P = 0.1 and 0.45 ± 0.3 vs. 0.56 ± 0.3, P = 0.5, respectively). AI also decreased ICAM-1 expression *in vivo* and *in vitro*, vascular leak (0.09 ± 0.01 vs. 0.06 ± 0.008, P = 0.003) and PMN adhesion (1,055 ± 179 vs. 751 ± 242, P = 0.04).
Conclusion AMPK activation by AICAR prevented sepsis-induced AKI. AICAR decreased cytokine release, endothelial activation and vascular leak, suggesting that organ protection may be mediated by modulation of the inflammatory response and protection of the microvasculature. However, AICAR's protective effect may be conditional to timing of administration.

P236

Study of the *ex vivo* immune response of polytrauma older patients in the ICU on admission: preliminary results

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Introduction Immunological status is differentiated with age, influencing treatment and outcome [1]. The aim is to determine the immune response of severely traumatized older patients compared

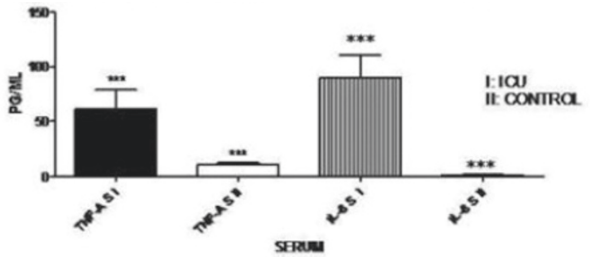

Figure 1 (abstract P236). Serum proinflammatory cytokines in older patients.

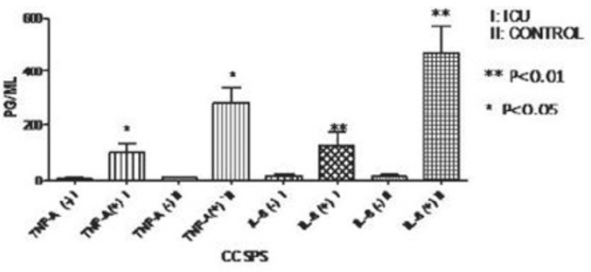

Figure 2 (abstract P236). *Ex vivo* proinflammatory cytokine release after whole-blood LPS stimulation in older patients.

with a group with arterial disease, expressed by proinflammatory cytokine release after *ex vivo* whole-blood LPS stimulation [2].

Methods The study comprised 16 polytrauma patients admitted to the ICU, aged 78 ± 8 (Group I) and 16 with arterial disease, aged 74 ± 5 (Group II). Ten milliliters of peripheral blood were collected from each patient, divided into two tubes with/without anticoagulant. Diluted 1:10 whole-blood samples were stimulated with 500 pg/ml LPS, at 37°C, for 4 hours. Serum and cell culture supernatants (CCSP) were removed and stored at –70°C. TNFα and IL-6 were measured in serum and CCSP by ELISA.

Results Serum proinflammatory cytokines were significantly elevated after severe trauma against control group (TNFα, P <0.001 and IL-6, P <0.001). *Ex vivo* cytokine release showed the opposite direction. There was a significantly lower TNFα and IL-6 release for Group I (TNFα, P <0.05 and IL-6, P <0.01) compared with Group II. TNFα *ex vivo* release from the samples of Group II was >300 pg/ml. See Figures 1 and 2.

Conclusion Older patients showed adequate immunological response, considering the limit of 300 pg/ml. The incidence of severe trauma was involved in the downregulation of immune activity and should be considered. Group I patients do not have the opportunity to precondition their immune status. Group II patients can better compensate operative therapies.

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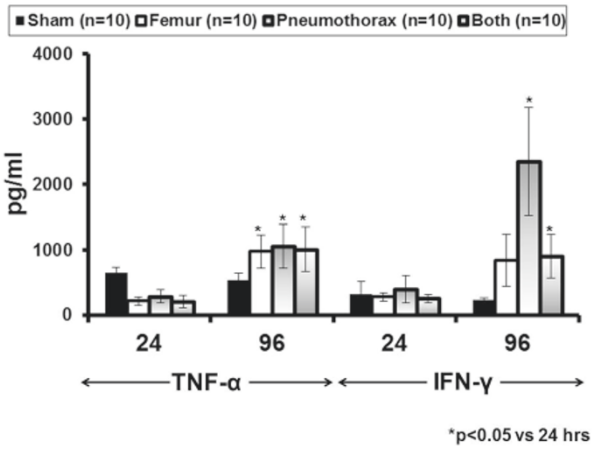

Figure 1 (abstract P237). Cytokine stimulations after sterile injury.

Methods Ninety-seven C56Bl6 male mice were subject to multitrauma after crush of the femur and chemical pneumothorax by turpentine. Mice surviving 72 hours after the injuries were challenged intravenously with one 7log$_{10}$ log-phase inoculum of *P. aeruginosa* and survival was recorded. In separate experiments, mice were sacrificed post injury; splenocytes were isolated and stimulated with 10 ng/ml LPS and cytokines were measured in supernatants by an enzyme immunoassay. Quantitative cultures of the right lung, kidney and liver were performed. The same procedures were done for sham-operated mice and for mice subject only to femur crush and to pneumothorax.

Results Initial experiments with 21 mice showed that the overall death rate for this model of multitrauma was 66.7% with most deaths occurring in the first 48 hours. In the second set of experiments, 12 mice remaining alive 72 hours post injury were challenged with *P. aeruginosa*; mortality was 37.5% compared with 75% of 12 non-injured and infected mice (log-rank: 5.77, P = 0.016). Respective mean production of TNFα from splenocytes isolated at sacrifice 24 hours and 96 hours post sham injury was 651 and 523 pg/ml (P = NS); post femur crush 217 and 916 pg/ml (P = 0.010); post pneumothorax 286 and 1,056 pg/ml (P = 0.018); and post both femur crush and pneumothorax 207 and 1,011 pg/ml (P = 0.019). Respective mean production of IFNγ from splenocytes isolated at sacrifice 24 hours and 96 hours post sham injury was 324 and 230 pg/ml (P = NS); post femur crush 278 and 840 pg/ml (P = 0.021); post pneumothorax 377 and 2,356 pg/ml (P = 0.025); and post both femur crush and pneumothorax 252 and 908 pg/ml (P = 0.019). Mean production of TNFα from splenocytes of injured mice sacrificed 24 hours after bacterial challenge was 1,184 pg/ml compared with 484 pg/ml non-injured and infected mice (P = 0.024). Similar differences were not found for IFNγ or for quantitative tissue cultures. See Figure 1.

Conclusion Mice survivors from multiple trauma become resistant to subsequent infection. This is probably linked with the induction of tolerance of the innate immunity to substances released after sterile tissue injury.

P237

Multiple trauma is linked with reversal of immunoparalysis and provides survival benefit from *Pseudomonas aeruginosa*

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Introduction Patients with multiple injuries are prone to hospital-acquired infections. We hypothesized that exposure to multiple injuries may modulate the innate immune response and the subsequent outcome of infections.

P238

Does clopidogrel change morbidity and mortality in ICU sepsis patients?

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Introduction The purpose of this study was to evaluate whether patients with sepsis exposed to clopidogrel have lower mortality and fewer days on mechanical ventilation compared with patients not exposed to clopidogrel. A recent *post-hoc* analysis of the PLATO trial suggests that the antiplatelet agent ticagrelor provided a significant

reduction in sepsis-related mortality and pulmonary adverse events compared with clopidogrel. It is unknown whether clopidogrel also provides benefit in patients with sepsis compared with no therapy. Knowing this information may help focus future research on determining the mechanism of ticagrelor's benefit.

Methods This retrospective cohort study included all patients over the age of 40 with a confirmed diagnosis of severe sepsis and an ICU stay at our academic medical center from 1 January 2005 to 31 March 2011. Clopidogrel use, patient demographics, and APACHE II score at the time of sepsis were collected from patient charts. Clinical outcomes included in hospital mortality, development of acute respiratory distress syndrome (ARDS), days on mechanical ventilation, in-hospital cardiac events, hospital cost, and length of stay.

Results We identified 824 patients who met the inclusion criteria for this study. Of these patients, 76 (9.2%) had been exposed to clopidogrel. The mean APACHE II score was similar for patients receiving clopidogrel and those who did not (23.4 vs. 22.6; $P = 0.426$). Patients exposed to clopidogrel had a similar rate of in-hospital mortality (26.3% vs. 33.2%; $P = 0.223$) and ARDS (43.4% vs. 38.6%; $P = 0.415$). While mortality was also similar between the groups for patients with a low APACHE II score (<25), mortality was lower in clopidogrel-exposed patients with an APACHE II score ≥25 (27.3% vs. 45.6%; $P = 0.045$). Patients exposed to clopidogrel did not have a higher use of blood products (65.8% vs. 65.9%; $P = 0.983$). Patients exposed to clopidogrel did not have significantly more days on mechanical ventilation, or ventilation-free days. Cardiac events during the hospital stay were not lower in patients on clopidogrel (4.0 vs. 2.4; $P = 0.432$). Hospital costs and length of stay did not differ between the groups.

Conclusion While clopidogrel may not increase the risk of bleeding in these patients, these data suggest that clopidogrel does not reduce adverse outcomes in patients with sepsis. A potential benefit in patients with APACHE II scores ≥25 may need further study. Future research into the mechanism of ticagrelor's benefit reported in the PLATO trial may be directed at the non-P2Y12 receptor mechanism.

P239

Continuous administration of corticosteroids in septic shock can reduce risk of hypernatremia

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Introduction Although the administration of hydrocortisone in septic shock generates adverse effects, the risk of corticosteroid-induced hypernatremia may be reduced by continuous administration of the drug [1,2].

Methods A total of 171 patients with septic shock were randomized into three study groups: group A ($n = 58$), 200 mg/day hydrocortisone hemisuccinate in four doses; group B ($n = 59$), same dose of hydrocortisone hemisuccinate in continuous administration; group C ($n = 54$), no hydrocortisone hemisuccinate. Mean serum sodium values, the number of hypernatremia episodes and variations in serum sodium (Na var) were investigated for 7 days. The local ethics committee approved the study.

Results There were no differences between the three groups at the beginning of the study regarding demographic data and the clinical characteristics. Mean values of natremia were normal in group C (140.35 ± 7.390 mEq/l to 144.79 ± 8.338 mEq/l) during the study period. High mean values appeared on day 4 in group A (147.21 ± 8.470 mEq/l to 149.37 ± 8.973 mEq/l on day 7) and on day 5 in group B (146.36 ± 8.272 mEq/l to 147.70 ± 8.865 mEq/l). Na var was 8.59 ± 5.960 mEq/l (–8 and 21 mEq/l) in group A, 6.63 ± 7.609 mEq/l (–17 and 23 mEq/l) in group B and 4.54 ± 7.455 mEq/l (–12 and 22 mEq/l) in group C. This variation is statistically significant when groups A and B are compared with group C ($P = 0.012$) and when only group A is compared with group C ($P = 0.0019$). The risk of hypernatremia after hydrocortisone hemisuccinate was almost three times higher than that of patients who did not receive this drug (RR 2.82, 1.35 <OR <5.90, $P = 0.0041$) and slightly higher when HHS was delivered as a bolus (RR 3.08, 1.32 <OR <7.25, $P = 0.0071$).

Conclusion Continuous administration of hydrocortisone hemisuccinate in septic shock is associated with a lower risk of hypernatremia than bolus administration.

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P240

Tissue oxygenation in patients with severe sepsis

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Introduction The aim of this study was to determine the correlation between regional tissue oxygenation (SrO_2) measured by near-infrared spectroscopy (NIRS), central venous oxygen saturation (SvO_2) and levels of serum lactate (SL) in patients with severe sepsis.

Methods An observational pilot study was performed in an ICU of a medium-sized teaching hospital. Adult patients admitted with severe sepsis were included and three NIRS electrodes were attached: on the left side of the forehead (LF), the right side of the forehead (RF) and the right forearm (RA). SL and SvO_2 measured in a jugular or subclavian central venous line sample were determined every 4 hours. Descriptive statistics were calculated. Pearson correlation coefficients (PCC) were calculated between SrO_2, SvO_2 and SL. Normal values for SrO_2 were defined as the median ± 1 interquartile range in patients with SL <1.7 mmol/l. Differences between groups were calculated by Pearson chi-square tests. $P < 0.05$ was considered statistically significant.

Results Twenty-five patients (12 men) were included. Mean age was 68 years, mean APACHE score 31. The most frequent reasons for ICU admission were abdominal sepsis ($n = 11$) and pneumosepsis ($n = 7$). Statistically significant correlations were found between SvO_2 and SrO_2: PCC SrO_2 LF, 0.46; PCC SrO_2 RF, 0.50; PCC SrO_2 RA, 0.21. Low, although statistically significant, correlations were found between SrO_2 and SL: PCC SrO_2 LF, –0.16; PCC SrO_2 RF, –0.15; and PCC SrO_2 RA, –0.20. Calculated normal values for SrO_2 LF were 60 to 80%, for SrO_2 RF were 60 to 76% and for SrO_2 RA were 64 to 84%. An out-of-range SrO_2 had a high positive predictive value (PPV) for an increased SL. The PPV for out-of-range SrO_2 LF was 85% versus 58% for normal SrO_2 LF (OR 4.27; 95% CI 2.09 to 8.72), the PPV for out-of-range SrO_2 RF was 77% versus 60% for normal SrO_2 RF (OR 2.32; 95% CI 1.25 to 4.31) and the PPV for out-of-range SrO_2 RA 75% versus 60% for normal SrO_2 RA (OR 1.94; 95% CI 0.95 to 4.00).

Conclusion This pilot study shows a statistically significant correlation between SvO_2 and SrO_2 in patients with severe sepsis. An out-of-range SrO_2 LF or RF had a high predictive value for increased serum lactate. We therefore conclude that NIRS could have a role in goal-directed therapy of patients with severe sepsis.

P241

Delayed admission to the ICU is associated with increased in-hospital mortality in patients with community-acquired severe sepsis or shock

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Introduction The aim of this study is to determine whether ward transfers causing delayed ICU admission are associated with increased in-hospital mortality in patients with community-acquired severe sepsis or shock. Community-acquired infections are among the leading causes of ICU admission [1]. The 30-day mortality for adult emergency department (ED) patients with a delay in ICU admission of up to

24 hours has been found to be significantly higher compared with patients admitted directly to the ICU from the ED [2].

Methods A retrospective cohort study of patients admitted with community-acquired sepsis to a 12-bed, tertiary ICU at a university-affiliated teaching hospital, November 2008 to October 2010. Patients were divided into two groups based on their ICU admission pattern: direct transfer from the ED (direct group); and one or more ward transfers between the ED and ICU within 48 hours (delayed group). Our primary outcome measure was mortality.

Results We identified 277 patients admitted to the ICU within 48 hours from arrival in the ED. Of these, 186 were admitted directly from the ED, and 91 patients had more than one ward transfer between the ED and the ICU. In-hospital mortality in the delayed group was 32% compared with 21% in the direct group (P = 0.0477). Patients with delayed admission had significantly lower APACHE II scores: 21 (16; 26) and 24 (18.75; 31) respectively (P = 0.0016). The in-hospital LOS was similar in the two groups. For patients in the delayed group, we found a trend toward increased 30-day mortality (P = 0.0723), 90-day mortality (P = 0.0838) and higher Charlson Comorbidity Index (P = 0.0609).

Conclusion We found that patients admitted with community-acquired severe sepsis or shock are more likely to die in-hospital if they experience redundant ward transfers within 48 hours of admission. However, the delayed group was significantly lower risk stratified in the ICU based on their APACHE II score. Identification of severe sepsis and risk assessment in the ED is crucial for patient outcome.

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P242

Effect of clarithromycin in patients with Gram-negative sepsis: subgroup analysis of a randomized trial

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Introduction A recent randomized trial of our group showed that blind treatment with clarithromycin decreased mortality from septic shock and multiple organ dysfunction, shortened time until resolution of infection in patients with severe sepsis/shock and decreased hospitalization costs [1]. The efficacy of clarithromycin in relation with the type of failing organs is analyzed.

Methods Six hundred patients with systemic inflammatory response syndrome due to primary Gram-negative bacteremia or acute pyelonephritis or intraabdominal infection were blindly assigned to placebo or clarithromycin for four consecutive days as adjunctive treatment to standard of care. Clarithromycin was administered at a dose of 1 g once daily in 1 hour of continuous infusion. Organ failures before allocation to blind treatment were defined according to the Surviving Sepsis Campaign 2003 definitions. Cox regression analysis was done to verify the effect of clarithromycin as a moderator. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated.

Results Forty-nine patients of the placebo arm and 55 patients of the clarithromycin arm had acute lung injury (ALI); mortality was 51.0% and 30.9% respectively (P = 0.046). Forty-seven patients of the placebo arm and 54 patients of the clarithromycin arm had acute coagulopathy; mortality was 44.7% and 44.4% respectively (P = 1.000). Twenty patients of the placebo arm and 19 patients of the clarithromycin arm had metabolic acidosis; mortality was 55.0% and 52.6% respectively (P = 1.000). Twenty-nine patients of the placebo arm and 39 patients of the clarithromycin arm had acute oliguria; mortality was 55.2% and 48.7% respectively (P = 0.631). ALI (HR = 2.42; 95% CI = 1.45 to 4.03, P = 0.001), acute coagulopathy (HR = 2.65; CI = 1.69 to 4.16) and cardiovascular failure (HR = 3.36, CI = 2.09 to 5.39) were independently associated with unfavorable outcome. Adding treatment with clarithromycin in the equation reduced the risk for death by ALI by 1.86-fold (HR = 0.54; CI = 0.29 to 0.99, P = 0.049).

Conclusion Clarithromycin is a major moderator of the physical course of Gram-negative sepsis complicated with ALI.

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P243

Benefit profile of recombinant human soluble thrombomodulin in sepsis-induced DIC

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Introduction Recombinant human soluble thrombomodulin (rhTM) demonstrated promising evidence suggestive of efficacy in a phase IIb, randomized, controlled trial [1] and is currently under evaluation in a phase III trial. However, the benefit profiles of rhTM have not been elucidated. The purpose of this study was to explore whether patients with a high disease severity (according to Acute Physiology and Chronic Health Evaluation (APACHE) II and Sequential Organ Failure Assessment (SOFA) scores) might have a treatment benefit from rhTM administration.

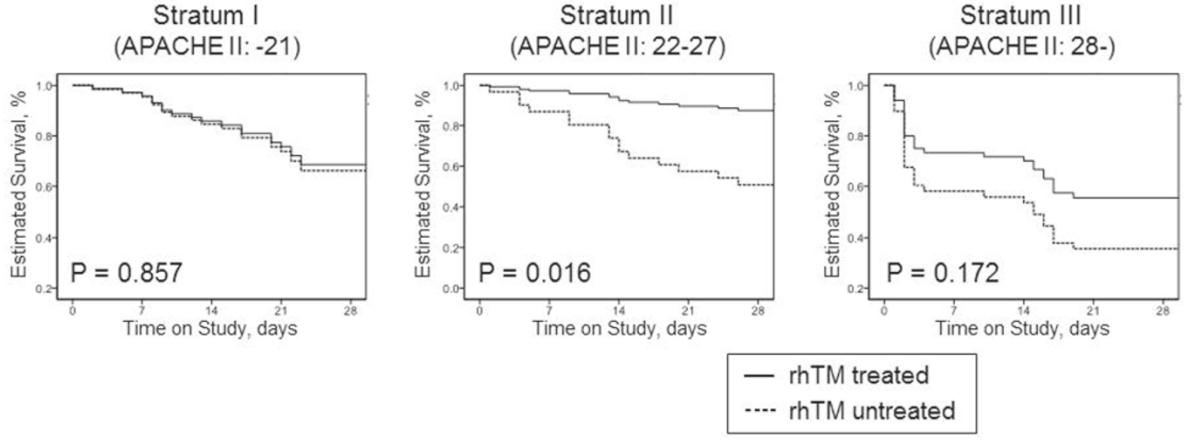

Figure 1 (abstract P243). Estimated survival curves for each of three disease severities.

Methods This was a *post-hoc*, subgroup analysis of a multicenter retrospective cohort study [2] conducted in three tertiary referral hospitals in Japan. All patients with sepsis-induced DIC who required ventilator management were included. We stratified all patients with different disease severity, as defined by APACHE II and SOFA scores to three strata. Intervention effects estimated as hazard ratios were analyzed by Cox regression analysis adjusted for propensity model to detect subgroup heterogeneity of the effects of rhTM on in-hospital mortality.
Results Eligible were 162 patients with sepsis-induced DIC; 68 patients received rhTM and 94 did not. After adjusting for imbalances, rhTM administration was significantly associated with reduced mortality only in patents in the stratum II group (APACHE II, 22 to 27) (adjusted hazard ratio, 0.20; 95% confidence interval, 0.05 to 0.74; $P = 0.016$), while not significant in stratum I and stratum III (Figure 1). A similar tendency was observed in analysis for SOFA score (stratum I (SOFA, −10), $P = 0.368$; stratum II (SOFA, 11 to 12), $P = 0.012$; stratum III (SOFA, 13–), $P = 0.673$).
Conclusion A survival benefit with rhTM treatment was observed in sepsis-induced DIC and a high risk of death according to baseline APACHE II and SOFA scores.
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P244

Comprehensive assessment of the true sepsis burden using electronic health record screening augmented by natural language processing

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Critical Care 2014, **18(Suppl 1):**P244 (doi: 10.1186/cc13434)

Introduction Interventional trials for sepsis have not shown an improvement in patient outcomes, often due to the lack of a diagnostic gold standard resulting in large heterogeneity of the patients enrolled. Electronic health record (EHR) screening tools have been applied to the sepsis population but limited to vital sign and laboratory data to identify target patients. Our objective was to describe an investigational database created through the application of a new EHR screening tool that applies natural language processing (NLP) analysis to clinical documentation to augment the identification of infection.
Methods We acquired data from the Clinical Vigilance for Sepsis EHR screen on consecutive patients from two hospital systems over 12 months at a 300-bed community hospital and 24 months from a 500-bed academic tertiary care center. A physician order for intravenous antibiotics was used as a surrogate for suspected infection, removing patients receiving a single dose of antibiotics without subsequent administration. Each patient's in-hospital course was tracked from arrival to final disposition, identifying vital signs, laboratory values, radiological results, and interventions as they occurred. Patients were followed for the primary outcome of mortality, with secondary outcomes of transfer to the ICU, vasopressor initiation and mechanical ventilation.
Results The EHR screen identified 216,550 patients over a total of 36 months from the two hospitals. A total of 37,160 (17%) patients were treated with i.v. antibiotics. Sepsis patients experienced a 3% (1,186/37,160) mortality rate relative to 0.5% (448/216,550) in patients without infection at any time. Sepsis at any time represented 73% (1,186/1,634) of all in-hospital deaths. ICU transfer occurred in 18% (6,865/37,160) of patients, with septic shock (vasopressor requirement) occurring in 10% (3,837), and 13% (5,072) requiring mechanical ventilation.
Conclusion Application of this novel EHR screening tool to identify sepsis patients utilizes NLP applied to clinical documentation, providing greater clinical context than laboratory and vital sign screening alone. This database represents the entire sepsis acuity spectrum, allowing for a more granular description of the infectious process as well as subgroups with adequate sample size. The dataset collected as a patient-centered time series will enable future studies to focus on the trajectory of clinical deterioration and shock before its occurrence.

P245

Outcomes of neutropenic patients with severe sepsis on a specialist cancer ICU

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Introduction The hospital survival rate for patients with septic shock remains at approximately 50% [1]. Critically ill cancer patients have often been considered poor candidates for ICU management due to the perception of poor outcomes for this group, in particular in the presence of neutropenia. There is a paucity of data supporting this. The objective of this study was to describe clinical outcomes for a group of septic neutropenic patients admitted to a cancer ICU.
Methods All neutropenic patients (neutrophils <1,000/mm^3) admitted to the ICU at the Royal Marsden hospital (London, UK) between October 2010 and December 2012 with a diagnosis of severe sepsis/septic shock were included retrospectively. Data were collated from patients' electronic records after approval by the hospital audit committee. Data are presented as the absolute value (%) or median (IQR). Fisher's exact test or the Mann–Whitney U test was used as appropriate.
Results Sixty-four neutropenic patients were admitted to the ICU during this period. Forty-seven (73%) patients survived to ICU discharge and 34 (53%) patients to hospital discharge. Twenty-two (34%) patients were alive at 6 months and 18 (28%) patients were alive at 12 months. Seventy-seven percent of patients had microbiologically documented infections. There was no significant difference between ICU survivors and nonsurvivors in duration of neutropenia, the presence of, or removal of, indwelling catheters, or the source of sepsis. Mechanical ventilation and need for vasopressors were associated with worse outcomes. Patient characteristics are presented in Tables 1 and 2.

Table 1 (abstract P245). Patient characteristics

	ICU survivors	ICU nonsurvivors
n	47 (73%)	17 (27%)
Age (years)	53 (38 to 65)	49 (33 to 62)
BM transplant	24 (51%)	7 (41%)

Table 2 (abstract P245). Characteristics on admission to the ICU

	ICU survivors	ICU nonsurvivors
Neutrophil count	0.5 (0.3)	0.2 (0.3)*
Days of neutropenia	3 (0 to 8)	6 (0 to 19)

*$P < 0.05$.

Conclusion In a group of oncology patients admitted to the ICU with neutropenia and severe sepsis/septic shock, we found an in-hospital mortality of less than 50%. This is similar to the general population.
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P246

Vitamin D and ICU outcome in septic patients: a difficult connection?

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Introduction Vitamin D, a secosteroid hormone, has roles in the optimal functioning of many organ systems and illnesses [1]. Recent reports show that most patients admitted to the ICU are vitamin D insufficient [2].
Methods In a 10-bed general ICU at the emergency department of a tertiary teaching hospital in Florence (Italy), 71 medical patients with severe sepsis or septic shock (51% men, 40% women) admitted to the ICU between January 2013 and September 2013 were studied. Vitamin D levels were measured by radioimmunoassay at admission, as well

Table 1 (abstract P246).

	Age	SAPS	Length of stay ICU (days)	Length of stay in hospital (days)	Vitamin D (ng/ml)	BMI
Mean	62.59	52.48	10.14	24.90	11.35	26.38
Median	67.00	54.00	6.00	20.00	9.60	24.83
Mode	77.00	40.00	3.00	8.00	4.00	24.69
Standard deviation	17.85	18.35	10.17	20.70	7.16	8.33

as demographic data (Table 1) and the Simplified Acute Physiology Score II (SAPS II). Exclusion criteria were: age <18 years, malnutrition state (body mass index (BMI) <18 kg/m^2), pregnancy. Statistical analysis was carried out by linear regression and *t* test with SPSS 13. This study was approved by the Internal Review Board. Informed consent was obtained.

Results Most patients showed vitamin D levels below 20 ng/ml, and we have not demonstrated a statistical significance correlation in the univariate regression between vitamin D level and both SAPS ($P = 0.300$) or length of stay in hospital ($P = 0.154$). Also our data do not demonstrate a statistical significance difference at *t* test between the value of vitamin D in the dead group and the alive group.

Conclusion Several groups have reported an inverse association between vitamin D levels in critically ill patients, severity of disease, outcome length of ICU stay and mortality [3,4]. In our experience we have not found an evident correlation between low vitamin levels and ICU outcomes. However, considering the prevalence of low vitamin D levels among the medical patients admitted to the ICU, further studies should be performed.

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P247

A meta-analysis of randomized controlled trials on the use of statins in septic patients

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Introduction Beneficial effects of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins) on vascular diseases have been demonstrated in several clinical trials. Recently discovered anti-inflammatory effects of statins seem to have an important role in counteracting the harmful effects of sepsis on the coagulation system. Many epidemiologic studies evidence that statin treatment may be associated with a better prognosis in severe bacterial infections, and a recent randomized trial found a reduced mortality in the statin group. We decided to perform a meta-analysis of all randomized controlled trials ever performed on statin therapy in septic patients to evaluate their effect on survival.

Methods Four trained investigators searched and assessed pertinent studies in BioMed Central, PubMed, Embase and the Cochrane Central Register (divergences resolved by consensus). Inclusion criteria were: random allocation to treatment; comparison of statins versus any comparator in septic patients. Exclusion criteria were: duplicate publications; nonadult studies; no data on main outcomes.

Results Data from 650 patients in five randomized controlled studies were analyzed. Overall analysis showed no difference in mortality between patients receiving statins (44/322 (14%)) versus control (50/328 (15%)), RR = 0.90 (95% CI 0.65 to 1.26), $P = 0.6$.

Conclusion Scientific evidence for the role of statins in septic patients is still limited and larger randomized trials should be performed on this topic. Published data, summarized by this meta-analysis of randomized trials, show that statin therapy has no detrimental effect on survival in the overall population of adult septic patients.

P248

Efficacy of early administration of thrombomodulin alfa in patients with sepsis-induced disseminated intravascular coagulation: subanalysis from post-marketing surveillance data

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Introduction We hypothesize that the early administration of thrombomodulin alfa (TM-alfa) (Recomodulin® injection; Asahi Kasei Pharma Corporation, Tokyo, Japan) could improve mortality in patients with sepsis-induced disseminated intravascular coagulation (DIC). TM-alfa has been approved for use as a curative medicine for DIC in Japan from 2008 that was examined in a multicenter, randomized, clinical trial [1].

Methods DIC was diagnosed based on the Japanese Association for Acute Medicine (JAAM) criteria. From May 2008 to April 2010, a total of 1,787 patients with sepsis-induced DIC from post-marketing surveillance data [2] were analyzed. The survival rates on day 28 after the last TM-alfa administration were evaluated.

Results The 28-day survival rate was 64.5%. Use of other anticoagulants before and after TM-alfa administration did not affect the survival rate (present vs. absent: 63.8% vs. 65.2% ($P = 0.782$) and 62.5% vs. 65.3% ($P = 0.606$) respectively). The survival rate decreased significantly in proportion to the duration of DIC before TM-alfa administration ($P < 0.001$). More precisely, the 28-day survival rate was 66.4% when TM-alfa was injected on the same day that DIC was diagnosed, whereas it was 48.5% and 31.1% when TM-alfa was started 4 days later and 7 days or more after DIC was diagnosed, respectively. These differences were significant ($P = 0.033$ and $P < 0.001$, respectively).

Conclusion The early administration of TM-alfa may be effective for patients with sepsis-induced DIC diagnosed based on the JAAM criteria.

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P249

Dynamic myocardial depression in septic cardiomyopathy

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Introduction Depression of left ventricular contractility appears in many diseases resulting from various etiology factors. One of the most interesting features of septic cardiomyopathy is the significant dynamic myocardial depression that is commonly observed. In this context, the objective of the present work is to characterize clinically, by laboratory, by echocardiography, and by invasive measures the patients with septic cardiomyopathy.

Methods A single-center database investigates all patients who were admitted and treated for severe sepsis or septic shock in the ICU over a period of 2 years (November 2011 to October 2013), and who were discharged with a diagnosis of septic cardiomyopathy or new left ventricular dysfunction. The clinical, laboratory, echocardiography, and invasive measures, and clinical outcome were recorded.

Results From the 105 patients that were investigated, 15 patients were found with septic cardiomyopathy. Septic cardiomyopathy is more prevalent among men (60%). Patients with septic cardiomyopathy have an increased prevalence of immune compromised disease (46%), and hypertension (40%). There was a need for mechanical respiratory support for 86% of patients. The improvement in cardiac function

occurred at an average of 6.9 days. *E. coli* is the commonest bacterial pathogen (33%). Laboratory findings show elevated liver enzyme and kidney function impairment in all patients. Thirty-three percent of patients were treated with N-acetyl cysteine, and 46% were treated with renal replacement therapy. High CRP was observed in all patients. Paroxysmal atrial fibrillation was diagnosed in 46%. Invasive measures in 50% of the patients have demonstrated high cardiac index (CI) and low systemic vascular resistant index (SVRI) on their admission, and 93% demonstrate low CI and high SVRI a few hours later. Hospitalization stay was between 3 and 42 days with an average of 14.6 days.

Conclusion Septic cardiomyopathy is more common among immune compromised patients. It is characterized by dynamic changes in the cardiac function based on echocardiography and invasive measures. A persistent hyperkinetic state was associated with high mortality rate. In addition to echocardiography follow-up, invasive monitoring even in their admission is of great importance for more effective and adequate treatment.

P250

Significant change in the practice of chest radiography in Dutch ICUs

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Introduction We performed a survey under Dutch intensivists on the current practice of chest radiography in their departments. Chest radiographs (CXRs) are obtained frequently in ICU patients, despite the diagnostic and therapeutic efficacy of routine CXRs being known to be low. The discussion regarding specific indications for CXRs in critically ill patients and the safety of abandoning routine CXRs is still continuing [1].
Methods A web-based questionnaire was sent to the medical director of all adult ICUs in the Netherlands. This survey contained questions regarding ICU characteristics, ICU patients, daily CXR strategies, indications for routine CXRs and the practice of radiologic evaluation.
Results Of the 83 ICUs that were contacted, 69 (83%) responded to the survey. Only 7% of ICUs still perform daily routine CXRs for all patients while 65% of ICUs say never to perform CXRs on a routine basis. A daily meeting with a radiologist is established in the majority of ICUs and is judged to be important or even essential. The therapeutic efficacy of routine CXRs was assumed by intensivists to be lower than 10% or to be between 10 and 20%. The efficacy of on-demand CXRs was assumed to be between 10 and 60%. There is consensus between intensivists to perform a routine CXR after endotrachial intubation, chest tube placement or central venous catheterization.
Conclusion The strategy of daily routine CXRs for critically ill patients has developed from a common practice (63%) in 2006 [2] to a rare practice (7%) nowadays. Intensivists still assume the value of routine CXRs to be higher than the efficacy that is reported in the literature. This might be due to the clinical value of negative findings, which has not been studied before.

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P251

Stating clear indications for chest radiographs after cardiac surgery increases their efficacy and safely reduces costs

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Critical Care 2014, **18(Suppl 1):**P251 (doi: 10.1186/cc13441)

Introduction We investigated the efficacy and safety of chest radiographs (CXRs) performed on specified indications only, directly after cardiac surgery. CXRs in the ICU are frequently obtained routinely for postoperative cardiosurgical patients, despite the fact that the diagnostic and therapeutic efficacy of these CXRs is now known to be low [1]. Routine CXRs may only be beneficial for certain indications and the discussion regarding these indications and the safety of abandoning routine CXRs is still continuing [2].
Methods We prospectively included all patients who underwent major cardiac surgery in the year 2012. A direct postoperative CXR was performed only for certain specified indications. An on-demand CXR could be obtained during the postoperative period according to other specified indications. For all patients who did not have a CXR taken before the morning of the first postoperative day, a control CXR was then performed. All CXR findings were noted and classified, including whether or not they led to an intervention. Diagnostic and therapeutic efficacy values were calculated.
Results A total of 1,351 patients were included who mainly underwent coronary artery bypass grafting, valve surgery or a combination of both. Eighteen percent of patients underwent a minimally invasive cardiac surgery. The diagnostic efficacy for major abnormalities was clearly higher for the postoperative and on-demand CXRs, performed on indication, when compared with the next-morning routine CXR (6.7% and 6.9% vs. 2.9%) ($P = 0.002$). The therapeutic efficacy was also clearly higher for the postoperative and on-demand CXRs (2.9% and 4.1%), while the need for intervention after the morning control CXR was now reduced to be minimal (0.6%) ($P = 0.002$).
Conclusion Stating clear indications for CXRs following cardiac surgery increases the efficacy of these CXRs and safely reduces the total number of CXRs significantly.

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P252

Evaluation of early graft function in a case series of lung-transplanted patients

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Introduction The aim of the study was to investigate early graft function in terms of biological and radiological variables in a case series of lung transplant (Ltx).
Methods We performed a prospective analysis of patients that underwent Ltx at Fondazione IRCCS Cà Granda Policlinico of Milan from 1 December 2012 to 10 December 2013. Donors' lung parameters were recorded. Recipients' clinical data were collected daily and lung computed tomography (CT) at end expiration was performed within 7 days after Ltx. On the same day, bronchoalveolar lavage was collected [1]. Quantitative CT analysis was run on separate lungs for each patient.
Results Out of 25 LTx, 12 paired data for donors and recipients were analyzed. Lung donors' PaO_2/FiO_2 was 392 ± 118, Oto score was 5 ± 3, and ICU length of stay was 2 ± 1 days. Recipients' age was 56 ± 11 years, and body mass index was 24 ± 4 kg/m^2. Four patients received double Ltx, and the warm ischemia time was 85 ± 16 and 94 ± 14 respectively for right lung and left lung. When the CT scan was performed (on

Table 1 (abstract P252). Quantitative CT scan analysis on transplanted lungs

Lung CT	Mean ± SD ($n = 16$)
Volume (ml)	1,639 ± 437
Weight (g)	761 ± 175
Hyper inflated (%)	0.0 ± 0.0
Normal (%)	38.9 ± 17.1
Poorly (%)	29.4 ± 8.4
Not inflated (%)	31.7 ± 14.9

day 4 ± 1), four patients were mechanically ventilated, PaO_2/FiO_2 was 270 ± 93 and $PaCO_2$ was 44.6 ± 10.0 mmHg. Primary graft dysfunction grade 2 or 3 at 72 hours post Ltx was diagnosed in six patients. All patients were discharged from ICU. Table 1 presents quantitative analysis of transplanted lungs. The alveolar protein concentration and not aerated tissue weight are significantly related (R^2 =0.69; P = 0.001).
Conclusion Alveolar protein concentration is related to morphological features of lungs early after Ltx.
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P253

Can laboratory blood tests be used to risk stratify patients admitted with pneumonia?

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Introduction Our objective was to determine whether an Early Warning Score (EWS) based on laboratory tests could risk stratify patients admitted to the Norfolk & Norwich University Hospitals NHS Foundation Trust with pneumonia. Physiological EWS systems producing an escalated response to an increasing score are used effectively within the Trust, yet mortality is high in patients admitted with a diagnosis of pneumonia. The CURB-65 score may not be an effective risk stratification tool for predicting mortality in the older patient nor to guide intensive care admission [1]. Jarvis and colleagues developed an EWS based on laboratory blood tests and used it in conjunction with physiological EWS to effectively risk stratify all medical patients [2].
Methods Of 2,158 patients admitted with pneumonia during 12 months from August 2012, data were collected for 1,598 who had received the required blood tests. Data included dates of admission, discharge and death if appropriate, gender, haemoglobin (g/dl), white cell count (10^9/l), sodium (mmol/l), potassium (mmol/l), urea (mmol/l), creatinine (mmol/l) and albumin (g/l) on admission. A composite EWS was calculated and measured against outcome.
Results Of 1,598 patients, 538 died during this admission. It is uncertain whether death was due to pneumonia as only admission diagnosis is recorded but overall mortality was 35%. Analysis of data showed a strongly positive relationship between increasing EWS and increased risk of mortality with a correlation coefficient of 0.97.
Conclusion Observational results suggest an EWS based on laboratory tests can be used to risk stratify patients with pneumonia and could be used to treat those with higher scores more aggressively earlier in their illness. Further analysis is required to determine whether age is a contributing factor and how this may modify the EWS. We need to determine whether laboratory-based EWS risk stratification can be used in isolation, or whether it contributes sufficiently to an existing physiological EWS that a combined system would improve outcome in our patients.
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P254

Lung function in the immediate postoperative period after video-assisted thoracoscopic and thoracotomy pulmonary resection

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Introduction Previous studies reported that video-assisted thoracoscopic surgery (VATS) is more beneficial for pulmonary lobectomy concerning the late postoperative period than open thoracotomy [1,2]. However, the early postoperative period when the rate of complications is highest has been scarcely examined. Our study aimed to compare the residual pulmonary function of pulmonary lobectomy patients after VATS and the standard thoracotomy approach in the immediate postoperative period.
Methods This prospective study included 14 VATS and 13 thoracotomy lobectomy (THOR) patients (age 58.8 ± 10.9 vs. 59 ± 8.9 years, P = 0.96; preoperative FVC 3.4 ± 1 vs. 3.4 ± 0.95 l, P = 0.98 and preoperative FEV1 2.7 ± 0.96 vs. 2.7 ± 0.6 l, P = 0.9, respectively). All patients received standard surgical and postoperative care with standardized pain management including i.v. diclofenac combined with epidural administration of bupivacaine and fentanyl. Spirometry was performed with a bedside MIR Spirolab II spirometer (Rome, Italy) preoperatively and 4, 8, 24, 48 and 72 hours after the surgery. FVC, FEV1, PaO_2, $PaCO_2$, complication rate, and length of ICU and hospital stay were recorded. Postoperatively measured FVC and FEV1 values were divided by preoperatively predicted values and multiplied by 100 to give the normalized FVC (nFVC) and FEV1 (nFEV1) [3].
Results The nFVC and nFEV1 values were significantly higher in the VATS group in the fourth and eighth postoperative hours compared with the THOR group (84.3 ± 14.4 vs. 64.3 ± 23.4, P = 0.013 and 84 ± 18.8 vs. 64 ± 22, P = 0.017, respectively). There was no statistically significant difference between the groups in the 24th, 48th and 72nd hours, although VATS patients showed higher values at each time points. The length of ICU stay was similarly 1 day, but the length of hospital stay was significantly longer in the THOR group (5 (3 to 6) vs. 7 (3 to 42) days (median and range) (P = 0.011)).
Conclusion Preoperative lung function prediction severely overestimates the real lung capacity of lobectomy patients in the immediate postoperative period. VATS lobectomy seems more beneficial from the point of early postoperative lung function. VATS lobectomy should be considered in patients with poor preoperative spirometry results to ensure better postoperative outcome.
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P255

Lung ultrasound reaeration score: a useful tool to predict non-invasive ventilation effectiveness

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Introduction The aim of our study is to evaluate the lung ultrasound (LUS) reaeration score (ReS) as a predictive tool for non-invasive ventilation (NIV) efficacy in general wards for acute respiratory failure (ARF) treatment. Even if ICUs are considered the safest place to perform NIV, a shortage of intensive beds has lead to NIV application outside the ICU. With appropriate patient selection, treatment-timing choice, adequate monitoring and staff training, NIV application in general wards can allow one to safely treat patients at an early stage with better cost-effectiveness [1]. Few data assessing the right tool to evaluate NIV treatment efficacy are available.
Methods We present preliminary data of a prospective observational ongoing study. Sixteen patients undergoing NIV treatment outside the ICU for ARF of any origin were evaluated with LUS at three times: before NIV application (T0), and at 5 minutes (T5) and 60 minutes (T60) of NIV treatment. US scan was performed in six regions for each emithorax. LUS patterns were defined as: consolidation (C); multiple coalescent B-lines (B+); multiple irregularly spaced B-lines (B) and normal aeration (A). A LUS-ReS [2] was calculated detecting changes in the US pattern when comparing T0 to T5 and T0 to T60 assessments. Outcome was defined as NIV failure in the case of tracheal intubation or death within 1 week from ARF outset, otherwise NIV success.
Results NIV treatment failed in five patients. Eleven patients have been successfully treated with NIV. Mean LUS-ReS (SD) at T0 to T5 was 0 (± 3.1) in group 0 and 2.5 (± 2.5) in group 1 (P = 0.15). Mean LUS-ReS (SD) at T0 to T60 was –1.2 (± 3.9) in group 0 and 4.2 (± 3.4) in group 1 (P = 0.03). ROC curves were obtained for the two LUS-ReS at T0 to

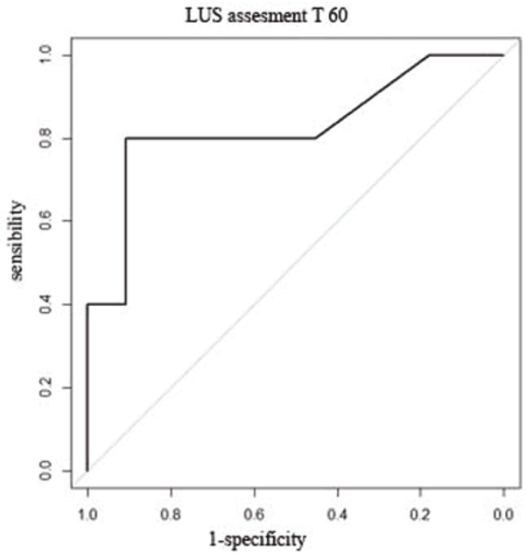

Figure 1 (abstract P255).

T5 (AUC 0.72) and T0 to T60 (AUC 0.83) (Figure 1). A LUS-ReS cutoff value of 0 can predict NIV effectiveness, with a sensibility of 91% and a specificity of 80%.

Conclusion If confirmed, our preliminary results suggest that LUS-ReS could be a useful tool in predicting NIV effectiveness for ARF treatment. Caution has to be applied when interpreting our results considered the small amount of patients enrolled.

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P256

Ultrasound in the diagnosis of pneumothorax: a survey of current practice

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Critical Care 2014, **18(Suppl 1):**P256 (doi: 10.1186/cc13446)

Introduction The purpose of this study was to survey current practice for the use of lung ultrasound (LUS) in the diagnosis of pneumothorax.

Methods Physician sonographers accredited by the German Medical Ultrasound Society (DEGUM) for ultrasonography in surgery, anaesthesia or medicine were invited to participate in an online survey. Frequency of exposure to patients with suspected pneumothorax, frequency of LUS use, assessment of diagnostic accuracy of LUS for ruling-out or ruling-in pneumothorax and preferences regarding technical aspects were enquired about.

Results Eighty-nine physicians responded. Average exposure to pneumothorax cases was 1/week. Fifty-five per cent of respondents used LUS 'always' or 'frequently'. Thirty-four per cent of physicians rated LUS as 'always accurate', and a further 54% as 'accurate in a majority of cases' in ruling out pneumothorax. Twenty-one per cent rated LUS as 'always accurate' and 69% as 'accurate in a majority of cases' in ruling in pneumothorax. Physicians reporting frequent exposure to pneumothorax patients used LUS in a higher proportion of cases ('high caseload sonographers') and were more confident to rule out pneumothorax (Figure 1). In total, 16 different combinations of transducers, probe orientations and scanning modes were reported. Linear transducers, sagittal probe-orientation, and B-mode and M-mode scanning were most often selected (38%).

Conclusion Physicians' use of LUS in the diagnosis of pneumothorax was modest. Assessment of diagnostic accuracy gave markedly lower scores than reported in clinical trials [1]. Correlation between frequency of exposure, likelihood of LUS usage and confidence in diagnostic accuracy warrants further research into the nature of the learning curve. Considerable variations regarding technical aspects of LUS reflect the ambiguity of current recommendations [2]. More research is required to establish the most efficient way of performing LUS for suspected pneumothorax and efforts need to be made to promote its use in these scenarios.

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P257

Computed tomographic assessment of airflow obstruction in smoke inhalation injury

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Critical Care 2014, **18(Suppl 1):**P257 (doi: 10.1186/cc13447)

Introduction Smoke inhalation injury (SII) is progress to pulmonary edema, pneumonia, and acute respiratory distress syndrome. SII may cause bronchial mucosal edema; we hypothesized that narrowing of luminal air bronchus due to bronchial wall edema correlated with respiratory deterioration of SII patients.

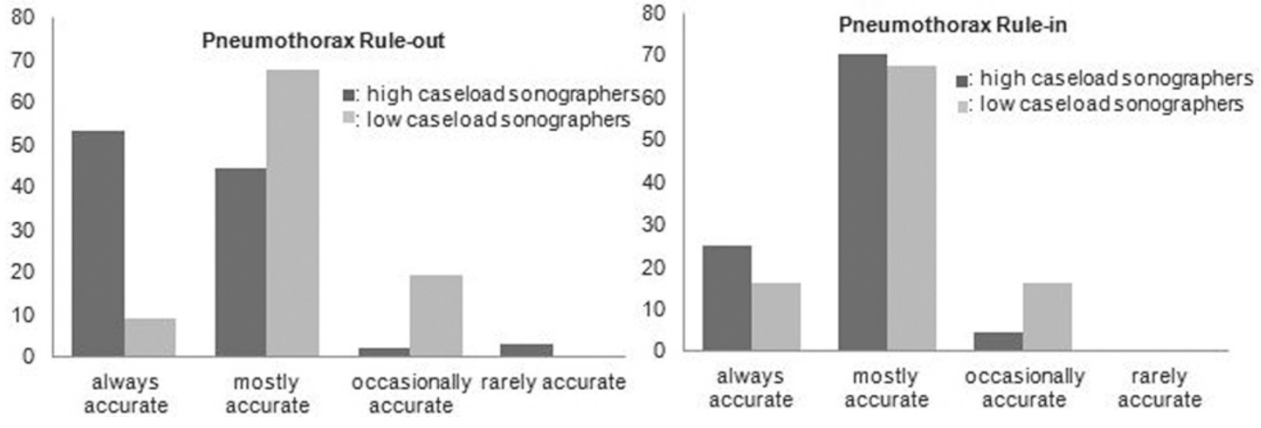

Figure 1 (abstract P256). Accuracy of LUS in pneumothorax.

Methods We prospectively studied 42 patients with a diagnosis of SII, according to visualized bronchoscopic findings at admission, and 15 control subjects. The thoracic high-resolution computed tomography (HRCT) scan was obtained within a few hours of admission to our hospital. Airway wall dimensions were calculated using a validated method. The images were viewed on a workstation using a magnification of ×5, and measurements of overall (D) and internal (L) diameter of the bronchi were made using electronic calipers, with wall thickness (T) being derived from these measurements (T = (D – L) / 2). Luminal area (Ai, mm^2) and total airway wall area (Ao) were calculated from L and D, respectively, using the formula: $A = \pi r^2$. We used both the ratio of airway wall thickness to total diameter (T/D ratio) and the percentage luminal area (LA% = (Ai / Ao + Ai) × 100).
Results The mean age of the patients was 59 years, 32 of the patients were men. The mean (SD) diameter of the bronchi in SII patients measured was 3.9 (1.5) mm (range 0.9 to 9.0 mm). There were statistically significant positive associations between wall thickening (expressed as T/D ratio) and luminal narrow (expressed as LA%) and the developed pneumonia (T/D ratio: $R^2 = 0.56$, $P < 0.01$ and LA%: $R^2 = 0.19$, $P = 0.005$) and mechanical ventilation days (T/D ratio: $R^2 = 0.37$, $P < 0.0001$ and LA%: $R^2 = 0.32$, $P < 0.001$, respectively). No statistically significant associations were identified between T/D ratio or LA% and initial P/F ratio, infusion volume initial 24 hours, ICU stay days, and outcome. The mean T/D ratio and LA% were 0.25 (0.04) and 25.9% (7.6) for patients with SII and 0.35 (0.04) and 44.7% (5.6) for controls.
Conclusion We have shown with the use of HRCT scanning on admission that patients with SII have airway wall thickening compared with normal controls. Furthermore, airflow obstruction due to bronchial wall edema related with developed pneumonia and mechanical ventilation days in SII patients.

P258

Semi-upright position improves ventilation and oxygenation in mechanically ventilated intensive care patients

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Introduction A semi-upright position (45° position) in ventilated patients is recommended to prevent ventilator-associated pneumonia (VAP) and is one of the first steps in progressive early mobility. We studied ventilated intensive care patients in a semi-upright position compared with a supine position to explore whether there was an improvement of oxygenation and ventilation.
Methods We retrospectively studied 60 patients in a mixed medical, surgical, neurological ICU during 2003 and 2007 [1-3]. In this study the effects of 45° position on the peripheral oxygen saturation (SpO_2) and the end-tidal carbon dioxide ($ETCO_2$) were measured. Body position was changed with a Total Care® bed (Hill-Rom) after results for the supine position (10°) were obtained. Half an hour after the body position was changed, measurements were taken, which included SpO_2 and $ETCO_2$. The results of body position change in the individual patients were analysed with paired-samples *t* test. A significance level <0.05 was considered significant.
Results Mean SpO_2 supine was 96.55% ± SD 2.404 versus mean SpO_2 semi-upright 97.4% ± SD 2.423, and mean ET-CO_2 supine was 4.62% ± SD 1.988 versus mean ET-CO_2 semi-upright 4.31% ± SD 1.060. The SpO_2 ($P < 0.0001$) and the $ETCO_2$ ($P < 0.0001$) improved significantly for the 45° position compared with <10° position.
Conclusion We demonstrated a significant increase in oxygen saturation and a significant decrease in end-tidal CO_2 when the head of the bed was elevated during mechanical ventilation. We believe positional therapy in intensive care patients is very important. The semi-upright position is an easy, effective and safe treatment in ICU patients. This position is effective in the bundle prevention of VAP, is the first step in progressive early mobility and is also effective in oxygenation and ventilation in mechanically ventilated patients. This clinical benefit of head-of-bed elevation >30° must lead to a standard of care in mechanically ventilated patients. Since 2009 the semi-upright position is a standard of care in our hospital.

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P259

Effects of sitting on the respiratory pattern, mechanics and work of breathing in mechanically ventilated patients

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Introduction The effect of sitting in an armchair on mechanically ventilated patients has not been studied enough. We study a group of patients ready for weaning for the respiratory pattern, mechanics and work of breathing during reclining in bed and after sitting in an armchair.
Methods Thirteen patients who needed mechanical ventilation after 18 days (1 to 60) were studied during volume assist-control mechanical ventilation and spontaneous breathing (O_2T, CPAP or PSV) in both positions. Airways, esophageal pressures and flow were registered for posterior analysis. Passive respiratory mechanics were measured by multiple linear regression methods, respiratory drive in esophageal pressure (P01) and respiratory effort using the pressure time product (PTP).
Results On controlled mechanical ventilation the respiratory system and chest wall elastance were significantly higher in sitting compared with reclining positions (Ers 39 ± 24 vs. 33 ± 25 cmH_2O/l and 10 ± 3 vs. 7 ± 3 cmH_2O/l), respiratory resistances were similar (15 ± 3 vs. 14 ± 5 cmH_2O/l/second) in both positions. Breathing pattern did not change significantly: tidal volume (0.406 ± 0.108 vs. 0.394 ± 0.118 l), inspiratory flow (0.74 ± 0.27 vs. 0.69 ± 0.23 l/second), inspiratory (0.97 ± 0.23 vs. 0.97 ± 0.28 seconds) and expiratory (1.43 ± 0.55 vs. 1.39 ± 0.44 seconds) times and respiratory frequency (27 ± 7 vs. 26 ± 7 bpm). Respiratory drive and effort tend to be higher in the sitting position, but not significantly. P01: 3.7 ± 1.9 versus 3.0 ± 1.4 cmH_2O, Δpes: 19 ± 10 versus 15 ± 8 cmH_2O, PTPmin: 373 ± 192 versus 284 ± 162 cmH_2O/second*minute.
Conclusion A sitting position for mechanically ventilated patients increased the rigidity of chest wall and the respiratory system. The effects of this mobilization must be evaluated because some patients show higher respiratory drive and effort in this position.

P260

The win ratio method: a novel hierarchical endpoint for pneumonia trials in patients on mechanical ventilation

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Introduction Development of novel antibiotics for VAP is hampered by the need for large phase 3 trials with mortality endpoints. With all-cause mortality rates decreasing, the large sample size for these trials, in particular for non-inferiority trials, has become a barrier to rapid drug development. Recently, a hierarchical approach to defining a composite endpoint for CV trials (win ratio method) has been described [1].
Methods We have adapted this approach in an ongoing superiority trial (Clinicaltrials.gov NCT01969799) comparing adjuvant use of a combination of fosfomycin and amikacin aerosol delivered by the PARI eFlow® Inline nebulizer in patients with Gram-negative pneumonia who are on mechanical ventilation. Both groups are receiving standard-of-care i.v. antibiotics. Patients from the active and placebo groups are matched in pairs based on presence of MDR Gram-negative bacteria, and disease severity by APACHE II score. Each pair has a winner and a

loser, or is a draw. The pair is first compared on mortality; if no difference, then ventilator-free days (VFD) are compared. If the outcomes are the same for both endpoints, a draw results. Active versus placebo groups will then be compared using the win ratio, defined as the number of pairs in which the active group was the winner divided by the number of pairs that did not result in a draw. We examined sample size and power characteristics of the win ratio endpoint using trial simulations.
Results Assuming a 15% 28-day mortality rate in the active arm and 20% in the control arm, to have 80% power with a two-tailed 0.05-level test for mortality would require 906 subjects per arm. Under the same assumptions with a difference in mean VFDs of 3 favoring the active arm (with common SD of 6), 130 subjects per arm provides 80% power. In approximately 32% of simulations, the win ratio result for each pair was determined by mortality. These simulation results assumed results within pairs were uncorrelated. If a positive correlation for each endpoint within pairs is assumed, power for the win ratio endpoint increases.
Conclusion The win ratio method is both clinically meaningful and straightforward to explain. This method could provide a new approach to powering both superiority and non-inferiority trials of novel antibiotics. In particular, this method allows for well-powered phase 2 trials, and potentially decreases the required size of phase 3 trials.
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P261

Failure to obtain admission sputum culture is associated with higher mortality and fewer ventilator-free days for intubated pneumonia patients: a quality improvement project

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Introduction The primary objective was to assess the impact of failure to obtain sputum culture (SC) among patients requiring intubation for pneumonia. For patients admitted to an ICU with severe pneumonia, guidelines recommend obtaining a lower respiratory tract sample for culture. Our experience suggested this is rarely ordered from the emergency department (ED).
Methods We retrospectively reviewed charts of all patients admitted through the ED with a diagnosis of pneumonia requiring intubation in the first 24 hours between January 2011 and November 2012. Patients were classified as SC collected or not collected. We recorded demographic data, SC results, antibiotic choice and de-escalation, ventilator-free days (up to day 14), and mortality in ICU and hospital. Inferential statistics were performed using SPSS version 20.0, with P <0.05 considered significant.
Results Of 50 patients we reviewed, 43 (86%) were intubated in the ED, 45 had SC ordered (only eight (18%) by ED physicians), and 37 (74%) had SC collected. There was no difference in age, gender or severity of illness as measured by APACHE score between the two groups. ICU mortality was lower in the SC collected group (24% vs. 69%, P = 0.007), as was hospital mortality (30% vs. 77%, P = 0.007) and antibiotics were de-escalated more often (89% vs. 8%, P <0.001). Patient with SC collected showed a trend toward significantly more ventilator-free days (6.5 vs. 0, P = 0.053).
Conclusion Sputum cultures were rarely ordered by ED physicians, and when not obtained in intubated patients with pneumonia, ICU and hospital mortality was higher, there was less antibiotic de-escalation, and a trend toward fewer ventilator-free days. Efforts to improve collection of sputum cultures in these patients are warranted.

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Nonventilatory factors affecting noninvasive mechanical ventilation success in hypercapnic critical care patients

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Introduction The aim was to determine the nonventilatory factors that affect the noninvasive mechanical ventilation (NIMV) success in patients with hypercapnic respiratory failure.
Methods A total of 41 patients were included in this prospective cohort study, who were followed for at least 96 hours in the ICU between January 2010 and November 2012 with the diagnosis of hypercapnic respiratory failure. Patients with ≥10 mmHg decrease in $PaCO_2$ in the first 72 hours were accepted as successful (Group 1) and those without this decrease were accepted as unsuccessful (Group 2). Among the patients with similar NIMV application characteristics, the effect of age, APACHE II score, infection, bronchospasm (daily respiratory function tests were performed with portable spirometry), heart failure, thyroid dysfunction and physiologic dead space ventilation (VD/VT) on success were evaluated. In statistical analysis, *t* test, Mann–Whitney *U* test and regression analysis were used.
Results Among the 41 patients, 28 (68%) were classified as Group 1 and 13 (32%) as Group 2. No differences were identified among the ventilatory parameters of the two groups (P >0.05). Patients in Group 1 were younger, had higher admission $PaCO_2$ levels, higher free T3 levels and ejection fraction in echocardiography (P <0.05). VD/VT values of Group 1 measured at admission and on the second and third days of NIMV were lower than Group 2 (P <0.05). Similarly, they had lower FEV1 percent predicted values in the stable period and on the first and second days of NIMV (P <0.05). FEV1/FVC was lower in Group 1 when measured in the stable period and on the third and fourth days of NIMV. In Group 2, CRP values measured during the first day (P = 0.014) and third day (P = 0.031) of NIMV were identified as higher. In multivariate regression analysis, admission $PaCO_2$ (OR: 1.59, 95% CI: 1.1 to 2.3, P = 0.014), free T3 (OR: 12, 95% CI: 1.51 to 101, P = 0.019), and VD/VT (OR: 1.23, 95% CI: 1.01 to 1.52, P = 0.048) were identified as independent risk factors affecting NIMV success.
Conclusion The results of this study revealed that among the NIMV nonresponsive hypercapnic patients, nonventilatory factors such as thyroid dysfunction and increased dead space ventilation should be considered.

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Physiologic comparison between NAVA, PAV+ and PSV in critically ill patients

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Introduction The aim of the present study was to compare, in a group of difficult to wean critically ill patients, the short-term effects of PSV, PAV+ and NAVA on breathing pattern, patient effort and patient–ventilator interaction.
Methods Seventeen patients were studied during NAVA, PAV+ and PSV with and without artificial increase in ventilator demands (challenge) using either dead space (DS, n = 10) or chest elastic load (CL, n = 7) application. Airway and transdiaphragmatic (Pdi) pressures, electrical activity of the diaphragm (EAdi), volume and flow were measured breath by breath, while inspiratory integral of Pdi (PTPPdi) and EAdi (∫EAdi) were calculated.
Results At resting conditions all modes provided equal support as indicated by a similar PTPPdi per breath, per minute and per liter of ventilation. Apart from triggering delay, which with and without the challenge was significantly higher with PAV+ than that with NAVA and PSV, patient–ventilatory synchrony did not differ among modes. Independent of challenging conditions, inspiratory effort to trigger the ventilator was significantly higher with PAV+ than with NAVA and PSV. Compared with PSV, PAV+ and NAVA favored a more variable breathing pattern as indicated by the significantly higher coefficient of variation of tidal volume (VT). CL increased PTPPdi significantly less with PAV+ than with PSV and NAVA, while the increase of PTPPdi after DS did not differ among modes. The relationship between VT and PTPPdi was weaker with NAVA (median (IQR) r^2 = 25.6% (2.7 to 58.1%)) than with PAV+ (55.6% (34.4 to 61.6%)) and PSV (53.9% (23.2 to 77.4%)) on account of a poor ∫EAdi–PTPPdi relationship (r^2 = 16.2% (1.4 to 30.9%)) during NAVA.
Conclusion Compared with PSV proportional modes favored breathing variability, while in the face of changing respiratory system mechanics PAV+ might be superior. However, significant drawbacks of both NAVA and PAV+ limit the effectiveness of these modes to proportionally assist the inspiratory effort.

P265

Does average volume-assured pressure support make any difference compared with BIPAP?

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Introduction Average volume-assured pressure support (AVAPS) has been developed to ensure a more fixed tidal volume along with the convenience and advantages of pressure support ventilation. In this study we compared the AVAPS with the BIPAP.
Methods Approval was obtained from the hospital's ethics committee for the study. Thirty-three patients over 18 years of age with acute respiratory failure as a result of either internal or surgical reasons were included in the study. This study was conducted with the Philips V 60 ventilator, which includes both BIPAP and AVAPS mode. The implementation protocol for non-invasive ventilation (NIV) included, firstly, a 2-hour BIPAP application (Period Bi) and then, without interruption, a 2-hour AVAPS application (Period AV). After measuring the basal blood gas analysis, patients were informed of how NIV would be practiced and what function it would have. In BIPAP mode, the ventilator parameters were adjusted as follows; EPAP: 5 to 7 cmH_2O, IPAP: 15 to 20 cmH_2O. Patient comfort was analyzed with a scale ranging from 0 to 2 (0: compatible, 1: medium-compatible, 2: noncompatible). During BIPAP ventilation, levels of arterial blood gases (pH, pO_2, pCO_2 and SPO_2), comfort scale and hemodynamic data were recorded at the 30th minute, first hour and second hour. After the patient was monitored for 2 hours in BIPAP mode, the mode was changed to the AVAPS by setting the required rates without removing the mask. EPAP settings were adjusted as follows for AVAPS: 5 to 7 cmH_2O, Pmin to max: 10 to 25 cmH_2O, tidal volume: 6 to 8 ml/kg. As in the BIPAP mode, we analyzed and recorded the rates of arterial blood gases, comfort scale and hemodynamic parameters at the 30th minute, first hour and second hour. In case of agitation that prevents NIV, patients were sedated by dexmedetomidine.
Results When we analyzed patients according to their body mass indexes (BMI), pH and pCO_2 values of the patients with BMI ≤30 showed a greater improvement at all three measurements in the AVAPS compared with BIPAP (P <0.001). When patient compliance was examined, the number of patients regarded as comfortable in the BIPAP period was 20 (66.7%), but this figure was 25 (83.3%) for the AVAPS.
Conclusion Patient comfort was higher and need for sedation was lower in AVAPS. According to the results obtained from this study, the AVAPS had positive effects on pH, gas variation and patient comfort; therefore, it can be confidently used in clinical practice.

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Oxygenation index outperforms the P/F ratio for mortality prediction

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Introduction The P/F ratio is widely used clinically and as part of research to categorise severity of respiratory failure [1]. However, no account is made of an important determinant of oxygenation; mean airway pressure (MAP). The oxygenation index (OI) incorporates the MAP and has been suggested as a more accurate means of determining severity of respiratory failure [2]. In addition, the optimal time for this assessment is unclear. We sought to answer these questions by analysing a large database of patient and ventilator data.
Methods The ICU of the Bristol Royal Infirmary has used an electronic clinical information system (CIS) since 2008, with every hour of care available for analysis as a result. Ventilated patients were identified, the P/F ratio and OI were calculated and the worst values for these determined for four time periods (first 12, 24, 36 and 48 hours of ventilation). Logistic regression analysis was used to create models to predict unit and hospital mortality.
Results Data for over 150,000 hours of care in 4,886 patients was available for analysis. Excluding nonventilated patients and those transferred ventilated from another ICU, 2,156 patients provided data. In comparison with survivors, nonsurvivors were older, with higher OI and 24-hour SOFA scores and lower P/F ratios. The optimal time for calculation of both OI and P/F ratio for mortality prediction is the first 12 hours of ventilation. The models using worst OI are better predictors of ICU and hospital mortality than those using worst P/F ratio (area under receiver operating curve 0.840 vs. 0.822).
Conclusion Our analysis suggests that the OI is a more sensitive descriptor of the severity of respiratory failure than the P/F ratio and that this calculation should be performed using data from the first 12 hours of ventilation.
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P267

Determining the mechanical ventilation mode and pressure support combination that is best compatible with the rapid shallow breathing index calculated in spontaneous ventilation

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Introduction Weaning from the mechanical ventilation (MV) composes about 40 to 50% of the total length of MV. Besides, there is no single reliable parameter indicating that patient will tolerate extubation safely. The rapid shallow breathing index (RSBI) is relatively the best predictive parameter for the initial assessment of readiness for discontinuation of MV support. But evaluation of the RSBI is valuable during T-tube ventilation; and in clinical practice it is not always possible to perform this assessment. In this study, we aimed to determine the best MV mode and pressure combinations that can predict successful RSBI closest to values calculated in spontaneous ventilation and estimate the patients' readiness for weaning.
Methods In this prospective cohort study, 25 mechanically ventilated patients were included. After 24 hours of MV, if the patients can successfully pass the daily screening test a spontaneous breathing trial (SBT) was initiated. RSBI and other weaning parameters were calculated in different combinations (PS:5 PEEP:5, PS:0 PEEP:5, PS:5 PEEP:0, PS:0 PEEP:0) before T-tube trial in all patients. Measurements in the spontaneous ventilation was performed with the COSMOPLUS Novometrix device that has both capnography and respiratory monitorisation function; other measurements were performed with ventilators.
Results The mean age of the study group was 73 ± 10 years; 11 of them were female and mean APACHE II score was 19 ± 6. RSBI did not differ significantly between spontaneous mode and other combinations, but the best correlation with spontaneous mode was found with PS:5 PEEP:0 (P = 0.0001, r = 0.719), and the worst with PS:0 PEEP:5 combination. RSBI calculated in each combination showed no predictive value for weaning success. Respiration rate (f) was higher in the SBT failure group than the SBT success group. When measured at PS:0 PEEP:5 and PS:5 PEEP:0 combinations, the threshold value of f was found to be 27/minute (P = 0.03).
Conclusion Although there was a correlation between RSBI measured in the T-tube and RSBI measured in different mode and pressure combinations, especially with the combination of PS:5 PEEP:0, a threshold value for RSBI cannot be detected during MV to predict SBT success.

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New setting of neurally adjusted ventilatory assist during mask noninvasive ventilation

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Introduction Noninvasive ventilation through a mask is commonly applied in pressure support ventilation (nPSV). Recent studies

showed that noninvasive neurally adjusted ventilatory assist (nNAVA) improves patient–ventilator interaction and synchrony. More recently we described a new setting for nNAVA (nNAVA15) able to reduce the peak of electrical activity of the diaphragm (EAdipeak) and dyspnea (assessed by a visual analogue scale, VASd), compared with both nPSV and nNAVA, in patients undergoing NIV through a helmet, by improving the rate pressurization. We therefore designed a physiological study to evaluate and compare the effects of nNAVA15 with nPSV and nNAVA on VASd, EAdipeak, pressurization rate and arterial blood gases (ABGs).
Methods Fourteen patients undergoing noninvasive ventilation because of acute respiratory failure underwent three randomized 30-minute trials: nPSV (inspiratory support above positive end-expiratory pressure (PEEP) ≥8 cmH_2O, fastest rate of pressurization); nNAVA (NAVA level to achieve a comparable EAdipeak as during nPSV); nNAVA15 (NAVA level at 15 $cmH_2O/\mu V$ and the maximum inspiratory airway pressure (Paw) set at the value corresponding to PEEP + inspiratory support during nPSV). Oxygen inspiratory fraction and PEEP remained unmodified throughout the study period. The last minute of each trial was analyzed. Paw-time products of the initial 200 ms from the onset of ventilator pressurization (PTP200), of the initial 300 and 500 ms from the onset of the EAdi swing indexed to the ideal PTP (PTP300i and PTP500i, respectively), and of the triggering area (PTPt) were computed. ABGs and VASd were assessed at the end of each trial.
Results nNAVA15 reduced VASd (3.0 (2.0; 3.0)), compared with both nPSV (5.0 (4.0; 5.2)) and nNAVA (4.0 (3.0; 5.0)) (P <0.001), without affecting ABGs and EAdipeak. nNAVA15 improved PTP300i and PTP500i (42% (32.5; 46.5) and 63% (54; 68)%, respectively) compared with nPSV (25 (4; 33)% and 44 (23; 52)%, P <0.001) and nNAVA (25 (20; 34)% and 46 (33; 57)%, P <0.001). PTP200 was lower in nNAVA (62 (46; 82) cmH_2O*second) with respect to both nPSV (87 (77; 112) cmH_2O*second) and nNAVA15 (85 (70; 127) cmH_2O*second) (P = 0.001). PTPt was significantly improved by both nNAVA (–00.9 (–3.2; –0.2) cmH_2O*second) and nNAVA15 (–0.6 (–2.3; –0.2) cmH_2O*second) as opposed to nPSV (–9.4 (–12.3; –5.9) cmH_2O*second, P <0.001).
Conclusion Compared with nPSV and nNAVA, nNAVA15 through a mask reduces VASd, assuring an optimal pressurization rate and triggering performance, without affecting the breathing pattern, neural drive and ABGs.

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A new setting to improve noninvasive neurally adjusted ventilatory assist by helmet

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Introduction Noninvasive neurally adjusted ventilatory assist by helmet (hNAVA) was shown to improve, compared with pressure support ventilation by helmet (hPSV), patient–ventilator interaction and synchrony in patients with acute respiratory failure without affecting peak electrical activity of the diaphragm (EAdipeak) [1]. Recently, a new helmet is available, which improves pressurization during hPSV. We propose a new setting of hNAVA (hNAVA15) to achieve further improvement. We compare hPSV, hNAVA and hNAVA15, all delivered using the new helmet, with respect to patient's dyspnea, assessed by a visual analogue scale (VASd), arterial blood gases (ABGs), EAdipeak, rate of ventilator pressurization and triggering performance.
Methods Fifteen patients underwent three randomized 30-minute trials: hPSV, set with an inspiratory support above positive end-expiratory pressure (PEEP) ≥10 cmH_2O and the fastest rate of pressurization; hNAVA, setting the NAVA level to achieve the same EAdipeak as during hPSV; hNAVA15 setting the NAVA level at 15 $cmH_2O/\mu V$ and the maximum inspiratory airway pressure (Paw) at the value corresponding to PEEP + inspiratory support during nPSV. Oxygen inspiratory fraction and PEEP remained unmodified throughout the study period. Paw-time products of the initial 200 ms from the onset of ventilator pressurization (PTP200), of the initial 500 ms from the onset of the EAdi swing indexed to the ideal PTPaw (PTP500i), and of the triggering area (PTPt) were computed. ABGs and VASd were assessed at the end of each trial.
Results hNAVA15 reduced the EAdipeak (10.2 (7.1; 16.2) μV) with respect to both hPSV (16.9 (12.7; 19.8) μV, P <0.001) and hNAVA (15.3 (10.7; 18.8) μV, P <0.001), while decreasing VASd (3.0 (3.0; 4.0) in hPSV, 3.0 (2.0; 4.0) in hNAVA and 1.0 (1.0; 2.0) in hNAVA15; P <0.01). PTP200 and PTP500i were improved by hNAVA15 (36 (28; 57) cmH_2O*second and 40 (30; 47)%, respectively) compared with hPSV (31 (24; 45) cmH_2O*second and 17 (9; 26)%, respectively) and hNAVA (23 (16; 30) cmH_2O*second and 23 (17; 37)%, respectively) (P <0.01). PTPt was lower in hNAVA15 (2.9 (1.6; 4.4) cmH_2O*second, P <0.01) compared with both hPSV and hNAVA, and lower in hNAVA (6.0 (2.7; 11.6) cmH_2O*second), compared with hPSV (18.5 (11.2; 22.5) cmH_2O*second, P <0.01). ABGs were no different between trials.
Conclusion In comparison with hPSV and hNAVA, hNAVA15 significantly reduced EAdipeak and VASd, improving the pressurization and triggering performance, without affecting ABGs.
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P270

Is neurally adjusted ventilatory assist feasible during anesthesia?

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Introduction Neurally adjusted ventilatory assist (NAVA) has so far been used in minimally sedated intensive care patients. NAVA has not been applied in patients in the operation room. The effect of different sedatives/anesthetics on the electrical activity of the diaphragm (Edi) has not so far been studied. The aim of our study was to compare the effect of sevoflurane and propofol on the Edi signal and breathing pattern during sedation and anesthesia and also in combination with remifentanil.
Methods A randomized cross-over study comparing sevoflurane and propofol sedation and anesthesia in 10 juvenile pigs. Remifentanil 0.1 μg/kg/minute was added after a period of anesthetic agent administration. The animals were ventilated with NAVA with fixed level throughout the study. Respiratory variables were measured for the last 5 minutes of each 15-minute exposure.
Results The Edi signal and spontaneous breathing were preserved with both anesthetics. The breathing variability, expressed as the coefficient of variation (SD/mean) of the tidal volume (CVvt), was high with both drugs. CVvt was greater during with propofol than with sevoflurane (CVvt 32 vs. 18% during sedation and CVvt 23 vs. 14% during anesthesia). The frequency of sighs was higher with propofol both during sedation (29 vs. 12 sighs/hour) and anesthesia (21 vs. 1 sighs/hour) than with sevoflurane.
Conclusion NAVA can be applied during propofol and sevoflurane anesthesia in pigs, with well-preserved Edi and spontaneous breathing. The natural variability is maintained with NAVA even during anesthesia. In contrast to sevoflurane, propofol sedation and anesthesia is associated with a high frequency of sighs and post-sigh apneas, probably due to a centrally induced mechanism. Our data warrant studies of NAVA in humans undergoing anesthesia and surgery when neuromuscular blockade is not required.

P271

Intensive alveolar recruitment after cardiac surgery: a randomized controlled clinical trial

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Introduction Protective mechanical ventilation has been associated with lower incidence of pulmonary and extrapulmonary complications in major surgery. The aim of the present study is evaluate whether adding an intensive alveolar recruitment protocol improves clinical outcomes and reduces healthcare utilization in patients undergoing cardiac surgery.

Methods In this single-center, parallel-group trial, we randomly assigned adult patients presenting signals of deficient gas exchange (PaO_2/FIO_2 <250 at a PEEP of 5 cmH_2O) in the immediate postoperative period to either intensive alveolar recruitment or a standard protocol, both using low-tidal volume ventilation (6 ml/kg/ibw). Our hypothesis was that an aggressive alveolar recruitment protocol will be translated to better lung compliance, better gas exchange, fewer pulmonary complications and reduced length of hospital stay when compared with the control group.
Results A total of 320 patients were enrolled in the study, 163 patients in the standard protocol group and 157 in the intensive alveolar recruitment group. Patients of the interventional group presented a higher incidence of pneumonia than patients for the control group (5 (3.3%) vs. 19 (22%), $P = 0.004$). The length of the hospital stay was shorter among patients receiving intensive alveolar recruitment than among those receiving standard care (10.9 (9.9 to 11.9) vs. 12.4 days (11.3 to 13.6); $P = 0.045$). There was no difference between groups according to extrapulmonary complications and mortality.
Conclusion In this trial, an intensive alveolar recruitment protocol associated with a protective mechanical ventilation strategy reduced pulmonary complication and length of hospital stay in patients undergoing cardiac surgery (NCT01502332).
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P272

Endomicroscopic analysis of time-dependent and pressure-dependent recruitment of subpleural alveoli

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Introduction We used transthoracic endoscopy [1] to continuously record images of subpleural alveoli during recruitment manoeuvres and different steady plateau pressures between the manoeuvres.
Methods We investigated two groups of 13 rats each. Animals were ventilated with ZEEP or PEEP of 5 mbar, FiO_2 of 1.0 and tidal volume of 10 ml/kg. A double low-flow manoeuvre was designed, consisting of two consecutive low-flow manoeuvres with a peak pressure of 30 mbar, interrupted by a 5-second plateau phase at different pressures (2, 4, 8 and 12 mbar). Alveolar size at the peak pressures and during the plateau levels was analyzed from the recorded videos frame by frame. Therefore the alveolar outline of 10 alveoli was marked manually and the outlined area was calculated [2]. Compliance of tidal breaths before and after the manoeuvres was calculated using two-point compliance.
Results In both groups, analysis of the alveolar area revealed that alveolar size at the second peak of the manoeuvre did not differ significantly compared with the first peak (100.97% in ZEEP group, 102.37% in the PEEP group). During the plateau phases there was a slight increase in alveolar size at higher plateau pressures (slope of linear regression at plateau 4 mbar: 0.1 %/500 ms for ZEEP group, 0.18%/500 ms for PEEP group; at plateau 8 mbar: 0.42%/500 ms for ZEEP group, 0.565%/500 ms for PEEP group). After the manoeuvres, compliance increased to 137.73% in the ZEEP group and 119.91% in the PEEP group.
Conclusion In the healthy lung, once recruited, alveoli stay stable in size over wide pressure ranges. Further recruitment manoeuvres do not lead to further increase of alveolar size, but increase of compliance. During plateau phases, alveolar size increases dependent on pressure. This leads to the assumption that recruitment is not only pressure dependent but also time dependent.
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P273

PEEP titration on the basis of intratidal resistance–volume profiles

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Introduction Lung-protective mechanical ventilation requires positive end-expiratory pressure (PEEP) and tidal volume (VT) to be chosen with regard to the individual state of the lung. The shape of the intratidal compliance–volume profiles might reflect the state of the lung (atelectatic, open, overdistended) and could therefore be classified into shape categories that translate into PEEP suggestions [1]. Intratidal resistance–volume profiles might reflect intratidal opening and collapse of the lung [2]. Using respiratory data from an animal study we suggest a classification into resistance shape categories based on the slope of the R(V) profiles.
Methods Fifteen pigs with lavage-induced lung damage were ventilated at two PEEP levels (0 and 12 mbar) and three tidal volumes (8, 12 and 16 ml/kg bodyweight). Compliance (C(V)) and resistance (R(V)) profiles for each individual animal and ventilation setting were calculated from respiratory data using the gliding-SLICE method [3]. C(V) profiles were associated with one of the six suggested shape categories. The dependency of the mean R(V) slope of all animals on the ventilation setting was used as a basis for classification into resistance shape categories. Resistance shape categories were compared with compliance shape categories for each individual animal to test whether similar PEEP suggestions result from both methods.
Results Small PEEP and VT were typically associated with increasing C(V), and decreasing C(V) corresponds to large PEEP and VT. A classification of each C(V) profile into one of six compliance shape categories was possible. The shapes of the R(V) profiles of individual animals were remarkably similar. The R(V) slope was typically largest for a PEEP and VT setting at which derecruitment was likely and smallest where overdistension was likely. Based on this a classification scheme was defined: 10 <slope <21 mbar s/L2 (category 1, 'increase PEEP'), slope ≥21 mbar s/L2 (category 2, 'keep PEEP') and slope ≤10 mbar s/L2 (category 3, 'decrease PEEP'). Comparison of resistance and compliance shape categories for single animals shows a good correlation.
Conclusion Resistance shape categories might provide additional guidance for PEEP setting. Combining compliance and resistance shape categories could improve lung-protective ventilation.
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P274

US study of gliding in nondependent lung regions: the dark side of the moon

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Introduction A protective ventilatory strategy should prevent VILI, but in patients with larger nonaerated areas hyperinflation may occur during tidal ventilation even during a protective ventilatory strategy [1]. The gliding sign is used as a marker of pneumothorax and, in a study [2], to quantify preoperatively the degree of pleural adhesion in thoracic surgery patients. In our study we measured the variations of gliding (G) and static compliance (Cstat) according to incremental/decremental variations of PEEP in patients with hypoxic respiratory failure.
Methods Ten patients with hypoxic respiratory failure (P/F <300) were ventilated in VCV (Vt of 7 ml/kg, FiO_2 100%, RR 10/minute); keeping Vt constant, PEEP was gradually increased from ZEEP to 22 cmH_2O, unless there was occurrence of hypotension or SpO_2 <90% or Pplat >45 cmH_2O or G no more visible, and then similarly reduced from 22 cmH_2O to ZEEP. The gliding was assessed at six points of intercostal

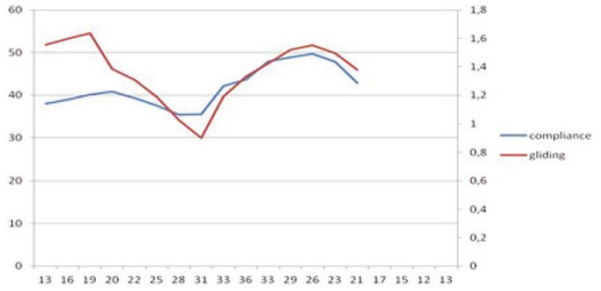

Figure 1 (abstract P274). PCC between mean G (cm) and mean Cstat at different PEEP, in axis Pplat.

spaces bilaterally and the movement of a hyperechoic point of pleura or a b-line was observed during tidal ventilation. For each step, the excursion of G during the inspiratory phase was measured and compared with the Cstat values. Statistical analysis was performed with the Pearson correlation coefficient (PCC).

Results All patients completed the study without adverse events. In all patients we observed a reduction of G and Cstat at the increase of PEEP and specularly an increase of G and Cstat during the reduction of PEEP (Figure 1). In five patients at the lower levels of PEEP (from 0 to 10) an increase of Cstat and G was observed. For all patients the PCC of Cstat and G and was >0.5 (P <0.03), ranging from 0.537 (P = 0.017) to 0.964 (P <0.0001).

Conclusion The variations of G at different levels of PEEP are consensual with those of Cstat. The study of G during tidal ventilation could help to identify hyperinflation in nondependent lung regions and to optimize lung-protective ventilatory strategies.

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P275

Protective ventilation reduces bacterial growth and lung injury in a porcine pneumonia model

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Introduction Bacterial pneumonia is a common indication for mechanical ventilation in the ICU. Ventilation with high positive end-expiratory pressure (PEEP) and low tidal volume (VT) is recommended in patients with adult respiratory distress syndrome. This improves clinical outcome compared with ventilation with low PEEP and medium-high VT [1]. However, the effect of VT and PEEP on bacterial growth in lung tissue is not known. This study contrasted the effect of a protective ventilator protocol with a standard medium-high VT and lower PEEP protocol on lung bacterial growth, lung edema formation and lung injury. It was performed in a porcine model of intensive care with the frequently found pathogen *Pseudomonas aeruginosa*.

Methods Sixteen pigs were anesthetized and randomized to mechanical ventilation with two different ventilator settings for 6 hours; Prot-V (PEEP 10 cmH_2O, VT 6 ml/kg, n = 8) and Control (PEEP 5 cmH_2O, VT 10 ml/kg, n = 8). At 0 hours, 1×10^{11} colony-forming units (cfu) of *P. aeruginosa* were instilled intratracheally. At the end of the experiment, six postmortem lung biopsies from predefined declivial locations were taken from each animal for cultures and weight measurements.

Results *P. aeruginosa* growth in lung tissue and wet to dry ratio were lower in the Prot-V group than in the Control group (P <0.05 and P <0.05). PaO_2/FiO_2 was higher in the Prot-V group than in the Control group (P <0.05) (Table 1).

Conclusion Protective ventilation with low VT and higher PEEP reduces *P. aeruginosa* growth in lung tissue, lung edema formation and lung injury in contrast with medium-high VT and lower PEEP ventilation in this porcine pneumonia model.

Table 1 (abstract P275). *P. aeruginosa* log mean, wet to dry ratio, and PaO_2/FiO_2 at 5 hours

	P. aeruginosa (cfu/g)	W/D	PaO_2/FiO_2 at 5 hours (mmHg)
Prot-V	3.5 ± 0.7	1.7 ± 0.2	434 ± 62
Control	4.2 ± 0.7	2.7 ± 1.3	343 ± 61

Data presented as mean ± SD.

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P276

Changes in computed tomography and ventilation/perfusion mismatch with positive end-expiratory pressure

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Introduction The purpose was to compare effects of PEEP on computed tomography (CT) and estimated ventilation/perfusion (V/Q) mismatch. Previously, an oxygenation-based method was shown more related to the CT-measured effect of PEEP than lung mechanics [1], indicating lung aeration is better quantified using V/Q mismatch. Pulmonary shunt and low and high V/Q mismatch can be estimated from varying FIO_2 and measuring ventilation and blood gas contents [2].

Methods Preliminary results in six ARDS patients. CT scans were taken in static conditions at PEEP 5, 45 and 15 to 20 cmH_2O. V/Q was estimated at 5 and 15 to 20 cmH_2O as: shunt, low V/Q as alveolar to lung capillary PO_2 difference ($\Delta AcPO_2$), high V/Q as alveolar to lung capillary PCO_2 difference ($\Delta AcPCO_2$) [2]. Nonaeration, poor aeration, and normal aeration plus hyperinflation were calculated from Hounsfield units. Aeration and V/Q were compared (Pearson, ρ).

Results PEEP improved V/Q in four patients, shunt reducing 7 to 42% with no/small increase in $\Delta AcPCO_2$. Two deteriorated, with large $\Delta AcPCO_2$ or shunt increase. No systematic changes in $\Delta AcPO_2$ were seen. Figure 1 shows response to PEEP in two patients. Changes in nonaerated regions and shunt were correlated (ρ = 0.94, P = 0.002). No correlations were found between poorly aerated regions and $\Delta AcPO_2$ (ρ = –0.09, P = 0.84) or hyperinflated regions and $\Delta AcPCO_2$ (ρ = 0.07, P = 0.88).

Conclusion In these preliminary cases, changes in shunt and nonaerated tissue correlated well. However, results indicate poor agreement between changes in low and high V/Q and lung morphology.

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P277

Ventilator settings in ICUs: comparing a Dutch with a global cohort

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Introduction In data collected during the Third International Study on Mechanical Ventilation, we compared data from the Netherlands with a global cohort. We hypothesized that tidal volumes (Vt) were smaller and applied positive end-expiratory pressure (PEEP) was higher in the Netherlands, compared with the global cohort. We also compared use of non-invasive ventilation (NIV) and outcomes in both cohorts.

Methods A *post-hoc* analysis of a prospective observational study of patients receiving invasive mechanical ventilation was conducted in

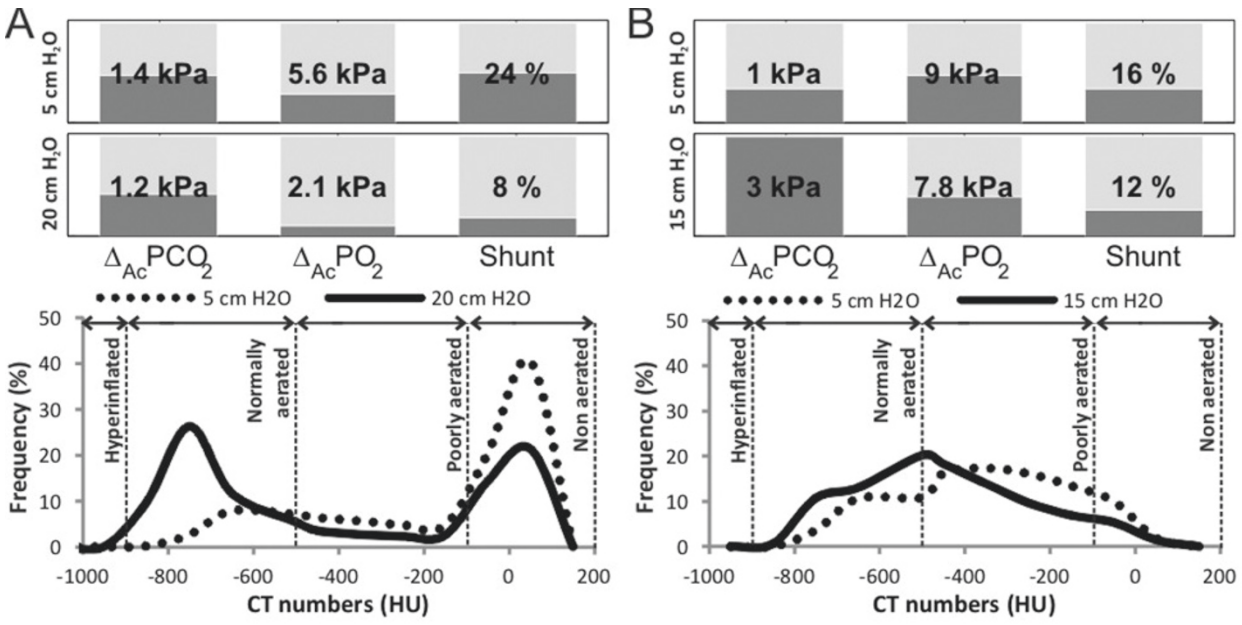

Figure 1 (abstract P276). Gas exchange and CT for patient improving **(A)** or worsening **(B)** with PEEP change.

494 ICUs around the world [1]. The Dutch cohort covered 196 patients and the global cohort 7,952.

Results Vt was 7.6 ml/kg predicted bodyweight in the Dutch cohort versus 8.0 ml/kg and the median applied PEEP was 8 cmH_2O versus 5.8 cmH_2O (both P <0.01). In the subgroup of patients with ARDS, Vt ml/kg was 7.6 and applied PEEP 8.8 cmH_2O in the Netherlands versus 8.6 ml/kg (P = 0.41) and 8.3 cmH_2O worldwide. In the Netherlands 7.1% of admitted patients received NIV as first mode of mechanical ventilation versus 15% in the global cohort. In both cohorts 18% of patients were hypercapnic at ICU admission. Fewer patients in the Dutch cohort showed an ICU-acquired pneumonia (4.1 vs. 9.4%, P = 0.007) and sepsis (5.1 vs. 9.0%, P = 0.042), but more patients evolved delirium (16 vs. 5%, P <0.01).

Conclusion According to our hypothesis, Vt was smaller and applied PEEP was higher in the Dutch cohort. Patients in both cohorts received larger Vt than recommended in prevention of ARDS [2]. Hypercapnia is a main criterion for the use of NIV [3], which suggests that NIV could be used more often in the Netherlands. The lower incidence of delirium worldwide could be caused by differences in sedation or may be due to the used methods of screening.

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P278

Graphical user interface for visualization of a decision support system for PEEP titration

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Introduction The analysis of dynamic volume-dependent compliance provides the rationale basis for PEEP titration during mechanical ventilation. Due to its volume dependence, the compliance of the respiratory system is nonlinear within each single breath (intratidal), which is reflected in the compliance–volume curve (CV curve). The shape of the CV curve is determined by the PEEP level. The mechanical stress for the mechanically ventilated lung is expected to be minimal when the lung is ventilated within the volume range of maximal compliance. We present a new graphical user interface (GUI) that supports the clinician to titrate the PEEP level by means of a shape category analysis of the CV curve.

Methods A decision support system in the form of a computer-based GUI was developed and tested using respiratory data obtained from patients of the University Medical Center Freiburg. The new clinician-oriented approach provides a breath-by-breath visualization of the patient's individual intratidal CV curve. The dynamic compliance was analyzed using the gliding-SLICE method [1]. The resulting intratidal CV curve was classified into one of six shape categories according to the definition from Mols and colleagues [2]. The actual shape category of the CV curve indicates whether PEEP setting should be changed or whether the volume range of maximal compliance is reached.

Results The GUI provided a breath-by-breath visualization of the intratidal CV curve and the intuitive individual compliance shape category. Based on the compliance shape category, different guidelines of PEEP titration were applied with the objective of ventilating the patient mechanically within the range of maximal compliance.

Conclusion The newly developed GUI allows a breath-by-breath visualization of the intratidal CV curve with high reliability. Automated classification of the intratidal CV curve into compliance shape categories provides the rationale basis for patient-individual PEEP titration.

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P279

Time-dependent apoptosis induction after spontaneous-breathing or ventilation-analogue experimental mechanostimulation of monolayer lung cell cultures

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Introduction The cyclic strain of lung tissue during mechanical ventilation compared with spontaneous breathing is associated with a largely increased mechanical load due to larger pressure amplitudes and higher acceleration forces. This additional load may change tissue mechanics and may lead to tissue damage. Although experimental mechanostimulation *in vitro* is a widely used method

to analyse mechanical load on cells or tissue, *in vitro* experiments with ventilation-analogue stimulation are missing. In this work we compare for the first time the changes of monolayer lung cells after ventilation-analogue stimulation with spontaneous-breathing analogue mechanostimulation. The aim of the study was to show time-dependent differences in the induction of apoptosis due to mechanical overload, by fluorescence microscopic observations.

Methods Alveolar epithelial cells (A549) were grown on RGD-coated, highly flexible polydimethyl siloxane membranes. After becoming approximately 100% confluent, cells were stained with Hoechst 33342/TMRE/caspase-3 and caspase-7/PI and continuously observed by fluorescence microscopy. The cells were stimulated either with ventilation-analogue or spontaneous-breathing analogue profile [1]. For both settings the frequency was 0.25 Hz, the surface increase 20% and the cell monolayers were stimulated over a time period of 2 hours in the bioreactor [2].

Results The analysis of fluorescence microscopic images showed the first evidence of apoptosis induction after 40 minutes of ventilation-analogue stimulation. In contrast, apoptosis induction after spontaneous-breathing analogue stimulation occurred after 90 minutes.

Conclusion The observation of cells during stimulation with continuous fluorescence microscopic imaging allowed us to analyse the time-dependent induction of apoptosis under the aspects of different stimuli. We could prove our hypothesis that ventilation-analogue stimulation was worse for the cellular viability then spontaneous-breathing analogue stimulation. In future, the direct optical tracking of cell damage should allow one to analyse other stimulation profiles as well, and thereby to improve the stimulation profiles and ultimately the ventilation profile as well.

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P280

Influence of positive end-expiratory pressure on cyclic recruitment and derecruitment during one breathing cycle in porcine acute lung injury

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Introduction Cyclic recruitment and derecruitment (R/D) of lung parenchyma during mechanical ventilation are responsible for atelectrauma. Theoretically, cyclic R/D can lead to varying degrees of pulmonary shunt fraction throughout the respiratory cycle. Measurements of dynamic pulmonary shunt fraction could help in assessing the degree of cylic R/D. However, common methods of measuring pulmonary shunt do not allow for dynamic serial measurements during one respiratory cycle. In this study, we measured serial dynamic pulmonary shunt fractions during one breathing cycle and investigated the effect of positive end-expiratory pressure (PEEP) on cyclic R/D in artificially ventilated pigs before and after saline washout induced acute lung injury.

Methods Pigs (n = 10) were anesthetized and ventilated at a tidal volume of 8 ml/kg and two levels of PEEP (0 and 15 cmH_2O – conditions: PEEP0; PEEP15). Hemodynamic, respiratory and multiple inert gas analysis by micropore membrane inlet mass spectrometery (MMIMS-MIGET; Oscillogy, USA) measurements were taken at PEEP0 and PEEP15 before and after saline washout. Retention of SF6, measured five times during one breathing cycle, was taken as a reflection of shunt fraction. MIGET sample acquisition was synchronized by electrical impedance tomography.

Results We observed dynamic changes in pulmonary shunt fraction, expressed as changes in SF6 retention, within all breathing cycles recorded, before and after induction of ALI. In healthy lungs at PEEP0 there was a decrease in SF retention at the end of inspiration and a return to baseline levels during expiration. In contrast, SF6 retention increased at PEEP0 in ALI during inspiration and decreased during expiration. In healthy pigs ventilated with PEEP15 there was an increase in SF6 retention at the end of inspiration and a return to baseline during expiration similar to the changes observed in pigs with ALI at PEEP0. In ALI at PEEP15, shunt decreased throughout inspiration and returned to baseline levels during expiration.

Conclusion Serial dynamic pulmonary shunt measurements during mechanical ventilation showed distinct variations over the respiratory cycle in both healthy and injured lungs. Increasing PEEP from 0 to 15 cmH_2O altered the patterns of dynamic pulmonary shunt before and after ALI. Thus, serial assessment of dynamic pulmonary shunt fraction by SF6 retention with MMIMS-MIGET could prove useful for optimization of mechanical ventilation in healthy and injured lungs.

P281

Effect of positive end-expiratory pressure on right ventricle function assessed by speckle tracking echocardiography

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Introduction We sought to determine in a swine model whether a novel echocardiography method, speckle tracking echocardiography (STE), could determine deterioration in right ventricle (RV) function induced by escalating levels of positive end-expiratory pressure (PEEP), and to compare STE with RV fractional area change (FAC). Acute cor pulmonale and hypotension can be induced by high levels of PEEP used in the management of acute respiratory distress syndrome [1]. Quantifying RV function by echocardiography can be challenging due to its shape and position. STE is a relatively new, feasible, sensitive, angle-independent method for describing cardiac deformation (strain) [2] and is particularly useful in analyzing RV function (RV free wall strain, RVfwS), as has been shown in pulmonary hypertension cohorts [3].

Methods Ten pigs, 40 to 90 kg, anaesthetized, fully mechanically ventilated at 6 to 8 mg/kg were subject to stepwise escalating levels of PEEP at 2-minute intervals (0, 5, 10, 15, 20, 25 and 30 cmH_2O). RV images were obtained using intracardiac echocardiography (for optimal frame-rate and endocardial definition) and were analyzed offline for FAC and RVfwS (using Velocity Vector Imaging; Siemens).

Results Escalating levels of PEEP were strongly associated with significant reductions in mean blood pressure (R^2 = 0.8, P <0.0001), FAC (R^2 = 0.8, P <0.0001) and RVfwS (R^2 = 0.9, P <0.001). Paired t tests indicated significant reductions in RVfwS with each step increase in PEEP. FAC only showed significant deterioration at 15 cmH_2O PEEP. Significant hypotension (a decrease of more than 20 mmHg) occurred after 10 cmH_2O PEEP. RVfwS decreased by a larger extent and earlier than FAC and mean blood pressure with increasing levels of PEEP.

Conclusion RVfwS measured by STE is a sensitive method for determining RV dysfunction induced by PEEP. RVfwS displays a stronger association, greater deterioration and earlier reduction than FAC and mean blood pressure with escalating levels of PEEP. This potentially has interesting implications for the role of STE in managing PEEP levels in critically ill patients with acute lung injury.

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P282

Airway pressure release ventilation restores hemodynamic stability in patients with cardiogenic shock: initial experience in cardiac intensive care

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Introduction Airway pressure release ventilation (APRV) is a pressure-limited, time-cycled mode of mechanical ventilation. It increases the cardiac index, resulting in improved organ perfusion, which is crucial in cardiogenic shock patients preventing organ failure secondary to inadequate perfusion [1]. The purpose of this study was to evaluate the effectiveness of APRV in restoring hemodynamic stability and

improving oxygenation in ventilated patients with cardiogenic shock and severe progressive hypoxemia.

Methods All cardiac and cardiac surgical patients with cardiogenic shock and ALI/ARDS admitted to our ICU were enrolled between January 2012 and September 2013. Data were collected on admission while the patients were on the conventional mode of ventilation and after 48 hours from switching to APRV. All enrolled patients were hemodynamically monitored with a pulmonary artery catheter and frequent echocardiography assessment. A retrospective analysis of these data was performed.

Results Completed datasets were obtained from 29 patients. The cardiac index was increased by 30% (P <0.013), serum lactate decreased by 37% (P <0.001), central venous saturation increased by 42% (P <0.001) and peak airway pressure decreased 19% (P <0.001), with 50% increase of mean airway pressure, hypoxemia improved within the first few hours of alveolar recruitment with PaO_2/FIO_2 increased by 23% (P <0.018), and there was less use of vasopressors, sedation and neuromuscular blockage over the course of APRV application.

Conclusion In our patient series, APRV significantly improved oxygenation and allowed for spontaneous breathing and a reduction in peak airway pressures. Furthermore, this strategy improved hemodynamics and facilitated weaning from MV. Therefore, our data suggest that this ventilation modality has favorable results and appears to be an effective alternative for lung recruitment in patients with cardiogenic shock and acute lung injury during their course of stay in cardiac ICU [2].

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P283

Experimental VILI begins with subpleural lung lesions

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Critical Care 2014, **18(Suppl 1):**P283 (doi: 10.1186/cc13473)

Introduction We developed an experimental model of VILI, ventilating piglets at a strain (TV/FRC) >2.5. It is possible that lung inhomogeneities act as stress raisers within the lung parenchyma, locally multiplying pressures. In a healthy lung the pleural surface, vessels and bronchi are detected as natural lung inhomogeneities. We studied the development of VILI with CT scan to determine where the first lung lesion developed.

Methods Piglets were sedated, orotracheally intubated and instrumented with arterial and central venous catheter and urinary catheter. The whole study was performed in the animal CT scan facility, which was equipped as an ICU, and CT scan was performed every 3 hours or if respiratory parameters (plateau/peak pressure) changed. We defined as new lesion lung regions the appearance of poorly inflated/not inflated lung regions not present in the previous CT scan image. We select the first CT scan in which a relevant number of new lesions appeared (>15) and manually delineated the lesions; the lesions were classified as close/not close to the pleural surface.

Results Six piglets were studied (22 ± 8 kg) that were ventilated with a TV of 750 ± 71 ml (41 ± 1 ml/kg) up to development of VILI, defined radiologically as infiltrates present in all pulmonary fields at CT scan plus development of lung edema. In the first CT scan where lesions appeared, a median of 28 lesions (IQ range 22 to 30) were present. Of these lesions, 18 (17 to 22) (72%) were located near the pleura and nine (6 to 11) (28%) near vessels/bronchi. See Figure 1.

Conclusion In an experimental model of VILI the first lung lesions appear below the pleural surface. Mutiple nonmutually exclusive possible explanations are possible: the pleural surface acts as a stress raiser; the mechanical friction of the lung with the ribs at very high tidal volume leads to parenchimal injury; and the lung skeleton is a fan-like structure starting from the hilum and going to the pleural surface, leading to increased stress/strain of the subpleural regions.

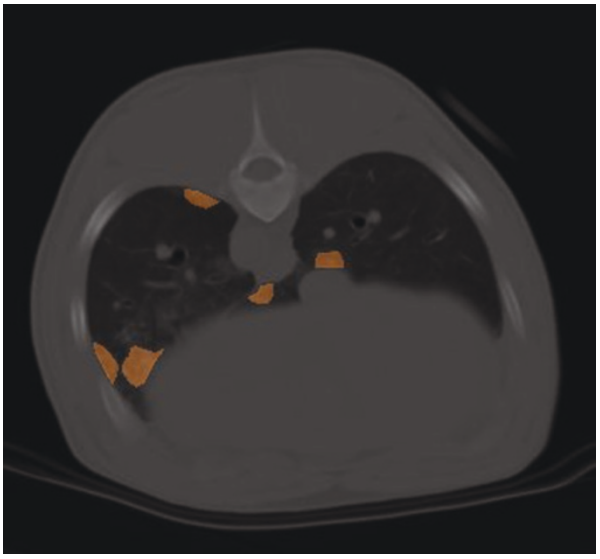

Figure 1 (abstract P283).

P284

Dissipated energy inside the respiratory system during mechanical ventilation

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Critical Care 2014, **18(Suppl 1):**P274 (doi: 10.1186/cc13474)

Introduction During mechanical ventilation some of the energy delivered to the respiratory system (RS) is dissipated within it, while some is recovered during expiration. The amount of unrecovered energy represents mechanical work done on the RS by the ventilator and may be related to the development of ventilatory-induced lung injury (VILI). The unrecovered energy is measured as the hysteresis area of the pressure–volume (PV) curve in static and dynamic conditions. We explored how and where the energy is dissipated inside the RS.

Methods In five piglets (weight 21 ± 2 kg) under general anesthesia, we recorded PV curves to quantify dynamic dissipated energy (DE) at increasing tidal volume (TV) (150, 300, 450, 600, 750, 900) and at increasing respiratory rate (RR) (3, 6, 9, 12, 15). We then recorded PV curves for the same TV inflated with a super-syringe (100 ml), to quantify static DE. We also quantified airway DE connecting the postmortem isolated tracheobronchial tree to the ventilator and recording PV curves at the respiratory setting previously described.

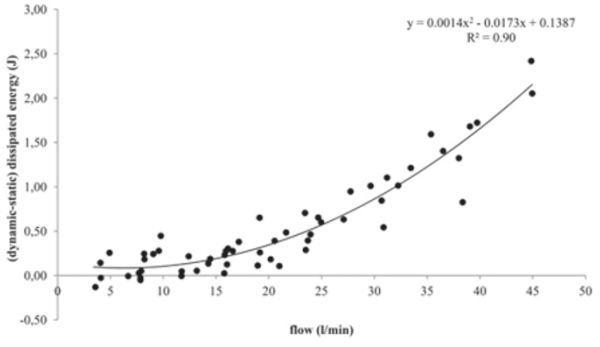

Figure 1 (abstract P284). Relationship between flow (l/minute) and (dynamic–static) dissipated energy (J).

Results Static DE(J) had a nonlinear relationship with the TV (ml/kg) applied: static DE = 0.0031*$TV^{1.5198}$, R^2 = 0.96. Subtracting from the PV curve hysteresis area of a single breath (dynamic DE) the airway DE, the resulting curve overlapped static DE at every RR considered, suggesting that the amount of energy spent on the RS is equal to the static DE. Static DE can be estimated knowing flow (l/minute) and dynamic DE(J) since:
(dynamic–static)DE = 0.0014*$[flow]^2$ – 0.0173*flow + 0.1387, R^2 = 0.90 (Figure 1).
Conclusion According to our data, the amount of energy that may be related to the development of VILI is static DE; it is a nonlinear function of TV and can be estimated knowing flow and dynamic DE.

P285

CT scan and ultrasound comparative assessment of PEEP-induced lung aeration changes in ARDS

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Introduction CT-scan quantitative analysis (qCT) represents the gold standard to assess lung aeration and recruitment in ARDS patients. Lung ultrasound (LUS) has been proposed as a bedside nonirradiating alternative to assess lung recruitability, identifying patients who may benefit from higher PEEP levels. We compared the two methods in the assessment of PEEP-induced lung aeration changes.
Methods LUS and whole-lung CT scan were performed on ARDS sedated, paralyzed, mechanically ventilated patients at PEEP 5 and 15 cmH_2O. LUS was performed considering six areas for each lung, with a comprehensive scan of the intercostal spaces in each area. We assigned to each area a score of aeration [1]: 0 (normal lung), 1 (≥3 noncoalescent B-lines), 2 (≥3 coalescent B-lines), 3 (consolidation). A cumulative LUS score (LUSS, ranging from 0 to 36 for the two lungs) was obtained as sum of all areas' individual scores, each area's score being the average of all pertaining LUS findings. LUS recruiters upon PEEP increase from 5 to 15 cmH_2O were defined by the switch of at least three areas to well aerated (area score 0). LUS-based assessment of lung aeration and lung recruitability was compared with qCT findings.
Results We enrolled seven patients (six males, age 54.1 ± 22.2 years, BMI 24.2 ± 4.9 kg/m^2, PaO_2/FiO_2 186 ± 78, tidal volume 445 ± 140 ml, RR 14.5 ± 3.4 breaths/minute, PEEP 12.5 ± 3.3 cmH_2O). In the 14 conditions evaluated, median LUSS was 19 (IQR 14 to 23); LUSS ≤19 (n = 8) corresponded to 34 ± 13% of nonaerated tissue at qCT; LUSS >20 (n = 6) to 48 ± 18% (P <0.05). A good linear correlation was found between reduction at LUS of consolidated areas (area score 3) versus reduction of qCT nonaerated volume (R^2 = 0.66), and between reduction at LUS of poorly aerated areas (area score 1 to 2) versus reduction of qCT poorly aerated volume (R^2 = 0.74). Change at LUS of at least three areas to well aerated (LUS recruiters, n = 4) corresponded to a qCT increase in well-aerated lung volume of 788 ± 262 g versus 431 ± 35 g in the LUS nonrecruiter group (n = 3) (P <0.05).
Conclusion These preliminary data suggest that LUS could be an accurate tool to assess lung aeration and recruitment at the bedside, avoiding the risks and workload related to the use of CT scan.
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P286

Effect of tidal volume and positive end-expiratory pressure on lung hysteresis of healthy piglets

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Critical Care 2014, **18(Suppl 1):**P286 (doi: 10.1186/cc13476)

Introduction Growing evidence suggests that, as long as the total lung capacity is not overcome, dynamic (that is, tidal volume, VT) is more injurious than static (that is, positive end-expiratory pressure, PEEP) lung deformation [1]. Because the lung behaves like a viscoelastic body [2], hysteresis may play a role in the development of ventilator-induced lung injury. The aim of the study was to investigate the effects of increasing VT or PEEP on lung hysteresis.
Methods In eight healthy piglets we measured total hysteresis and the peak inspiratory pressure (Ppeak) while randomly increasing VT (with no PEEP) or PEEP (with fixed VT). P1 was extrapolated from the drop in airway pressure during an end-inspiratory pause [3]. Hysteresis attributable to lung parenchyma was computed as: total hysteresis – ((Ppeak – P1) × VT).
Results The main findings are shown in Figure 1. P values refer to one-way repeated-measures analysis of variance.
Conclusion Lung hysteresis increases with VT, but not with PEEP. Further studies are needed to prospectively evaluate the role of lung hysteresis in the pathogenesis of ventilator-induced lung injury.
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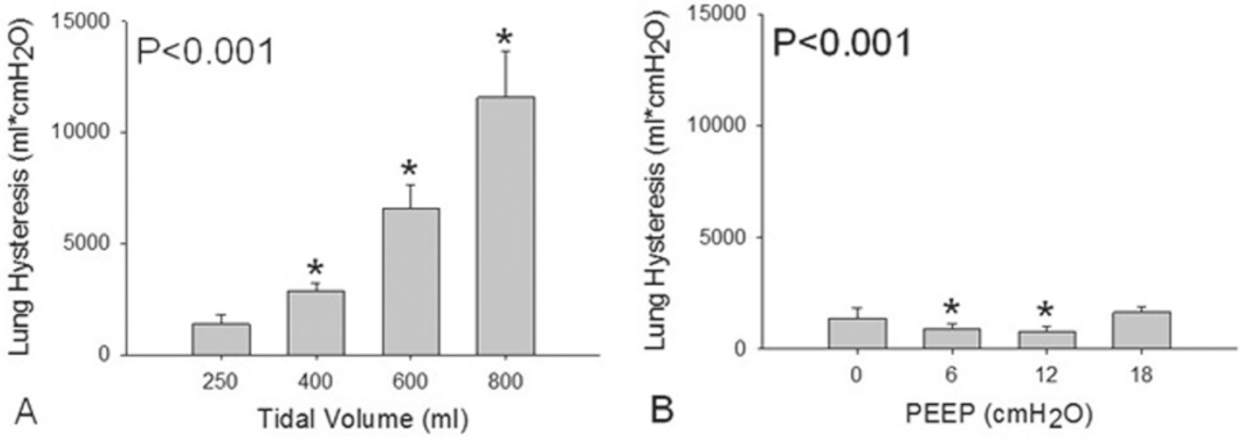

Figure 1 (abstract P286). Lung hysteresis as a function of VT **(A)** and PEEP **(B)**. *P <0.05 versus VT 250 ml or PEEP 0 cmH_2O (Holm–Sidak method).

P287

Evaluation and quantification of pulmonary hyperinflation in three gravitational zones of domestic felines by computed tomography

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Critical Care 2014, **18(Suppl 1):**P287 (doi: 10.1186/cc13477)

Introduction Mechanical ventilation (MV) aims to enhance blood oxygenation and to remove carbon dioxide. However, excessive hyperinflation by MV may cause lung injury.
Methods Eighteen cats (4 ± 1 kg) were anesthetized with propofol (loading dose of 6 mg/kg and constant rate infusion of 0.5 mg/kg/minute) and neuromuscular blockade was achieved with rocuronium at 1 mg/kg/minute. Their lungs were initially mechanically ventilated in FiO_2 of 40%, with peak inspiratory pressure (Ppeak) of 5 cmH_2O for 20 minutes, and then the Ppeak was increased by 5 cmH_2O increments until 15 cmH_2O every 5 minutes. Following that, Ppeak was decreased by 2 cmH_2O every 5 minutes until reaching Ppeak of 5 cmH_2O. The ventilator maintained the respiratory rate and inspiratory time at 15 breaths/minute and 1 second, respectively. Between the Ppeak increments, we applied a 4-second pause for a 5-mm computed tomography (CT) scan of the thorax area. The radiographic attenuation (in Hounsfield units, HU) was classified as over-insufflation (1,000 to 900 HU), normal insufflation (900 to 500 HU) and atelectasic (500 to 100 HU). We split the lungs into three proportional gravitational zones (I, II and III) from apex to base.
Results The three zones presented increased over-insufflated areas and decreased areas with normal insufflation with increasing Ppeak from 5 to 15 cmH_2O. At 5 cmH_2O, the areas of over-insufflation and normal insufflation in zones I, II and III were 13% and 36%; 4% and 22%; and 0.7% and 15%, respectively. At 15 cmH_2O, the areas of over-insufflation and normal insufflation in zones I, II and III were 74% and 55%; 81% and 57%; and 82% and 71%, respectively.
Conclusion The higher proportion of overly distended pulmonary areas in high Ppeak may increase the risk of lung injury. The lowest Ppeak (5 cmH_2O) showed less potential to lung injury as it has higher areas of normal insufflation and less areas of over-insufflation in all gravitational zones.

P288

Effect of inhaled nitric oxide on apoptosis of lymphocytes in newborns in a critical state

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Critical Care 2014, **18(Suppl 1):**P288 (doi: 10.1186/cc13478)

Introduction Activation of lymphocyte apoptosis while reducing the endogenous nitric oxide is a predictor of adverse outcome in newborns on mechanical ventilation [1]. With the aim to improve the results of treatment we studied the effect of inhalable nitric oxide on the immune system in newborns with respiratory diseases on mechanical ventilation [2].
Methods With the permission of the ethics committee in a controlled, randomized, blind clinical trial we included 27 newborns with respiratory diseases on mechanical ventilation. Randomization was performed by the method of envelopes. Group I ($n = 17$), patients receiving inhalation of nitric oxide at a concentration of 10 ppm for 24 hours controlling the level of methemoglobin (Pulmonox mini; Messer II NO Therapeutics, Austria). Group II ($n = 10$) did not receive inhaled NO. At admission and at 3 to 5 days we studied subpopulations of lymphocytes by one-parameter immunophenotyping using reagents (Immunotech Beckman Coulter, USA): fitz-labeled CD3, CD4, CD8, CD14, CD19, CD34, CD56, CD69, CD71, CD95 monoclonal antibody, the relative content of lymphocytes in early and late apoptosis using Annexin V^+-labeled FITK and propidium iodide (PL^+), labeled with PE (Saltag, USA), with results on the Beckman Coulter Epics XL cytometer (USA). The statistical power of the study was 80% ($\alpha \leq 0.05$).
Results In Group I relative to group II at 3 to 5 days we registered an increase in mature monocytes (CD14) – 23.1 ± 0.8% ($P < 0.05$); reduction in the relative content of CD69 – 3.8 ± 0.21%, lymphocyte of apoptosis: (Annexin $V^-FITC^+PI^-$) – 7.12 ± 0.46% and (Annexin $V^-FITC^+PI^+$) – 0.79 ± 0.07% ($P < 0.001$). The duration of mechanical ventilation was 4.1 ± 1.4 days ($P < 0.05$). All patients survived. None of the patients showed clinical or laboratory evidence of adverse effects of inhaled nitric oxide. In Group II seven newborns died, and the duration of mechanical ventilation in survivors was 18 ± 3.4 days.
Conclusion Inhalable of nitric oxide activates monocyte–macrophage immunity, stabilizes the apoptosis of T-lymphocytes, and reduces mortality and duration of mechanical ventilation in newborns with respiratory diseases on mechanical ventilation.
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P289

Diaphragm microcirculatory dysfunction and lipid accumulation in endotoxemic rabbits during mechanical ventilation

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Introduction Sepsis-induced diaphragm dysfunction (SIDD) has been widely described in the literature as a condition affecting the diaphragm muscle characterized by contractility loss of function and associated with a high mortality, assessed at around 54% [1]. Previous studies have investigated the pathogenesis of ventilator-induced diaphragmatic dysfunction (VIDD), its lipid metabolic alterations [2] and microcirculatory function processes. This study was designed to investigate on diaphragm muscle the effects of LPS-induced endotoxemia in rabbits undergoing two different modes of mechanical ventilation.
Methods A prospective randomized animal study in 25 invasively monitored and mechanically ventilated New Zealand White rabbits. The rabbits were randomized to control ($n = 5$), controlled mechanical ventilation (CMV) ($n = 5$), pressure support ventilation (PSV) ($n = 5$), or CMV or PSV with LPS-induced endotoxemia (CMV-LPS and PSV-LPS respectively) ($n = 5$ for each). The endotoxemia was induced by LPS injection in the CMV-LPS and PSV-LPS groups. Rabbits were anesthetized and ventilated for 24 hours, except for the control (30 minutes). A catheter able to detect the electrical activity of the diaphragm was placed to evaluate the diaphragm contractility at baseline and after 6, 12 and 24 hours. After 24 hours, we evaluated: the diaphragm microcirculation assessed by a sidestream dark-field videomicroscopy; the mitochondria membrane potential; the lipid accumulation; and the diaphragm muscular fiber structure.
Results In endotoxemic animals, after 24 hours, the diaphragm contractility and fiber structure, the microcirculation, mitochondrial membrane potential and lipid accumulation were severely compromised, but not in the CMV and PSV groups. Moreover, a slight but significant increase of lipid accumulation was observed in the CMV and PSV groups in comparison with control ($P < 0.05$).
Conclusion In endotoxemic rabbits, the impaired microcirculation resulted in an increased lipid accumulation and in a disturbance of the mitochondria membrane potential and contractility of the diaphragm. No microvascular alterations have been observed in ventilated non-endotoxemic animals. Moreover, the diaphragm contractility dysfunction was more pronounced in endotoxemic animals.
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P290

High-frequency oscillatory ventilation use in patients with H1N1: a single-centre review

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Critical Care 2014, **18(Suppl 1):**P290 (doi: 10.1186/cc13480)

Introduction Limited evidence exists as to the value of high-frequency oscillatory ventilation (HFOV) for patients with H1N1 [1,2]. We describe a subgroup of patients, from a single UK centre, who received HFOV and had H1N1-positive virology.
Methods Local permissions for research were obtained. Patients with confirmed H1N1 who underwent HFOV between 2008 and 2012 were included. Data collected retrospectively included demographics, diagnosis, illness severity and outcome measures.
Results We identified 10 patients (Table 1) who received both HFOV and had confirmed H1N1. Two patients were transferred to a tertiary centre to receive ECMO and both critical care and 6-month mortality were 40%.

Table 1 (abstract P290). Patient characteristics

Male (%)	60
Age (years)	39.4 ± 9.75
Mean APACHE II	19.5 ± 4.88
Pre-HFOV neuromuscular blockade infusion (%)	40
Pre-HFOV vasoactive drug infusion (%)	50
Mean pre-HFOV V_T exp (ml/kg)	8.54 ± 2.68
Median P/F ratio (mmHg)	
Pre HFOV	67.5
0 hours	94.35
4 hours	110.4

Conclusion This study adds to the literature on the use of HFOV in H1N1 patients. We managed to replicate some of the existing evidence in respect to the population age [1,2] and the incidence of mortality. Whilst P/F ratios improved on initiation of HFOV, these patients subsequently had long critical care and hospital stays. There is uncertainty regarding the use of HFOV in ARDS, but it may be a valuable treatment for H1N1 patients. The ventilation strategies employed and the subsequent consequences for H1N1 patients require further evaluation.
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P291

EIT comparison of airway pressure release ventilation and conventional ventilation

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Critical Care 2014, **18(Suppl 1):**P291 (doi: 10.1186/cc13481)

Introduction The aim was to study EIT as a monitoring tool for tidal ventilation (TV) redistribution following switching patients from volume-controlled ventilation (VCV) to airway pressure release ventilation (APRV) in patients with severe ARDS.
Methods Six patients with severe ARDS having Pplat ≥30 cm were included in the study. Patients ventilated with the ARDSnet strategy were subjected to EIT analysis. Regional TV distribution was monitored by an EIT system (PulmoVista 500®; Dräger Medical GmbH, Lübeck, Germany), dividing the lung field into four same-size regions of interest (ROIs): ventral right (ROI 1) and left (ROI 2) and dorsal right (ROI 3) and left (ROI 4). In step 1, patients ventilated with VCV as per the ARDSnet protocol were subjected to EIT analysis. In step 2, patients were switched to APRV. Ventilation parameters, arterial blood gas analysis and percentage of tidal ventilation distribution in the four ROIs were recorded at steps 1 and 2. Analyses were performed by paired *t* test.

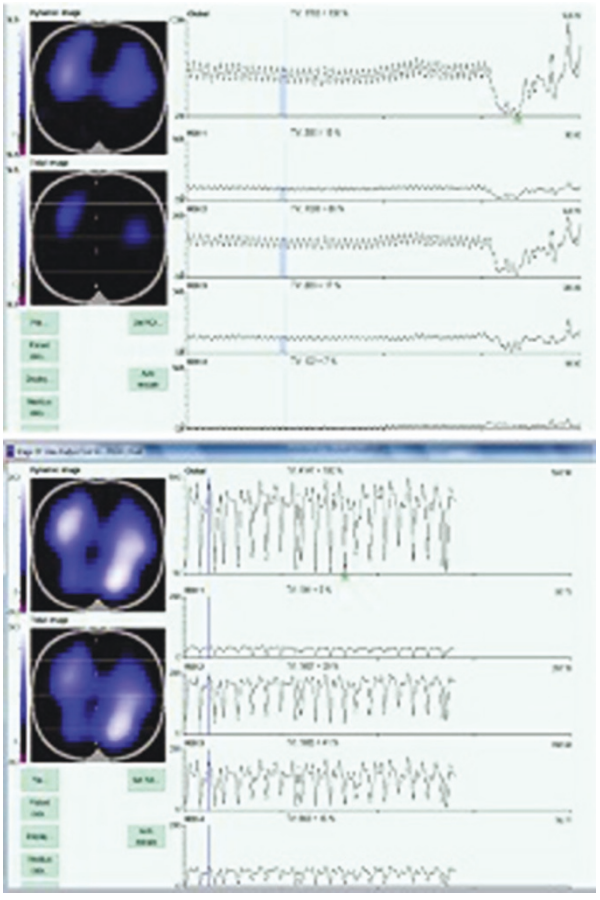

Figure 1 (abstract P291). EIT comparison of VCV and APRV.

Results Patients on VCV had P/F ratio of 79.5 ± 12.5 with PEEP of 14.16 ± 1.32 There was a significant improvement in P/F ratios on switching to APRV (126.16 ± 23.69, $P = 0.002$) at 30 minutes of ventilation on APRV. There was a trend to decrease in FiO_2 (0.82 ± 0.15 vs. 0.68 ± 0.10, $P = 0.068$) and PCO_2 (52.5 ± 6.15 vs. 45.00 ± 8.67, $P = 0.071$) and increase in PaO_2 (65.83 ± 14.53 vs. 84.83 ± 12.22, $P = 0.056$) at step 2. The proportional distribution of ventilation in the dorsal ROI 3 and ROI 4 also improved on switching to APRV. TV in ROI 3 during VCV, 12.76 ± 6.76%, improved to 24.58 ± 6.61% ($P = 0.067$). Similarly TV in ROI 4 during VCV, 24.58 ± 6.61%, improved to 26.6 ± 6.09% ($P = 0.068$). Due to small sample size, improvement in TV in dorsal ROIs was not statistically significant. Upper panel of Figure 1 shows end-inspiratory and end-expiratory images of EIT on VCV with poor TV in dorsal ROI 3 and ROI 4. Lower panel of figure shows two EIT images at Phigh = 30 cm showing improved TV in dorsal ROIs.
Conclusion EIT may help to identify patients with severe ARDS on VCV with a potential of increasing recruitment by tidal redistribution of ventilation with APRV.

P292

Lung-protective ventilation suppresses plasma levels of cell-free DNA in porcine experimental postoperative sepsis

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Introduction Mechanical ventilation affects systemic inflammation where protective ventilation attenuates the response [1]. Plasma

levels of cell-free DNA (cfDNA) increase and have prognostic value in sepsis [2]. In the present study, the effect of tidal volume and PEEP on arterial and transorgan levels of cfDNA was investigated in a porcine postoperative sepsis model.
Methods Two groups of anaesthetised pigs were ventilated with either protective ventilation (VT 6 ml/kg, PEEP 10 cmH_2O; $n = 20$) or controls (VT 10 ml/kg, PEEP 5 cmH_2O; $n = 10$) for 7 hours. An artery, the hepatic vein, the portal vein and the jugular bulb were catheterized. Continuous endotoxin infusion at 0.25 μg/kg/hour for 5 hours was started after 2 hours of laparotomy that simulated a surgical procedure.
Results The group receiving protective ventilation showed lower levels of cfDNA in arterial blood compared with controls ($P = 0.02$). Trans-hepatic levels of cfDNA were higher compared with trans-splanchnic levels during the experiment ($P = 0.02$), but this effect was attenuated in the group receiving protective ventilation. No difference between the groups was detected in blood samples from the jugular bulb.
Conclusion In experimental postoperative sepsis, protective ventilation suppresses arterial levels of cfDNA. The liver seems to be a significant contributor to systemic cfDNA levels, an effect that is suppressed during protective ventilation.
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P293

Comparison of HFOV and conventional ventilation in H1N1 influenza ARDS

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Critical Care 2014, **18(Suppl 1):**P293 (doi: 10.1186/cc13483)

Introduction HFOV is a promising rescue therapy for refractory hypoxia in severe ARDS.
Methods This is a retrospective comparative study. We retrieved data for all patients with H1N1 influenza-related severe ARDS treated in the ICU during October 2009 to April 2013. Our ICU had only one HFOV machine during the pandemic. Patients were divided into two groups: HFOV group (received HFOV at first eligibility) and conventional lung protective ventilation (CLPV) group (did not receive HFOV at first eligibility due to nonavailability of HFOV). Eligibility criteria for rescue therapy by HFOV were: P/F ratio ≤100; PEEP needed above 12 cm; Pplat ≥30 cm on CLPV. There was no selection or omission bias for HFOV application and HFOV was applied to the first eligible patient. Patient demographic data, laboratory parameters, hemodynamic variables, and oxygenation and ventilator settings were recorded while on CLPV at first HFOV eligibility in all patients.
Results The total of 43 patients who met the rescue therapy criteria were further grouped into the HFOV group (24 patients) and the CLPV group (19 patients) depending upon modality of ventilation received after satisfying first-time HFOV eligibility criteria. Both groups were comparable for differences with Fisher's *t* test for qualitative variables and ANOVA for quantitative variables (Table 1), except for higher mortality in the CLPV group (16/19 (84.4%) vs. 12/12 (50%), $P = 0.026$). On logistic regression analysis to find independent variables differentiating the two groups, mortality was higher in the CLPV group ($P = 0.02$, odds ratio (CI) 71.60 (1.85 to 2,766.59)) compared with the HFOV group.

Table 1 (abstract P293).

Variable	CLPV ($n = 19$)	HFOV ($n = 24$)	*P* value
Age	41.15	32.83	0.07
SOFA	4.95	4.62	0.41
Pplat	29.57	30.46	0.26
O.I.	38.88	35.70	0.54
P/F	70.63	76.79	0.50
PCO_2	59.89	59.92	0.99
Death	16	12	0.02

Conclusion HFOV when applied as rescue therapy for refractory hypoxia due to severe ARDS caused by H1N1 influenza pneumonia is associated with better outcome compared with CLPV.

P294

Opening pressures and intratidal opening and closing in ARDS lung

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Introduction Intratidal opening/closing is believed to be one of the main triggers of ventilator-induced lung injury; the application of higher PEEP united with the limitation of plateau pressure at 30 cmH_2O may limit this phenomenon. We aim to evaluate the intratidal opening/closing at different PEEP levels and the amount of lung parenchyma that regains inflation going from 30 (pressure limit of tidal ventilation) to 45 cmH_2O.
Methods Patients with ARDS underwent whole-lung low-dose (60 mAs, 120 kV) computed tomography at PEEP 5 cmH_2O end expiration and end inspiration, PEEP 15 cmH_2O end expiration and end inspiration, and airway pressure 30 and 45 cmH_2O end inspiration. Quantitative analysis of CT data was performed and recruitability was defined as the fraction of lung parenchyma that regains inflation going from 5 cmH_2O end expiration to 45 cmH_2O end inspiration. Patients were classified as high recruiters (HR) and low recruiters (LR) according to the median lung recruitability (14% of lung parenchyma).
Results Eighteen patients (male 12, age 56.0 ± 18.6 years, BMI 25.6 ± 5.2 kg/m², PaO_2/FiO_2 166 ± 70, tidal volume 496 ± 84 ml, RR 19 ± 7.4 breaths/minute, PEEP 11.4 ± 3.7 cmH_2O) were enrolled. The fraction of lung parenchyma that could be recruited at plateau pressure above 30 cmH_2O was highly variable with a median of 5% (IQ range 1 to 17%) corresponding to a median 16% (IQ range 10 to 47%) of total lung recruitability. Indeed we observed a statistically relevant difference in lung recruitment between airway pressures of 30 and 45 cmH_2O ($P = 0.016$). With PEEP 5 cmH_2O, median opening/closing was 129 g (IQ range 124 to 145 g) in the HR group and 50 g (IQ range 24 to 76 g) in LR ($P = 0.006$), corresponding to 8% of lung parenchyma (IQ range 6 to 8%) in HR and 4% (2 to 7%) in LR ($P = 0.053$). Increasing the PEEP level to 15 cmH_2O, median opening/closing was 67 g (IQ range 24 to 95 g) in the HR group and 45 g (0 to 80 g) in the LR group ($P = 0.512$), corresponding to 3% (1 to 5%) in HR and 3% (0 to 5%) in LR ($P = 0.93$). We observed a statistical difference between recruitments with PEEP 5 and PEEP 15 in the HR group ($P = 0.013$) but not in the LR group ($P = 0.781$).
Conclusion A highly variable and significant fraction of lung parenchyma is always closed with tidal ventilation at 30 cmH_2O plateau pressure, regardless of the PEEP level applied; this implies that sigh or periodic recruitment maneuvers may lead to opening and closing. Intratidal opening/closing was reduced but not abolished in all patients while ventilating at higher PEEP level (15 cmH_2O).

P295

Compliance with protective lung ventilation in an Irish teaching hospital

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Introduction The importance of protective lung ventilation in reducing mortality in adult respiratory distress syndrome (ARDS) patients is well described [1]. However, suboptimal compliance with the recommended tidal volumes has been reported [2]. Therefore, we wished to assess our compliance in adhering to protective lung ventilation in patients with, or at risk of developing, ARDS.
Methods A retrospective review was done on all mechanically ventilated patients in the ICU of Tallaght Hospital over a 6-month period (February to July 2013). Hourly tidal volumes were recorded

automatically in electronic charts. Compliance was assessed by calculating the total time patients with, or at risk of developing, ARDS were ventilated with tidal volumes <6 ml/kg, 6 to 8 ml/kg, and >8 ml/kg during the first 72 hours on mechanical ventilation. ARDS is defined as per the Berlin criteria [3]. Exclusion criteria were patients who did not receive invasive ventilation or who were ventilated for less than 72 hours. We also assessed whether patients' height was documented.
Results A total of 72 patients were ventilated for >72 hours. Of these patients (44 males, 28 females, mean age 65.5 years), ARDS criteria were met in 17 patients and 22 patients were determined to be at risk of developing ARDS. For patients with ARDS, the ventilated time with tidal volumes <6 ml/kg, 6 to 8 ml/kg, and >8 ml/kg was 25.3%, 31.7% and 43% respectively. For patients at risk of developing ARDS, the ventilated time with tidal volumes <6 ml/kg, 6 to 8 ml/kg, and >8 ml/kg was 15.7%, 29.3%, 55%, respectively (Table 1). A total of 16 patients (nine who had ARDS) had no documentation of their height.

Table 1 (abstract P295).

Tidal volume	With ARDS (%)	At risk of ARDS (%)
<6 ml/kg	25.3	15.7
6 to 8 ml/kg	31.7	29.3
>8 ml/kg	43	55

Conclusion Compliance with protective lung ventilation in our ICU is suboptimal. This may be due to the lack of education and guidelines in the unit regarding protective lung ventilation. Moreover, accurate recording of patient height and determination of predicted body weight should be documented to facilitate accurate tidal volume calculation and protective lung ventilation.
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P296

Mechanisms underlying the lung-protective effects of FLow-controlled EXpiration

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Introduction During mechanical ventilation the expiration occurs passively and is determined by the recoil forces of the respiratory system. In an experimental study in pigs we could find that linearization of the expiratory flow via FLow-controlled EXpiration (FLEX) [1] is lung protective [2]. Utilizing electrical impedance tomography (EIT) we aimed at investigating the mechanisms underlying the lung-protective effects of FLEX.
Methods All experiments were approved by the local animal welfare committee. Twelve pigs with oleic acid-induced lung injury were ventilated in the volume-controlled mode (VCV). In six animals, expiratory flow was linearized via FLEX. PEEP was set to achieve similar mean airway pressure in the control group ($n = 6$) and in the FLEX group ($n = 6$). Using EIT, the local distribution of ventilation was measured and alveolar derecruitment during the no-flow phase in late expiration was quantified.
Results During ventilation with FLEX the no-flow phase in late expiration was reduced by 50% compared with passive expiration. Derecruitment during the no-flow phase was clearly reduced by FLEX compared with VCV. Furthermore, intratidal ventilation was more homogeneously distributed during ventilation with FLEX compared with conventional passive expiration.
Conclusion In comparison with conventional VCV with passive expiration, the no-flow phase in late expiration is reduced and so is the time the lung persists on the lowest pressure level (PEEP) during the breath. The reduced low-pressure time is associated with reduced end-tidal derecruitment. In a lung mechanically stabilized and recruited by sustained airway pressure throughout the expiration phase, the distribution of ventilation is more homogeneous. These mechanisms of alveolar recruitment maintenance can explain the lung-protective effects of FLEX.
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P297

Value of peak flow rates measured during a spontaneous breathing trial to predict success of weaning from mechanical ventilation

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Introduction Numerous parameters have been suggested for the prediction of weaning from mechanical ventilation; however, these parameters have limited success in the prediction of weaning outcome. The aim of this study is to assess the success of minute peak flow rates (spontaneous peak inspiratory flow rate (SPIF) and spontaneous peak expiratory flow rate (SPEF)) measured during a spontaneous breathing trial (SBT) in the prediction of weaning outcome.
Methods Patients managed and receiving mechanical ventilation support for at least 24 hours in the medical and surgical ICUs of Erciyes University between March 2011 and May 2012 were included in the present study. Over 30 minutes, SPIF and SPEF values were measured during a SBT in patients spontaneously breathing by T tube. Patients who tolerated 30 minutes of SBT were extubated. Patients who did not need reintubation for 48 hours after extubation were considered successful weaning, while those needing reintubation were considered weaning failure.
Results The study was completed with 36 patients overall, being 11 patients in failure and 25 patients in the success group. In both groups, areas under the curve (AUCs) were calculated for each minute via ROC analysis using minute SPIF and SPEF values measured during SBT. The maximum AUC was calculated at minute 23 for SPIF (0.564; 95% CI: 0.363 to 0.764) and at minute 9 for SPEF (0.542; 95% CI: 0.316 to 0.376). Cutoff values were determined for the minutes in which maximum AUC values for SPIF and SPEF were detected; and sensitivity and specificity values were calculated. When the cutoff value for SPIF was accepted as >26.7 l/minute at minute 23, sensitivity and specificity was calculated as 72.0% and 28.0%, respectively. When the cutoff value for SPEF was accepted as >24.7 l/minute at minute 9, sensitivity and specificity were calculated as 63.6% and 48.8%, respectively.
Conclusion We think that minute SPIF measurement which has better sensitivity and minute SPEF measurement which has better specificity compared with available traditional predictors [1] may be used as a potential bedside weaning predictor when evaluated in comprehensive studies.
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P298

Lung ultrasound findings predict weaning failure from mechanical ventilation

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Introduction Lung ultrasound is increasingly becoming a diagnostic tool in the critical care setting. The B-line is an artifact that correlates with interstitial edema. Decreases in intrathoracic pressure during a spontaneous breathing trial (SBT) will augment venous return and impede left ventricular ejection, increasing intrathoracic blood volume.

Therefore, the presence of cardiovascular dysfunction can contribute to weaning failure (WF). A randomized trial concluded that bedside lung ultrasound could predict post-extubation distress through changes in aeration during a T-tube test; however, it could not screen patients before submission to a SBT [1]. We aim to assess the reliability of lung ultrasound as a predictor of weaning outcomes.

Methods We conducted a prospective, multicenter, observational study in two adult medical–surgical ICUs. Lung ultrasound was performed immediately before SBT. Three or more B-lines in a single view were called a B-pattern. B-predominance was defined as a B-pattern on at least one of the four anterior chest wall zones. All enrolled patients met eligibility criteria for ventilation liberation. Patients with tracheostomy were excluded.

Results During 2 years, 250 SBTs were analyzed. WF, defined as an inability to tolerate a T-tube trial during 30 to 120 minutes, occurred in 51 (20.4%). There was a higher prevalence of chronic obstructive pulmonary disease in the WF group as well as higher duration of mechanical ventilation. WF patients were also younger. Patients succeed at SBT and were extubated at first time in 75.9% of cases. We observed a significant association between B-predominance prior to submission to SBT and WF (OR = 1.99 (1.04 to 3.84)). For diagnosing WF, B-predominance showed 69% sensitivity, 48% specificity, 25% positive predictive value, and 86% negative predictive value.

Conclusion The finding of B-predominance at bedside lung ultrasound performed before SBT predicts WF, although it shows low accuracy.

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P299

Fluid balance predicts weaning failure in chronic obstructive pulmonary disease patients

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Introduction Fluid balance (FB) has been associated with weaning and extubation failure, particularly of cardiac origin. Also, the increased right ventricular afterload, a feature common in chronic obstructive pulmonary disease (COPD) patients especially during a weaning test, may hinder diastolic filling of the left ventricle through a biventricular interdependence mechanism. We aimed to investigate the relationship of the FB in the 48 hours prior to a spontaneous breathing trial (SBT) and weaning outcomes in a subgroup of COPD patients admitted to a medical–surgical ICU.

Methods We conducted a 2-year prospective, multicenter, observational study in two adult medical–surgical ICUs. All enrolled patients met eligibility criteria for ventilation liberation. Patients with tracheostomy were excluded. We collected demographic, physiologic, 48-hour FB (measured inputs minus outputs) and lung ultrasound findings immediately before a SBT in 29 COPD patients. Our main outcome of interest was weaning failure (WF), defined as the inability to tolerate a T-tube trial during 30 to 120 minutes, in which case patients were not extubated.

Results Weaning success (WS) (n = 19) and WF (n = 10) patients were similar in relation to age, sex, APACHE II score, reason for mechanical ventilation (MV) and comorbidities. Mean duration of MV was 11 days. FB in the 48 hours prior to the SBT did not differ between the WS and WF groups (1,091.11 ± 2,195.89 ml and 2,398.80 ± 1,533.15 ml, respectively). Nevertheless, comparing individuals with 48-hour FB above and under the cutoff value of 0 ml according to weaning outcomes resulted in significant association between positive FB and WF in COPD patients (odds ratio = 1.77 (1.24 to 2.53)). That cutoff point was obtained on the ROC curve. See Figure 1.

Conclusion Positive FB in the 48 hours preceding the SBT predicted WF in COPD individuals. We recognized that no intervention was performed in order to accelerate the weaning process. Brain natriuretic peptide levels were not available.

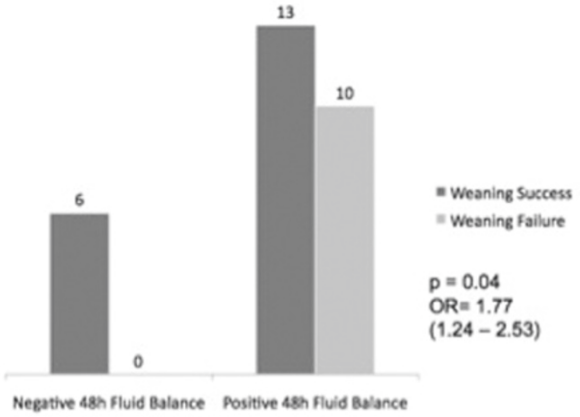

Figure 1 (abstract P299). Association between positive fluid balance WF in COPD patients.

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P300

Role of the rapid shallow breathing index to predict the success of mechanical ventilator liberation in acute respiratory failure

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Introduction The rapid shallow breathing index (RSBI) is considered a good parameter to predict mechanical ventilator liberation. We hypothesized that the RSBI provides no benefit when clinical readiness criteria are met.

Methods Adults with acute respiratory who required MV for more than 24 hours, excluding COPD, were assessed daily as a liberation protocol (Figure 1). During the RSBI step, RSBI was recorded and blinded to the

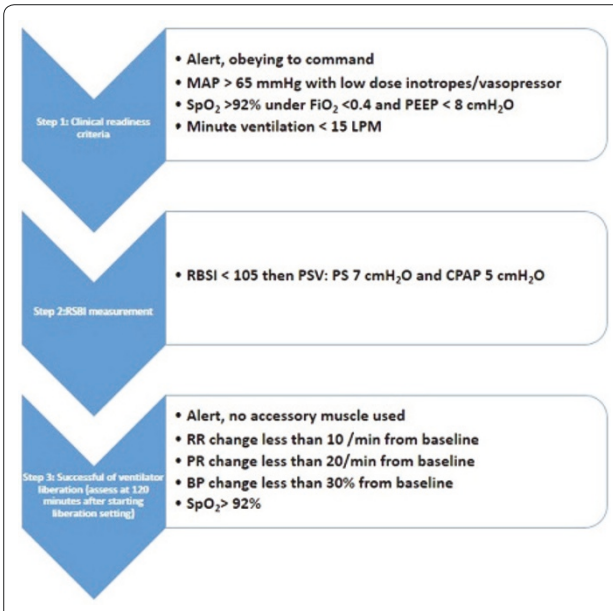

Figure 1 (abstract P300). Standard mechanical ventilator weaning protocol.

Table 1 (abstract P300).

Character	CR	CR + RSBI	*P* value
Age	55.79 ± 19.6	56.62 ± 19.4	0.74
Male sex (%)	58.3	59.1	0.90
Success rate (%)	89.2	92.2	0.43

researcher. The liberation process was continued regardless of the RSBI result. The primary outcome was the success rate of mechanical ventilator liberation with or without RSBI.
Results Analysis of 120 cases with clinical characteristics as presented in Table 1. There was no statistically significant difference between using only clinical readiness and using clinical readiness and the RSBI (92% vs. 89%, $P = 0.43$).
Conclusion The inclusion of RSBI in our standard mechanical ventilator liberation protocol for patients who met the clinical readiness criteria did not significantly increase the success rate of mechanical ventilator liberation.

P301

Determinants of ventilator weaning outcome in a medical–surgical ICU

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Introduction The purpose of this study is to prospectively evaluate the determinants of weaning outcome in a selected sample of ventilator-dependent patients.
Methods After fulfilling a set of inclusion/exclusion criteria, 46 patients treated in a single medical–surgical ICU were prospectively evaluated between October 2011 and January 2013. The study protocol followed the generic course of mechanical ventilatory support and its discontinuation. A period of CMV was followed by stepwise reduction in pressure support. The outcomes were recorded at the second and 24th hour after the beginning of the PSV (8 cmH_2O PS) spontaneous breathing trial (SBT). A short period of ZEEP breathing was introduced after the CMV as an additional respiratory stressor. A large number of parameters (including those derived via indirect calorimetry and esophageal balloon catheter) were analyzed. The following statistical methods were used: Student's *t* test or its nonparametric alternatives for intergroup comparisons, repeated-measurements ANOVA for intragroup comparisons, cross-tabulation and Fisher's exact test to compare categorical variables. Logistic regression analysis was conducted with regard to success/failure classification.
Results Twenty-two (63.04% of all) patients successfully passed the 2-hour SBT. Of them, five failed the subsequent 24-hour SBT. Almost all of the latter (four out of five) were ventilated due to chronic respiratory or cardiac diseases. The following parameters were significantly different between the groups of patients who successfully and unsuccessfully completed 2-hour SBT: pre-inclusion body weight; PEEPi (end-expiratory occlusion method), peak and mean airway pressures during CMV; PaO_2, PaO_2/FiO_2 and oxygenation index during the SBT; respiratory rate, tidal volume, f/Vt, patient work of breathing (modified Campbell method), total body oxygen consumption, respiratory quotient and energy expenditure during ZEEP and the SBT. The logistic regression model devised to predict the outcome of the 2-hour SBT included the following parameters: type of artificial airway (tracheotomy vs. translaryngeal), oxygen consumption, f/Vt and energy expenditure during the SBT.
Conclusion The presence of serious respiratory and/or cardiac comorbidities might require longer duration of the SBT. In our study, respiratory load–muscle capacity balance and metabolic activity appear to play a major role in determining the weaning outcome. A short period of ZEEP breathing is safe and might have prognostic utility regarding the outcome of mechanical ventilatory support discontinuation.

P302

Microbiology and outcomes of severe pneumonia in critically ill cancer patients

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Introduction Pneumonia is the most frequent types of infection in cancer patients. The presence of multiresistant pathogens (MR) is often associated with inadequate antimicrobial therapy. The aims of this study were to describe the microbiology and outcomes of cancer patients with severe pneumonia requiring ICU admission.
Methods A secondary analysis of a prospective cohort study was performed from 2002 to 2011 at Instituto Nacional de Cancer and Hospital Sirio-Libanes, Brazil. Adult patients with a diagnosis of cancer with pneumonia (not acquired in the hospital setting) were evaluated at ICU admission. Demographic, clinical and laboratory data were collected during the first day in the ICU, severity scores, comorbidities, performance status, cancer-related data, microbiologic identification, empiric antibiotics and the adherence to treatment guidelines.
Results A total of 268 patients were enrolled: 187 (69.8%) patients with solid tumors and 81 (30.2%) patients with hematological malignancies. In total, 167 (62.3%) patients had septic shock, and ICU and hospital mortality rates were 45.5% and 67.9%. Microbiological confirmation was present in 140 (52%) patients with 56% Gram-negative. The most frequent pathogens were methicillin-sensitive *S. aureus* (36 (26%)), *P. aeruginosa* (35 (25%)) and *S. pneumoniae* (16 (12%)). Low incidence of MR (16 (11.4%)) was observed. Adequate antibiotic therapy based on microbiological identification was prescribed in 120 (85.72%) patients. Adherence to ATS/IDSA guidelines was observed in 41 (15.3%) patients. There were no differences regarding ATS/IDSA guideline adherence (MR 3 (18.8%) vs. no MR 38 (15.1%), $P = 0.719$). We observed a trend towards higher hospital mortality in the MR patients (MR 14 (87.5%) vs. no MR 168 (66.7%), $P = 0.101$). In multivariate analysis, mechanical ventilation (OR 2.52 (1.19 to 5.32)), dialysis (3.86 (1.23 to 12.10)) and higher SAPS2 (OR per point 1.03 (1.01 to 1.05)) were associated with increased hospital mortality whereas successful noninvasive ventilation was associated with lower mortality (0.32 (0.13 to 0.77)). MR were forced into MV analysis but were not associated with outcomes.
Conclusion Severe pneumonia in cancer patients presents high hospital mortality, with particular clinical and microbiology features. Despite low adherence to ATS/IDSA guidelines, antibiotic therapy was adequate in most of patients following local guidelines based on local bacterial profiles. Further investigation is needed to clarify the impact of MRs in clinical outcomes of cancer patients with severe pneumonia.

P303

Biomarker-based exclusion of ventilator-associated pneumonia: a multicentre validation study

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Introduction Ventilator-associated pneumonia (VAP) remains a leading cause of nosocomial infection in the ICU [1]. VAP is confirmed by positive microbiology in approximately one-third of patients with suspected VAP [2], implying that there is scope to improve antibiotic stewardship. In a single-centre study, bronchoalveolar lavage fluid (BALF) inflammatory mediators (in particular interleukin-1 beta (IL-1β)) [3] and neutrophil proteases [4] demonstrated potential as biomarkers to exclude VAP. We aimed to validate these findings in a multicentre study.
Methods We conducted a prospective, multicentre observational study of 167 patients with clinically suspected VAP from 12 ICUs across the UK. VAP was confirmed by growth of a potential pathogen in BALF at $>10^4$ colony-forming units/ml. IL-1β, IL-8, matrix metalloproteinase-8 (MMP-8), MMP-9 and human neutrophil elastase (HNE) were measured in BALF by cytometric bead array. IL-6, IL-8, MMP-8, MMP-9 and HNE were measured in serum. Patients were dichotomised into VAP and

non-VAP groups and receiver operating characteristics (ROC) curves were constructed for individual biomarkers and combinations of markers before optimum cutoff points were determined.
Results A total of 150 patients had paired semi-quantitative culture and biomarker results. Fifty-three (35%) patients had VAP and 97 (65%) patients formed the non-VAP group. All BALF biomarkers were significantly higher in the VAP group (P <0.001). The area under the ROC curve for IL-1β was 0.81, for IL-8 was 0.736, for MMP-8 was 0.758, for MMP-9 was 0.785 and for HNE was 0.777. Using a cutoff value of 17 pg/ml, IL-1β had a sensitivity of 96.2%, a specificity of 43.3%, a negative predictive value (NPV) of 95.5% and a post-test probability of 4.5% (95 CI: 1 to 16%). A combination of IL-1β and IL-8 excluded VAP with a sensitivity of 100%, a specificity of 44.3% and a NPV of 1. There was no significant difference in serum biomarkers between the VAP and non-VAP groups.
Conclusion This study demonstrates that IL-1β effectively excludes VAP when validated in a multicentre study. The performance is further improved by the addition of IL-8, and the combination could form a rapid diagnostic assay to exclude VAP. Biomarker analysis appears to have the potential to improve antibiotic stewardship, and this concept should be formally tested in the setting of a randomised controlled trial.
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P304

Clinical pulmonary infection score calculator in the early diagnosis and treatment of ventilator-associated pneumonia in the ICU

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Introduction Ventilator-associated pneumonia (VAP) is a frequently occurring nosocomial infection in ICU patients and has been associated with increased morbidity, prolonged duration of ventilation and ICU stay and increased costs for healthcare. It was shown that early diagnosis of VAP and immediate initiation of appropriate antibiotics is associated with reduced morbidity and mortality. The aim of this study is to evaluate the potential ability of a screening test based on the clinical pulmonary infection score (CPIS) to identify and treat patients with VAP.
Methods All files belonging to patients between 18 and 80 years old admitted to the ICU and supported by mechanical ventilation for longer than 48 hours were evaluated retrospectively. Demographic data of the patients, the time of mechanical ventilation, duration of the ICU stay and results (survival or death) were recorded. The CPIS was calculated after 48 hours for the diagnosis of VAP. The patients with CPIS >5 intubated were evaluated VAP(+) and the others with CPIS ≤5 were thought VAP(–). The diagnosis of VAP was bacteriologically confirmed with the culture of endotracheal aspirate. Statistical evaluations were done according to the results on the day of intubation and the results on days 2, 3, 5, 8 and 10 after intubation. Scores of APACHE II and CRP levels were also recorded on the same days.
Results The duration of mechanical ventilation and ratio of death were significantly higher in the patients with VAP(+). CPIS levels in the patients with VAP(+) were significantly higher than the patients with VAP(–) in the days after the diagnosis. CPIS levels were also higher in the patients with VAP(+) on the day of diagnosis. At the same day the parameters, which included the CPIS, body temperature, leukocyte number, tracheal secretions, PaO_2/FiO_2 levels and the presence of infiltrates on the chest radiograph, were significantly higher in VAP(+) patients (P <0.05). ROC curves were formed for CPIS scores to be used in diagnosis VAP and the cutoff point had a sensitivity of 97.44% and a specificity of 100% for diagnosing VAP.
Conclusion At the end of the study, it was concluded that using the CPIS for early diagnosis and treatment of VAP and thinking that the patients with CPIS >5 were VAP(+) are guiding factors to resolve the problems associated with VAP in ICU patients.

P305

Validation of the 2005 American Thoracic Society/Infectious Diseases Society of America guidelines for ventilator-associated pneumonia: a Japanese multicenter observational study

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Introduction To select the empirical antimicrobial treatment for patients with ventilator-associated pneumonia (VAP), the 2005 American Thoracic Society/Infectious Disease of America (ATS/IDSA) guidelines classify patients according to time of onset and risk factors for potential multidrug-resistant pathogens (MDRPs). This study aimed to evaluate the effectiveness of microbial prediction and validate the adequacy of these guidelines for antibiotic strategy in VAP patients.
Methods We retrospectively analyzed 296 patients who received empiric antimicrobial treatment for VAP between January 2006 and December 2010 in 10 ICUs of Japanese tertiary hospitals. VAP was diagnosed according to CDC criteria. After assigning patients to the ATS/IDSA risk group (n = 250; late onset or risk factors for MDRPs) or non-risk group (n = 46; early onset without risk factors for MDRPs), we determined the accuracy of the guidelines for predicting pathogens and the impact of guideline adherence on patient outcome.
Results Median age and SOFA scores on ICU admission were 66 (interquartile range: 50 to 77) years and 6 (4 to 8) years, respectively. Primary diagnosis on ICU admission was coma including post-cardiac arrest syndrome (31%), trauma (29.4%), and sepsis (9.8%). Prediction of MDRPs was significantly higher in the risk group than in the nonrisk group (36.8% vs. 15.2%, P = 0.004). Guideline adherence was lower in the risk group (45.6% vs. 65.2%, P = 0.016). Treatment adequacy was greater with guideline adherence than with nonadherence (75.7% vs. 55.9%, P <0.01). Hospital mortality was not affected by guideline adherence (P = 0.70). Multivariate analysis revealed that the independent factors related to hospital mortality were adequate antimicrobial treatment (odds ratio: 0.53, 95% CI: 0.29 to 0.95; P = 0.034), age (1.02, 1.00 to 1.04; P = 0.004), history of malignancy (8.59, 1.48 to 49.6; P = 0.016), trauma (0.41, 0.2 to 0.87; P = 0.02), acute kidney injury (5.54, 2.69 to 11.4: P <0.001), and severe sepsis at VAP onset (2.7, 1.4 to 5.1; P = 0.002).
Conclusion The prediction of MDRPs using the 2005 ATS/IDSA guidelines was acceptable. To ensure adequate antimicrobial treatment, strict guideline adherence is required in the Japanese setting.

P306

Surveillance and evaluation of ventilator-associated events as per Centers for Disease Control and Prevention guidelines

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Introduction While ventilator-associated pneumonia (VAP) can affect all patients ventilated for >2 days in an ICU, an issue during the last two decades has been identification of a universally accepted definition. The Centers for Disease Control and Prevention (CDC) in Atlanta, GA, USA, have designed a new surveillance paradigm aiming to increase the objectivity of VAE diagnosis ranging from ventilator-associated condition (VAC), infective VAC to possible and probable VAP [1]. We assessed the feasibility and accessibility of the audit tool developed from the CDC guidelines as a marker of quality assurance.
Methods A prospective audit of patients admitted to University Hospital Lewisham ICU for intubation and ventilation was performed for September and October 2013. Recording of minimum PEEP and FiO_2, minimum and maximum temperatures, WBC count, specimens sent, antibiotics administered and date of organisms found was performed on a daily basis. VAEs were recorded as per modified CDC criteria (absence of quantitative microbiological testing) and compared

against a surrogate marker of clinically diagnosed VAEs based on information available to the clinician.

Results Forty patients were admitted with 29 fulfilling inclusion criteria. Of n = 29, mean age was 58 (SD 21) with a median number of 5 (2 to 29) ventilator-days. We recorded eight VAEs based on CDC criteria, one VAC, four IVAC and three VAPs. Clinical decision-making indicated seven VAEs, of which five were VAPs. CDC and clinical criteria correlated in only five of eight VAPs and clinical criteria alone would have indicated 40% more VAPs than CDC criteria. Median time to VAE trigger was 8 days (4 to 20), median number of ventilator-days if a CDC VAE triggered was 14 compared with 3 if no CDC VAE was triggered (P <0.01), and 11 compared with 3 (P <0.01) for clinical VAEs.

Conclusion While similar numbers of VAEs are triggered using CDC and clinical criteria, we noted a disparity in the VAP incidence. Four clinical VAPs were not triggered due to the hierarchical nature of the CDC criteria because the initial criterion of sustained minimum PEEP or FiO_2 rise was not met despite clear clinical criteria based on increased inflammatory markers, temperature spikes and new microbiology. We are therefore doubtful of the robustness of this tool in its current format as an accurate measure of quality assurance and agree with recent statements from the CDC [1] that modifications may be necessary.

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P307

Extracorporeal carbon dioxide removal as a bridge to lung transplantation in life-threatening hypercapnia

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Critical Care 2014, **18(Suppl 1):**P307 (doi: 10.1186/cc13497)

Introduction The introduction of the lung allocation score has resulted in a growing number of patients who are considered for lung transplantation (LTX) while being acutely decompensated. In the sickest of these patients, mechanical ventilation (MV) alone may not be sufficient to establish adequate gas exchange. Thus, different modes of extracorporeal life support have come to the focus of interest in this setting.

Methods A retrospective analysis of 17 patients (male/female ratio: 6/11; median age: 35 (range 16 to 63)) who underwent arteriovenous or venovenous interventional lung assist (iLA; Novalung, Germany) support as bridging to primary LTX (n = 11) or re-LTX (n = 6) between 2005 and 2013.

Results The underlying diagnosis was bronchiolitis obliterans syndrome III in re-LTX patients (n = 6), cystic fibrosis (n = 5), idiopathic pulmonary fibrosis (n = 2), emphysema (n = 1), adult respiratory distress syndrome (n = 1), hemosiderosis (n = 1), and chronic obstructive lung disease (n = 1), respectively. The type of iLA was arteriovenous in 10 and venovenous (iLA active) in seven patients. The median bridging time was 14 (1 to 58) days. The type of transplantation was bilateral LTX (n = 6), size-reduced bilateral LTX (n = 5), lobar bilateral LTX (n = 4), and right single LTX with contralateral pneumonectomy (n = 1), respectively. Hypercapnia was effectively corrected in all patients within the first 12 hours of iLA therapy: $PaCO_2$ levels declined from 145 (70 to 198) to 60 (36 to 99) mmHg, P <0.0001. iLA was initiated during non-invasive ventilation in three patients, of whom one was intubated prior to LTX. All other patients (n = 14) were placed on iLA while on invasive MV. Of those, three patients were extubated and remained on iLA until LTX, one patient was weaned from iLA and remained on MV until LTX, and one patient was weaned from iLA and MV prior to LTX. Five patients were switched to extracorporeal membrane oxygenation (venovenous n = 2, venoarterial n = 3) after 5 (1 to 30) days on iLA support. One patient died prior to LTX due to septic multiorgan failure (SMOF). All others (n = 16; 94%) were successfully transplanted. Of these, two patients died in the ICU due to SMOF. The remaining 14 patients (82%) survived to hospital discharge and were alive at a median follow-up of 20 (1 to 63) months.

Conclusion In patients with life-threatening hypercapnia, bridging to LTX with iLA is feasible, and results in favorable short-term and long-term outcome.

P308

Difference in physiological parameters between sitting out of bed into a chair or sitting up on an electric bed in the adult ICU

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Introduction The primary aim of this study was to identify in adult intensive care patients whether there was a difference in the acute physiological response when a patient is sat out into a chair compared with when a patient is placed in a chair position using an electric bed. The secondary aim of this study was to observe the functional outcome of these patients [1].

Methods The study was conducted in an adult tertiary referral ICU over a 3-month period. Patients that met predetermined inclusion/exclusion criteria were allocated to either sitting in a chair or sitting up in an electric bed. Heart rate, respiratory rate, tidal volume and mean arterial pressure were obtained for all patients when they were supine in bed, at 1 minute and at 1 hour in the new position. Arterial blood gases were obtained at 1 hour in their new position. A functional outcome measure known as the Chelsea Critical Care Physical Assessment Tool (CPAX) was also taken on the day of admission, on the day of sitting out, on the day of discharge from intensive care and at ward level. All data were analysed using Student's t test.

Results Sixteen subjects were recruited for this study. There was a significant increase in paO_2 (13.6 ± 2.35 kPa, P = 0.01) and decrease in $paCO_2$ (4.82 ± 1.27 kPa, P = 0.02) in the chair group at 1 hour after sitting out in the chair when compared with baseline (10.9 ± 2.44 kPa; 5.41 ± 1.32 kPa). Also there was a significant increase in tidal volume in the chair group after 1 minute of sitting out (403 ± 118 ml) compared with baseline (314 ± 105 ml). There was no difference in the electric bed group for all physiological parameters. The chair group had a better CPAX score on discharge from intensive care (chair group 24; electric bed group 13) and on discharge from the hospital (chair group 39; electric bed group 16). There were no adverse cardiovascular responses to either position.

Conclusion Sitting suitable critically ill patients out into a chair is safe and can significantly improve the arterial blood gas measurement and the tidal volume when compared with sitting a patient into the sitting position in an electric bed.

Reference

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P309

Quantifying sputum production in intensive therapy

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Critical Care 2014, **18(Suppl 1):**P309 (doi: 10.1186/cc13499)

Introduction Sputum is essential for the protection of the respiratory tract but also plays a significant role in the pathophysiology of lung disease [1]. This is evident in critical care where high sputum loads contribute to respiratory failure [2]. The quantity of sputum produced by a patient can impact on key decisions such as weaning, extubation and discharge. We undertook a survey to establish whether there was a consensus on how we quantify sputum on our intensive therapy unit (ITU).

Methods We conducted a multidisciplinary team questionnaire of our 28-bed tertiary ITU. Staff were asked how they quantified sputum load in intubated patients. They were also asked to rate statements on a five-point scale pertaining to sputum characteristics. The results were analysed in Excel 2010.

Results One hundred members of staff completed the sputum production in intensive therapy (SPIT) questionnaire (21% doctors, 71% nurses, 8% physiotherapists). Sputum load was deemed to be important or essential by more than 95% of respondents when making

decisions to extubate or decanulate. The quantification of sputum was inconsistent: 39% of respondents counted the frequency of suctioning, 24% measured the quantity of sputum in the suction tubing, whereas 25% used another method. An effective cough, consistency and colour were felt to be more important features of sputum than blood staining.
Conclusion Our results showed a very high level of agreement on the importance of knowing sputum load for decisions to extubate, decanulate or discharge from the ITU. In contrast, there was little consensus on how we should quantify sputum load in ventilated patients. This lack of standard approach may contribute to uncertainty in the clinical decision-making process. We have developed an objective sputum scoring system. Components identified as important by our survey such as suction frequency, sputum consistency and colour are included. We have recognised the benefits of the standardised Bristol stool chart to facilitate communication and believe this can be achieved with sputum load in ventilated patients.
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P310

Outcomes of patients with acute respiratory failure of mixed aetiology treated with non-invasive ventilation in a large teaching hospital critical care unit

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Introduction Bilevel non-invasive ventilation (NIV) is an established therapy in chronic obstructive pulmonary disease (COPD) and cardiogenic pulmonary oedema but evidence for its use in other acute respiratory conditions is less robust. Reported ICU mortality after NIV treatment of pneumonia ranges between 18 and 33% [1,2], compared with 10% in exacerbations of COPD [3]. We aimed to study the outcomes of patients with acute respiratory failure of mixed aetiology treated with NIV in our critical care unit and compare findings with those already published.
Methods Data were collected retrospectively on patients admitted to our critical care unit with acute respiratory failure requiring NIV over a 3-year period using the Metavision electronic patient record system. Patients with a primary surgical problem and those who received continuous positive airway pressure as a primary intervention were excluded. We recorded: primary respiratory diagnosis causing respiratory failure; patient demographics; serial arterial blood gas results; success of NIV as defined by the British Thoracic Society (BTS) [4]; and mortality statistics.
Results In total, 113 consecutive patients were identified. Mean age was 64 and 50% (56/113) were male. The primary diagnosis was pneumonia in 55 patients and exacerbation of COPD in 40 patients. The overall mortality on critical care, in hospital and at 1 year was 19% (22/113), 34% (38/113) and 41% (46/113) respectively. Success of NIV as defined by BTS criteria (pH >7.3 or reduction in $PaCO_2$ by 0.5 kPa) in the first 6 hours was seen in 72% (80/111) of patients. In NIV responders, 1-year mortality was 31% (25/80) compared with 65% (20/31) in nonresponders.
Conclusion NIV is used to treat acute respiratory failure due to a wide range of aetiologies in our unit with comparable mortality rates to large published series [1,2,5]. A successful response to NIV in the first 6 hours is associated with a reduction in 1-year mortality when compared with nonresponders.
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P311

Effect of nasal high flow for postoperative respiratory failure: a prospective observational study

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Critical Care 2014, **18(Suppl 1):**P311 (doi: 10.1186/cc13501)

Introduction We studied the effect of nasal high flow (NHF) for postoperative respiratory failure after extubation in our general surgical ICU. Recently some studies have reported that NHF improves oxygenation and reduces respiratory rate. However, the usefulness of NHF in the general surgical ICU has not been fully determined.
Methods A prospective observational study was conducted in our general surgical ICU to investigate the effect of NHF on respiratory parameters in patients with postoperative respiratory failure. Patients who were admitted to the ICU for postoperative respiratory failure (defined as oxygen saturation as measured by pulse oximetry <96% and/or respiratory rate>24 beats/minute while receiving more than 6 l/minute oxygen through a facemask) were eligible in this study. Pre and 1 and 6 hours after NHF treatment, we collected PaO_2, $PaCO_2$, respiratory rate, heart rate, and blood pressure. Data were presented with means and standard deviations. P <0.05 was considered statistically significant.
Results Forty-two patients were treated using NHF in our ICU from February 2013 to November 2013. The mean age of the patients was 62.8 ± 15.8 years, and the male:female ratio was 22:19. PaO_2 values after 1 and 6 hours of NHF (104 ± 34 mmHg, 107 ± 26 mmHg, respectively) were significantly higher than that before NHF (89 ± 38 mmHg; P <0.02). The PaO_2/FiO_2 ratio was increased from 1 hour to 6 hours of NHF (from 218 ± 90 mmHg to 236 ± 86 mmHg, P <0.05). Respiratory rate after NHF (19.6 ± 4.7/minute) was significantly lower than that at baseline (22.3 ± 4.8/minute; P = 0.0006), whereas $PaCO_2$ after NHF was reduced compared with baseline (from 41 ± 7 mmHg to 39 ± 5 mmHg, P <0.02). Thirty-two (76%, success group) patients did not need other positive ventilation. On the other hand, 10 (24%, failure group) patients required non-invasive positive pressure ventilation or intubation. We compared the failure group with the success group. However, there were no significant differences in vital signs, total bleeding, operative duration and preoperative respiratory function between the groups.
Conclusion In this study, NHF gradually improved oxygenation. Additionally, NHF reduces the respiratory rate and the value of $PaCO_2$. This result might suggest that NHF decreased dead-space ventilation. There was no difference between the success group and the failure group. So we can use NHF as the first choice for postoperative respiratory failure, but it is difficult to predict success or failure.

P312

Inhalation injury and clinical course in major burned patients

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Critical Care 2014, **18(Suppl 1):**P312 (doi: 10.1186/cc13502)

Introduction Inhalation injury is the primary determinant of mortality in major burned patients, particularly when associated with pneumonia. This study sought to describe the association between severity of inhalation injury on bronchoscopic examination and clinical course among fire victims of Santa Maria, RS, Brazil. Two hundred and forty-two people were killed in the disaster.
Methods Eighteen patients with inhalation injury secondary to smoke and fire exposure in an enclosed space admitted to Hospital de Clínicas de Porto Alegre were divided into groups according to the severity of injury as determined by bronchoscopic criteria: grade 1 (moderate edema and hyperemia), grade 2 (marked edema and hyperemia, with or without carbonaceous debris), or grade 3 (mucosal ulceration or necrosis). Duration of mechanical ventilation (MV), length of ICU stay, overall length of hospital stay, and PaO_2/FiO_2 ratio on days 1 and 3 were compared among these groups by means of ANOVA with Tukey's *post-hoc* correction.
Results Three patients had grade 1 injury, four had grade 2 injury, and 11 had grade 3 injury. Seven patients developed ventilator-associated pneumonia. Mean duration of MV increased progressively in relation

to injury severity (grade 1: 2.7 ± 0.6 days vs. grade 2: 5.7 ± 2.1 days vs. grade 3: 13.0 ± 5.4 days; $P = 0.004$), as did length of ICU stay (grade 1: 4 days vs. grade 2: 7.2 ± 2.2 days vs. grade 3: 19.9 ± 7.7 days; $P = 0.001$) and overall length of hospital stay (grade 1: 5 days vs. grade 2: 14.5 ± 5.0 days vs. grade 3: 63.4 ± 43.6 days; $P = 0.025$). There were no significant differences in PaO_2/FiO_2 ratio between groups at day 1. However, as expected, differences in PaO_2/FiO_2 ratio were found on day 3 (grade 1: 501 vs. grade 2: 424 ± 115 vs. grade 3: 318 ± 120; $P = 0.049$).
Conclusion In this cohort of patients with major burns, the severity of inhalation injury was associated with prolonged MV, length of ICU stay, and overall length of hospital stay, as well as with deterioration in oxygenation on day 3.
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P313

Severe respiratory failure in multiple trauma patients: extracorporeal support as a salvage therapy – a single-center experience

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Critical Care 2014, **18(Suppl 1):**P313 (doi: 10.1186/cc13503)

Introduction Use of extracorporeal life support (ECLS) in trauma casualties is limited by concerns regarding hemorrhage, particularly in the presence of traumatic brain injury (TBI). We report usage of ECMO/interventional lung assist (iLA) as salvage therapy in 13 trauma patients. A high-flow technique without anticoagulation was used in cases with coagulopathy or severe TBI.
Methods Data were collected from all adult trauma cases referred to one center for ECMO/iLA treatment due to severe hypoxemic respiratory failure. Thirteen consecutives cases are reported. The type of assistance was chosen based on a flowchart. Type of study: therapeutic, level of evidence IV. We analyzed patient data, injury data, blood gases before connection, methods of assistance, coagulation study, complications, survival and neurological outcome.
Results Thirteen casualties had an average Injury Severity Score of 50.3 ± 10.5 (age 27.7 ± 8.6 years, 69.2% male) and were supported 9.9 ± 4.8 days on ECMO ($n = 7$) and 7.16 ± 5.9 days on iLA ($n = 6$). All suffered severe chest injuries, including one cardiac perforation. Most were coagulopathic prior to initiation of ECMO/iLA support. Among the seven patients with TBI, four had active intracranial hemorrhage. Only 30% of the patients received continuous anticoagulation during the first 24 hours of support without clotting of the system or diagnosis of a thromboembolic event. Complications directly related to support therapy were not lethal; these included hemorrhage from a cannulation site ($n = 1$), accidental removal of a cannula ($n = 1$) and pressure sores ($n = 3$). Deaths occurred due to septic ($n = 3$) and cardiogenic shock ($n = 1$). Survival rates were 57 and 83% on ECMO and iLA, respectively. Follow-up of survivors detected no neurological deterioration.
Conclusion ECMO/iLA therapy can be used as rescue therapy in adult trauma cases with severe hypoxemic respiratory failure, even in the presence of coagulopathy, bleeding and/or brain injury. The benefits of oxygenation and circulatory support must be weighed individually against the risk of hemorrhage. Further research should determine whether ECMO therapy also confers survival benefit.

P314

Advanced respiratory care techniques in a severe adult respiratory failure unit

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Introduction Outcome is improved when patients with severe adult respiratory distress syndrome are transferred to an extracorporeal membrane oxygenation (ECMO)-capable unit [1]. Not all patients transferred require ECMO, and this service evaluation examines which techniques are utilised in patients who ultimately do not require ECMO.

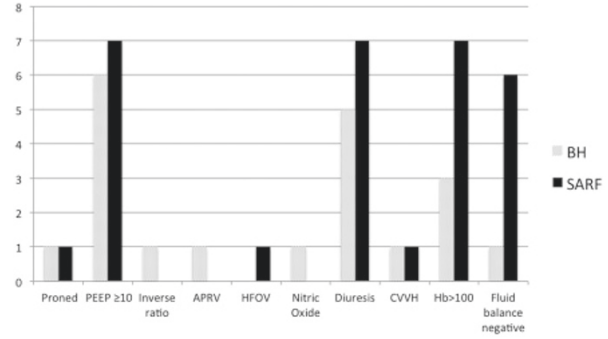

Figure 1 (abstract P314). Frequency of interventions in the base hospital (BH) and SARF centre.

Methods All patients transferred to the Severe Adult Respiratory Failure (SARF) unit between April 2012 and April 2013 for advanced respiratory care who did not require ECMO, identified from the ECMO database, underwent retrospective notes' review to identify the advanced respiratory techniques performed at the SARF unit and the base hospital.
Results Ten patients were admitted for advanced respiratory care who did not require ECMO. Eight patients had community-acquired pneumonia, one had an inhalational injury and one had a previously undiagnosed cardiac sarcoma. The techniques utilised in the SARF unit and base hospital are shown in Figure 1. Nine patients were discharged from the SARF unit alive (90%).
Conclusion A negative fluid balance and targeting higher haemoglobin are more frequently achieved in a SARF unit. Further studies are required to fully elucidate the advanced respiratory care techniques undertaken at specialist SARF units.
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P315

Nebulized C1-esterase inhibitor treatment does not attenuate pulmonary complement activation in a rat model of severe *Streptococcus pneumoniae* pneumonia

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Introduction While complement protein deficiencies are associated with severe and recurrent pulmonary infections, excessive complement activation plays a role in the pathogenesis of lung injury. We hypothesized that inhibition of the complement system by repetitive treatment with nebulized plasma-derived human C1-esterase inhibitor (C1-INH) reduces pulmonary complement activation and subsequently attenuates lung injury and lung inflammation in a model of severe *Streptococcus pneumoniae* pneumonia.
Methods Thirty-two male rats were intratracheally challenged with *S. pneumoniae* to induce pneumonia. Rats were repeatedly exposed to nebulized C1-INH or saline, 30 minutes before induction of pneumonia and every 6 hours thereafter. Rats were sacrificed 20 or 40 hours after inoculation to investigate early and late effects. BALF and lung tissue were obtained for measuring levels of complement activation (C4b/c in BALF), lung injury (total protein levels in BALF), and inflammation (IL-6 levels in lung tissue).
Results Pneumonia was characterized by bilateral macroscopic infiltrates, bacterial outgrowth in the lung and clinical signs of illness. Pneumonia was associated with pulmonary complement activation. In rats treated with nebulized C1-INH, a functional fraction of C1-INH was detectable in BALF. However, C1-INH treatment did not affect

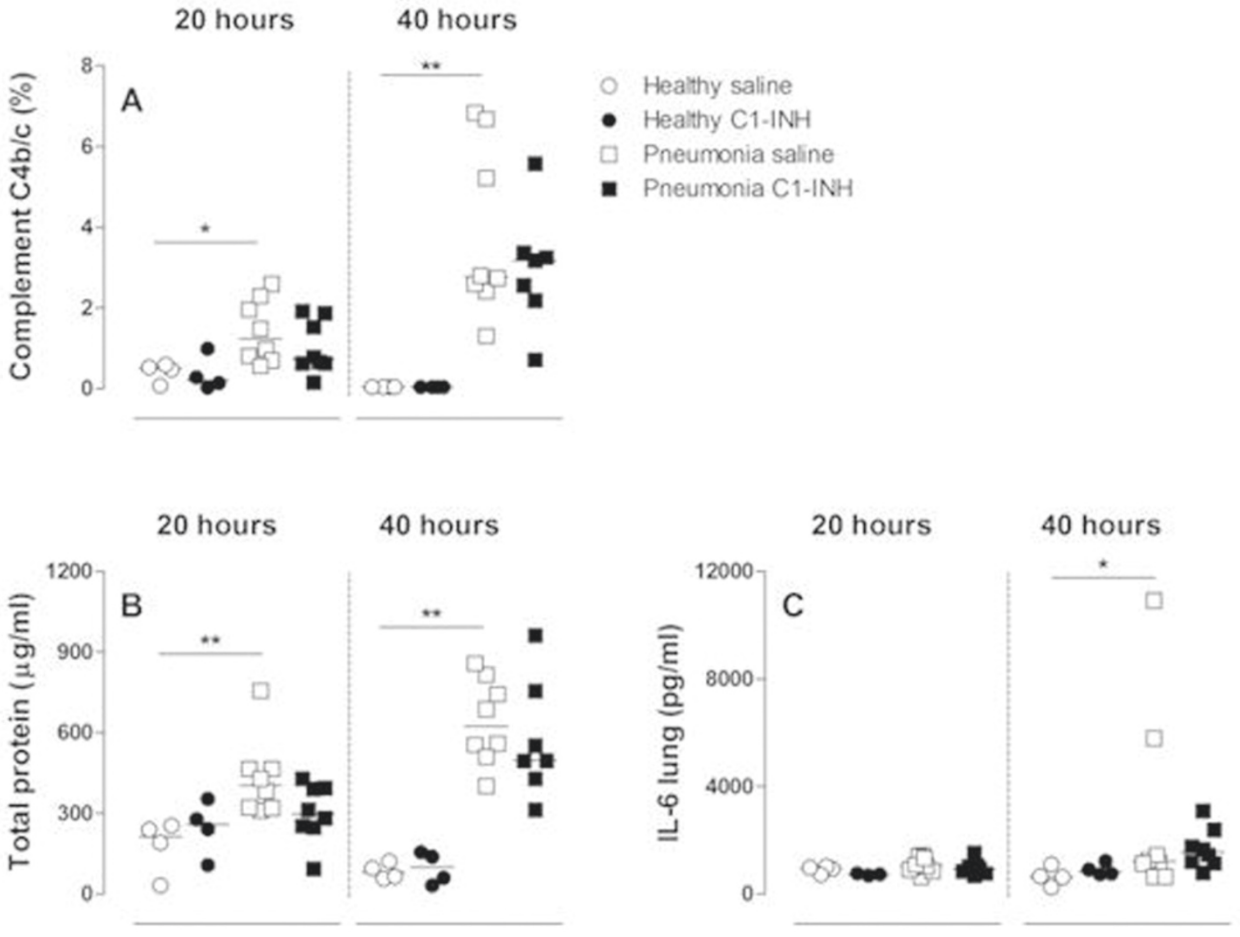

Figure 1 (abstract P315).

pulmonary complement activation (Figure 1A), lung injury (Figure 1B) or inflammation (Figure 1C).

Conclusion Severe *S. pneumoniae* pneumonia is associated with pulmonary complement activation in rats. Nebulized C1-INH treatment, in an attempt to reduce pulmonary complement activation, neither affects pulmonary complement activation or lung injury and inflammation.

P316

Novel carbon dioxide removal device driven by a renal-replacement system without hemofilter: an experimental approach and validation

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Critical Care 2014, **18(Suppl 1):**P316 (doi: 10.1186/cc13506)

Introduction Management of acute respiratory diseases must avoid ventilator-induced lung injuries along with the rise of $PaCO_2$ and respiratory acidosis [1]. Efforts are made to find devices assisting protective ventilation and able to remove arterial CO_2 and correct acidosis [2]. An extracorporeal CO_2 removal device driven by the widely used Prismaflex® platform called PrismaLung® was tested *in vivo*.

Methods Five hypercapnic ventilated pigs were equipped with the PrismaLung® system designed to remove CO_2 from the bloodstream through a decarboxylation membrane mounted on a renal replacement device without any hemofilter. Experiments examined the potential for blood decarboxylation by gas-exchanger membrane with different sets of parameters (blood flow rate: 200, 300 and 400 ml/minute, sweep gas flow: 2, 5, 10 and 50 l/minute, FiO_2: 21 and 100%). Statistical analysis was performed with the Student *t* test.

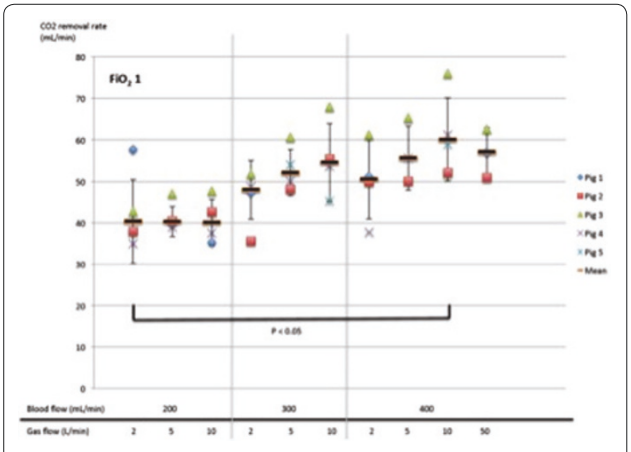

Figure 1 (abstract P316). CO_2 removal rates at FiO_2 1.

Results The extracorporeal device allowed efficient CO_2 removal rates at FiO_2 1 (Figure 1) and 0.21 (Figure 2), ranging from 40 to 60 ml/minute. Efficiency was increased with blood and sweep gas flows. Carbia and pH of animals were significantly modified after 10 minutes

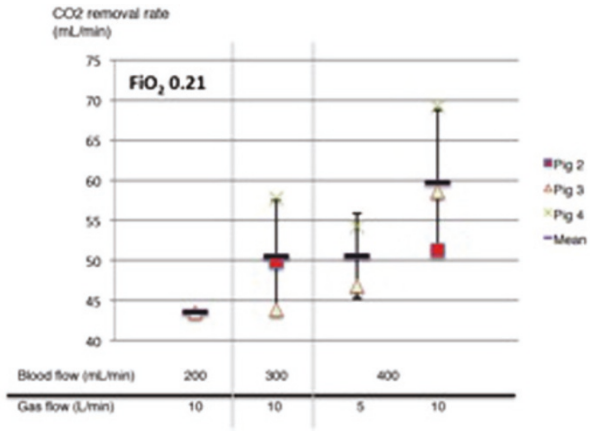

Figure 2 (abstract P316). CO_2 removal rates at FiO_2 0.21.

of treatment. No significant modification of blood oxygenation was obtained with pure oxygen, allowing the use of ambient air as the sweep gas through the membrane. No side effects or filter clotting occurred during experiments.

Conclusion The device based on the Prismaflex® platform efficiently removed CO_2 from blood and decreased $PaCO_2$ and acidosis of hypercapnic pigs. Benefits for patients with acute to chronic respiratory diseases need evaluation.

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P317

Does geography affect referral rates for extracorporeal membrane oxygenation in England?

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Critical Care 2014, **18(Suppl 1):**P317 (doi: 10.1186/cc13507)

Introduction Referral for ECMO has been demonstrated to reduce mortality in severe hypoxic respiratory failure [1-3]. The numbers of patients that undergo ECMO is still small and the service depends on timely referral from regional ICUs. There is evidence that intensivists' views on the role of ECMO are mixed [4]. The purpose of this study is to determine whether there are variations in the geographical distribution of patients that receive ECMO.

Methods NHS England provided the home primary care trust (PCT) of all adult patients referred for ECMO for potentially reversible respiratory failure from 2008 to 2012. The referrals from each PCT were indexed to the population of each area to produce a referral rate per 1,000,000 people.

Results See Figure 1. ECMO services have expanded rapidly in the last 5 years in England following the publication of evidence for its efficacy and concerns regarding an influenza pandemic. The referral rates for ECMO for severe hypoxic respiratory failure vary greatly around the country from 88 per 1,000,000 population in Leicester City to no referrals in 32 PCTs. Possible explanations could include: the distributions of swine flu around the country, referring doctors' beliefs about the efficacy of ECMO, local access to high-frequency oscillation ventilation and possible reluctance of teaching hospitals to refer to specialist centres. Further investigation to account for this variation appears indicated.

Conclusion The referral rates for ECMO vary greatly around the country.

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P318

Assessment of an endotracheal tube cleaning closed-suctioning system by micro-computed tomography: preliminary clinical data

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Introduction Using micro-computed tomography (MicroCT), we assessed the effectiveness of a cleaning closed-suctioning system (CSS) to remove secretions from the endotracheal tube (ETT) lumen. Biofilm growing within the ETT, soon after intubation, increases the patient's risk to develop ventilator-associated pneumonia, and new cleaning devices have been designed to keep the ETT clean from secretions [1].

Methods In a bench test, we injected a water-based gel into unused ETTs to evaluate MicroCT scan (SkyScan 1172; Bruker, Belgium) effectiveness to measure secretions. In six critically ill patients, a cleaning CSS (Airway Medix Closed Suction system; Biovo, Tel Aviv) was used three times a day to keep the ETT clean. After extubation, we measured ETT secretions volume by MicroCT scanning over a length of 20 cm from the ETT tip. We also collected ETTs from 11 patients treated with a standard CSS as controls, and evaluated ETT microbial colonization.

Results The volume of gel measured by MicroCT strongly correlated with the volume of injected gel (P <0.001, R^2 = 0.99). At extubation, a lower amount of secretions was measured in the ETTs treated with the cleaning CSS as compared with controls (0.031 ± 0.029 vs. 0.350 ± 0.417 mm^3, P = 0.028), corresponding to a smaller occupation of the cross-sectional area (average 0.3 ± 0.4 vs. 3.8 ± 4.5% respectively, P = 0.030). Microbial colonization tended to be reduced in the ETTs treated with the cleaning CSS (total bacterial charge 1.3 ± 1.7 vs. 3.6 ± 2.7 log(CFU/ml), P = 0.08).

Conclusion MicroCT scan showed high precision and accuracy in measuring the volume of secretions in bench tests and can thus be used to evaluate the effectiveness of actions or devices studied to reduce ETT biofilm accumulation. In a small nonrandomized population of critically ill patients, the use of an ETT cleaning device appeared effective to reduce the volume of secretions present in the ETT at extubation.

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P319

Does cost affect endotracheal tube performance?

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Introduction Today's healthcare environment has forced providers to constantly evaluate the materials used, and to find less expensive alternatives. Recently, low-cost endotracheal tubes (ETTs) have been introduced to the market. The aim of this study was to test these tubes (Portex AirCare and Cardinal Health ETT) compared with endotracheal tubes with known performance (Hi-Lo Covidient pre ISO standard and Taper-Guard Covidient, post ISO standard).

Methods We used the required test setups according to the ISO standard for cuff sealing performance. The tubes were tested versus each other in size 7.0, 7.5 and 8.0 mm. Kink performance was done in the routine manner.

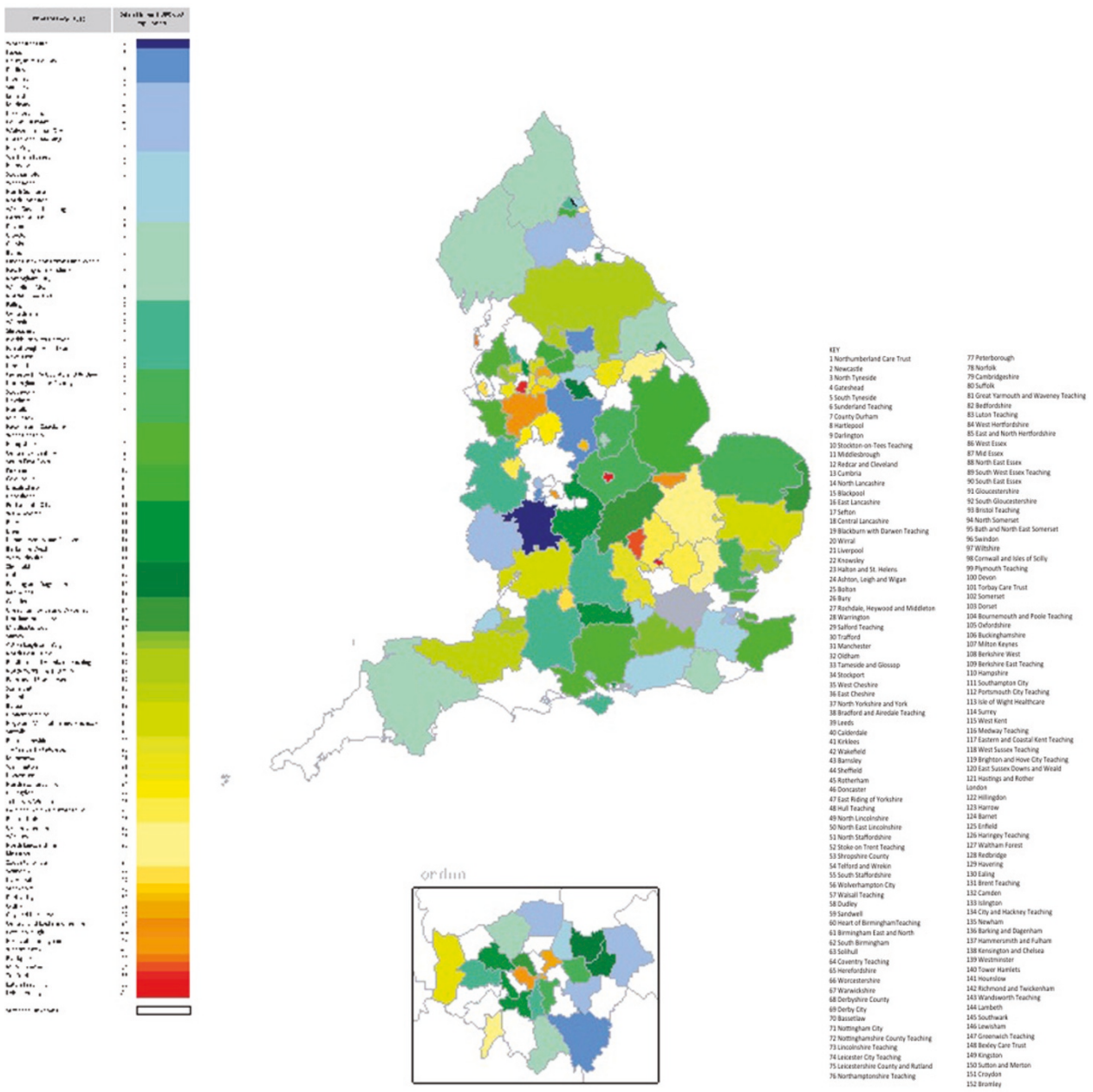

Figure 1 (abstract P317).

Results The leak test showed that the Portex AirCare ETT leaked significantly more compared with both the Hi-Lo (P <0.05) or Taper-Guard (P <0.001) ETTs. The standard deviation leak rate for AirCare was large, suggesting varying seal performance between tubes from various lots. The kink test showed no difference among tubes.

Conclusion Although tubes look the same there may be differences in performance. This study demonstrated that the new cheaper ETTs had greater cuff leak compared with the two tubes used for comparison. We can only speculate whether differences found in this study is a result of cost cutting. However, the great variability in sealing performance between ETTs of the same size from different lots would indicate that manufacturing controls may be less stringent. Although we cannot demonstrate that the higher incidence of leak will result in adverse patient outcomes, one can surmise that the possibility exists. Thus, selection of endotracheal tubes should not be based on purchase price alone but should take into account documented performance in standardized tests.

P320

Tracheostomy in obese patients: the best tube choice issue

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Introduction Obesity is not an absolute contraindication for percutaneous tracheostomy (PDT). Video-endoscopy (video-FBS) and ultrasound (US) facilitate PDT techniques and reduce complications in obese patients (OPs) [1,2]. OPs may have a higher trachea–skin distance that makes it difficult to place or to manage a tracheostomy tube (TT).

Methods A retrospective review was performed using data in the last 5 years. All OPs were from the ICU of our university hospital. Only OPs who underwent a PDT were selected with BMI >30 kg/m^2. All OPs needed prolonged mechanical ventilation. A total of 67 OPs were identified, with 60 PDTs placed using the Ciaglia Blue Rhino (CBR) Introducer Kit and seven PDTs with the UniPerc PDT Kit. All PDTs were performed by dedicated staff including residents. Valuation of clinical anatomical and physio-pathological features of the OPs and US scan of the neck came before the procedure. At the beginning of the procedure we placed a 5 mm ID orotracheal tube by tube exchange with video-FBS assistance, as already described [3]. An 8 to 9 mm ID wire-reinforced silicone tracheostomy tube (rTT) with adjustable flange was chosen instead of a standard PVC or silastic TT (sTT) in all OPs treated with CBR because of the anatomical particularities of OPs and because of external traction by the weight of the tubing attached to the TT. An extralong TT (eTT) was chosen because the pretracheal tissue was too thick for a regular-sized TT in 16 OPs with BMI >40 kg/m^2 treated with CBR. For three OPs treated with CBR we needed to change rTT to eTT because of tube dislodgement and subocclusion X-ray and video-FBS diagnosis. The UniPerc technique was chosen for OPs with BMI >40 kg/m^2.

Results No major complications (aborting procedure, >50 ml bleeding, TT misplacement, death) were observed. We had only minor complications (<50 ml bleeding: 3%; ring fracture: 2%; difficult insertion: 21% only with CBR rTT because of the step between the tip of the rTT and its introducer). UniPerc eTT placement has always been easy.

Conclusion In our experience, the data do not support what previous studies have shown suggesting increased risk of complication in OPs [1,2]. We know that the sTT could not be effective in OPs. The use of US, video-FBS assistance [3], and rTT with an adjustable flange allows a safe and effective adjustment to anatomical OP particularities, avoiding collected risks.

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P321

Impact of high-flow oxygen therapy delivered through a tracheostomy on arterial blood gases and endotracheal pressure

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Introduction High-flow oxygen therapy (HFOT) delivered through nasal cannulas can improve oxygenation as compared with low-flow oxygen devices. It has been shown that nasal HFOT can generate a positive airway pressure, which increases linearly with the gas flow rate. Data on the use of HFOT delivered through a tracheostomy are scarce. The aim of the present randomized, controlled, cross-over trial was to assess the effects of HFOT delivered through a tracheostomy on arterial blood gases and endotracheal pressure in critically ill patients.

Methods Tracheostomized patients underwent HFOT with three gas flow rates (10 l/minute, 30 l/minute and 50 l/minute), randomly applied for 20-minute periods. At the end of each period, arterial blood gases, respiratory rate, and endotracheal pressure (Ptrach) were measured. Ptrach was recorded over the last 3 minutes of each study period: the maximum expiratory pressure (MEPtrach) and mean expiratory pressure were measured and averaged for all respiratory cycles during 1-minute recording with stable breathing. FiO_2 was kept constant during the whole study.

Results Seventeen tracheostomized patients were enrolled (SAPS II 52 ± 10, PaO_2 96 ± 27 mmHg, $PaCO_2$ 33 ± 10 mmHg). Increasing the gas flow rate from 10 l/minute to 30 l/minute was associated with an increase in PaO_2/FiO_2 that did not improve further when 50 l/minute was used (259 ± 66, 317 ± 79, and 325 ± 76, respectively, P <0.001). The same trend was observed with PaO_2 (89 ± 19 mmHg, 109 ± 26 mmHg, and 113 ± 29 mmHg, respectively, P <0.001) and SaO_2 (96 ± 3%, 98 ± 2%, 98 ± 2%, respectively, P <0.001). $PaCO_2$ (32 ± 8 mmHg on average) and respiratory rate (27 ± 7 breaths/minute on average) did not change with different gas flow rates. MEPtrach (0.96 ± 0.43 cmH_2O, 1.32 ± 0.4 cmH_2O, and 1.89 ± 0.5 cmH_2O at 10 l/minute, 30 l/minute and 50 l/minute, respectively, P <0.01) and mean expiratory pressure (0.54 ± 0.27 cmH_2O, 0.91 ± 0.29 cmH_2O, and 1.36 ± 0.35 cmH_2O, at 10 l/minute, 30 l/minute and 50 l/minute, respectively, P <0.01) increased with flow. Changes in PaO_2/FiO_2 were not correlated with changes in expiratory pressures.

Conclusion When HFOT is used through a tracheostomy at increasing gas flow rate, oxygenation increases up to 30 l/minute while CO_2 clearance and the respiratory rate do not vary. Tracheal expiratory pressure increases with flow, but changes are small and probably of limited clinical relevance. Changes in oxygenation are not related to the variations of tracheal expiratory pressure. HFOT through a tracheostomy has different effects from when a nasal interface is used.

P322

Development of the novel Tracoe Twist Plus tracheostomy tube

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Introduction The 4th National Audit project, conducted by the Royal College of Anaesthetists in 2011, reviewed major airway complications in the UK [1]. It highlighted tracheostomy tube displacement as a significant risk in critical care patients. Prior to 2011, at the Royal London Hospital ICU, the Tracoe Twist (marketed by Kapitex) was primarily used as the default choice of tracheostomy tube. However, over a 5-year period, there were a significant number of critical incidents related to tracheostomy tube displacement or blockage. On investigation of these incidents, root-cause analysis identified inadequate length of the Tracoe Twist as a major contributing factor. As a consequence of this, there was also an increasing requirement for the use of adjustable flange tubes. This was particularly apparent in obese patients. Our objective was to develop a new tracheostomy tube that would reduce the number of incidents related to inadequate length. An additional aim was to maximise the inner diameter for a given external diameter, thus reducing airway resistance and potentially aiding weaning.

Methods We formed a consultation committee, consisting of consultants in critical care, a consultant surgeon and a consultant anaesthetist with a specialist interest in head and neck anaesthesia and tracheostomy care. We collaborated with the Kapitex design team to develop a new tracheostomy tube which addressed some of the perceived deficits of existing devices.

Results We developed a prototype tracheostomy tube that had an increased length for a given internal diameter. We also increased the mobility to flange, in order to reduce pressure areas and assist with fixation. A third modification was to ensure a maximal internal diameter for a given external diameter. We piloted its use in 20 patients. No adverse events were observed and the clinical impression was that the increased length was beneficial to the patients.

Conclusion Following the success of the pilot study, this new tracheostomy tube was developed and then marketed by Kapitex. This tube was named the Tracoe Twist Plus. We have now used this tube for 2 years. We have since performed an extensive retrospective audit of tracheostomy usage and the effect of the introduction of the novel Tracoe Twist Plus, and the complication rate was reduced in terms of displacement and obstruction.

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P323

Ability to speak in ventilator-dependent tracheostomized ICU patients

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Introduction Mechanical ventilation (MV) and inability to speak increases psycho-emotional distress [1]. Although not commonly used

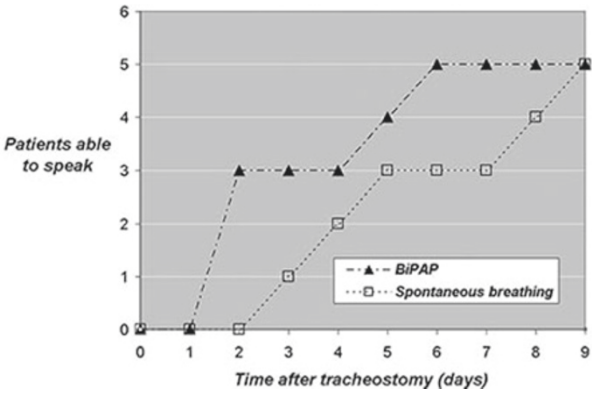

Figure 1 (abstract P323). Number of patients able to speak.

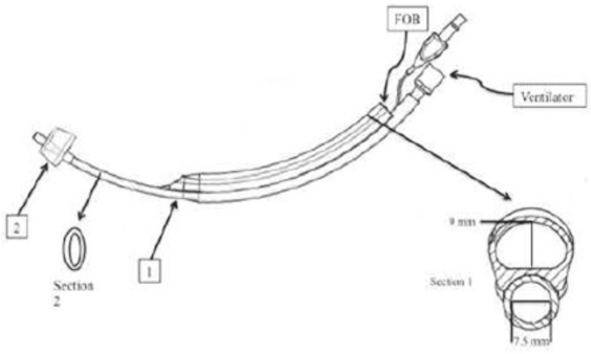

Figure 1 (abstract P324). Point 1 just before vocal cord, point 2 asymmetric elliptical cuff just before the carena.

in ICU patients, MV with a deflated cuff in patients with a tracheostomy can be provided safely and comfortably, by use of a BiPAP Vision®. Air leakage to the upper airway enables speech [2]. By adding a Passy-Muir® speaking valve as second step, the quality of speech and cough will improve. The ability to speak provides an important improvement in communication.

Methods The aim of this study was to compare weaning from MV by gradually decreasing the level of support in cuff-deflated ventilation with use of a BiPAP Vision® and a Passy Muir® speaking valve, or by trials of spontaneous breathing with use of a speaking valve, both for progressively longer periods of time. We examined the differences in the ability to speak, the duration of the weaning period, the occurrence of delirium and the frequency of tracheal suctioning. We performed a single-centre retrospective and prospective observational study in a 22-bed mixed ICU during 1 year. Data were collected using the patient data management system. Baseline criteria were age, gender, APACHE IV score, ICU length of stay and duration of MV before placement of the tracheostomy.

Results Ten patients were included, five in the BiPAP group and five in the spontaneous group. There were no significant differences in the baseline criteria. On the second day after tracheostomy, three out of five patients in the BiPAP group were able to speak compared with one in the spontaneous method group. A difference in speaking ability remained until day 9 (see Figure 1). At first time of speaking, the BiPAP group had higher PEEP level (10 vs. 7.5 cmH_2O) and higher SOFA score (6.2 vs. 4.6) compared with the spontaneous group. There was no significant difference in delirium, duration of weaning and tracheal suctioning between both groups.

Conclusion Cuff-deflated MV in ICU patients enables speaking during ventilator dependence. With this technique the ability to speak started in an earlier phase of weaning compared with weaning with spontaneous breathing trials and a speaking valve.

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P324

Double-lumen endotracheal tube for percutaneous tracheostomy: *in vitro* and *in vivo* preliminary data

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Introduction A double-lumen endotracheal tube (DLET; bilumen ventilation tube, PCT/IT2012/000154; Deas S.r.l., Italy) (Figure 1) has been developed to improve the safety of patients and procedural comfort during percutaneous tracheostomy (PT). The DLET is divided into an upper channel, for placement of a fiberoptic bronchoscope (FOB), and a lower channel exclusively dedicated to the patient's ventilation. The aim of this study is to achieve an *in vitro* and an *in vivo* evaluation of PT performed with the DLET.

Methods The nonlinear constant of the Rohrer equation (K_2) was calculated as resistive properties, during a continuous flow of 10 to 90 l/minute, for a conventional endotracheal tube (ETT) with and without FOB (ETT size 7, 7.5, 8, 7f, 7.5f, 8f), ventilation tube of TLT (F4 and F5) and DLET. The variation of gas exchange (Δ) was measured with arterial blood gas samples obtained before and after the PT. During PT, all patients received sedation, analgesia, neuromuscular blocking and volume-controlled ventilation set with FiO_2 100%, TV 500 ml, RR 15 breaths/minute, PEEP 5 cmH_2O.

Results *In vitro* evaluation showed that the DLET had the lowest K_2 (7 = 11.33; 7.5 = 8.74; 8 = 7.57; 7f = 6.13; 7.5f = 10.52; 8f = 12.28; F4 = 130.0; F5 = 11.12; DLET = 5.25 cmH_2O/l/minute). During *in vivo* evaluation, PT was performed with the conventional ETT with FOB and DLET for five patients in each group (age 69 ± 13 vs. 71 ± 16; SAPS II: 56 ± 14 vs. 52 ± 20; GCS 3 vs. 4). Gas exchange before and after the procedure did not differ between the groups, but the Δ values of pH, PaO_2 and $PaCO_2$ measured before and after the procedure were, ETT+FOB versus DLET: ΔpH: −0.05 ± 0.05 versus 0.01 ± 0.02, $P = 0.04$; ΔPaO_2: −112.6 ± 112.6 versus 41.6 ± 25.3, $P = 0.01$; $\Delta PaCO_2$: 14.5 ± 10.8 versus 0.6 ± 1.1, $P = 0.02$; ΔHCO_3: 0.5 ± 2 versus −0.04 ± 0.3, $P = 0.6$.

Conclusion The DLET resulted in adequate airway patency and minimal obstruction due to the lower channel exclusively dedicated to patient's ventilation. Gas exchange in PT with the DLET remained stable without any variation in oxygenation and carbon dioxide levels, although the same settings of mechanical ventilation.

P325

National survey of ICUs in the UK: discharging patients with tracheostomies

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Introduction Respiratory weaning in ICUs can be a lengthy and expensive process [1], but may be facilitated by the use of tracheostomies. Discharging patients with tracheostomies to general wards improves ICU bed availability but raises potential patient safety issues. This is demonstrated by the increased mortality compared with patients decannulated before discharge from the ICU [2]. We investigated how often ICUs in the UK discharge patients with tracheostomies to wards, which wards these are and whether systems are in place to ensure adequate safety on discharge.

Methods We telephoned 217 ICUs in the UK. Nursing staff answered a series of questions regarding the discharge of patients with tracheostomies to the wards and their follow-up.

Results We obtained information from 203 ICUs. A total of 201 units used tracheostomies for respiratory weaning. In total, 151 routinely discharged patients to wards with tracheostomies, 11 never did and

39 did occasionally. Five discharged to the high dependency unit only, 60 to respiratory wards only, 70 to specialist wards and 15 to any or most wards. Eighty-five out of 190 units discharged patients with tracheostomy cuffs both up and down, 72 discharged with the cuff down or cuffless and 16 with the cuff 'usually down'. A total of 141 hospitals had routine follow-up for tracheostomy patients from critical care outreach or other services. Critical care outreach was available 24 hours a day in 65 hospitals.

Conclusion The vast majority of ICUs in the UK perform tracheostomies for respiratory weaning and many routinely discharge patients to the wards prior to decannulation. Routine follow-up is usually available, but cover may only be available during the day. Patients may go to a specialist ward with trained nurses but this is not always the case. Patients are often discharged to wards with their tracheostomy cuff up, raising major safety issues if their tracheostomy tubes block and nurses are not trained for such emergencies. Twenty-four hours a day critical care outreach cover may improve patient safety, but further research and the production of guidelines is needed to facilitate the safe discharge of patients with tracheostomies from ICU to the wards.

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P326

Percutaneous dilatational tracheostomy in patients with severe coagulopathy or thrombocytopenia

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Introduction Percutaneous dilatational tracheostomy (PDT) is the standard airway access in critically ill patients who require prolonged mechanical ventilation. However, patients with severe coagulopathy or thrombocytopenia might have an increased risk of periprocedural bleeding.

Methods We retrospectively reviewed the records of all patients who underwent PDT (using the Ciaglia technique with bronchoscopic guidance) on our cardiothoracic ICU between January 2004 and February 2013. Patients were stratified into two groups: no coagulopathy (group 1), and coagulopathy/thrombocytopenia defined as international normalized ratio >1.5, partial thromboplastin time >50 seconds and/or platelet count $<50 \times 10^9$/l (group 2).

Results From a total of 1,001 patients (46% male, mean age 68.1 years) that underwent PDT, we identified 441 patients (44.1%) with a severe coagulopathy (group 2). There were no procedure-related deaths. Major procedure-related complications included a severe bleeding (requiring transfusion and/or surgery) in two patients in each group (one laceration of the brachiocephalic trunk, one venous bleeding, two bleedings from a thyroid vessel), injury of the membranous wall of the trachea in two patients in group 2 as well as a pneumothorax and a device failure in group 1. The incidence of moderate periprocedural bleeding was comparable between the two groups ($n = 43$ (9.75%) vs. $n = 41$ (7.3%), P = NS).

Conclusion Periprocedural bleeding complications during and after PDT are rare, even in patients with a severe coagulopathy, and thus PDT can be safely performed in these patients.

P327

Repeat bedside percutaneous tracheostomy: still a contraindication?

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Introduction Percutaneous tracheostomy has become an established procedure in airway management of critically ill patients. Repeat PDT is considered a (relative) contraindication as a result of distorted anatomy.

Methods A retrospective review of all repeat bedside percutaneous dilatational tracheostomies (Ciaglia technique with direct bronchoscopic guidance) performed on our cardiothoracic critical care unit from January 2004 to February 2013 was conducted.

Results From a total of 1,001 patients undergoing PDT, we identified 36 patients with repeat PDT. Patients' previous tracheostomies dated back between 5 days and 2.7 years (mean 122 days). Mean age was 60.3 ± 14.3 years, 42% of patients were female. The mean time from intubation to PDT was 3.7 ± 3.9 days. There were no deaths associated with PDT but one major procedure-related complication: one patient suffered from a periprocedural laceration of the brachiocephalic trunk. After emergency surgery and surgical tracheotomy (ST), the patient recovered completely. In all other patients, no conversion to ST, no loss of airway, no paratracheal insertion, and no accidental tracheal extubation was observed. No pneumothorax, pneumomediastinum, hypotension, hypoxemia, or arrhythmias were recorded. A mild bleeding was observed in 13 patients (36%). A moderate but not significant bleeding was observed in only one patient (2.8%). A tracheal ring fracture occurred in six patients (16.7%). Fourteen patients (38.9%) could be weaned successfully from the respirator and the tracheostomy could be removed. Thirteen patients (36.1%) were transferred to another ICU with the tracheostomy in place. The functional and cosmetic outcomes of PDT were excellent.

Conclusion Repeat PDT is a safe procedure in experienced hands and should not be generally considered a contraindication. However, special attention should be paid to the anatomical situation with an increased risk of vascular complications.

P328

National UK survey: a review of percutaneous tracheostomy and auxiliary subglottic suction port use

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Critical Care 2014, **18(Suppl 1):**P238 (doi: 10.1186/cc13518)

Introduction The tracheostomy is an ancient technique that more recently has developed a percutaneous technique. Percutaneous tracheostomies (PCT) have been shown to be safer and reduce infection, cost and other complications over surgical techniques [1-3]. Ventilator-associated pneumonia (VAP) is a serious complication resulting from the use of endotracheal tubes (ETT) and tracheostomies. Changes in design of these tubes by the addition of a subglottic suction port have been shown to improve VAP rates in mechanically ventilated patients [4,5]. A large meta-analysis review showed that subglottic drainage reduced the number of days of mechanical ventilation required and reduced the number of days stayed on the ICU [4].

Methods We contacted all ICUs in the UK by telephone and spoke to the nurse-in-charge to ascertain their normal practice with regards to PCT and subglottic suction use.

Results We contacted a total of 246 general ICUs, 72% of which we received a response. The average number of beds per ICU from all units who responded was 11. Ninety-eight per cent of ICUs that we questioned did use PCT. For three units, the average bed number per unit was 11 and the other 2% of ICUs who did not use PCT had five beds per unit on average. The proportion of ICUs that employed subglottic suction ports on their ETTs was 43% having on average 11 beds per unit, whilst the proportion of ICUs that did not employ subglottic suction ports was 57%, also with 11 beds per unit on average. Regarding PCT subglottic suction ports, 38% of ICUs did utilise these tubes whilst 62% did not. Of the group of ICUs that did use subglottic suction ports on their tracheostomy tubes, the average beds per unit was 12. Of the group of ICUs that did not use subglottic suction ports on their tracheostomy tubes, the average beds per unit was 10.

Conclusion Significant differences in practise exist with PCT and subglottic suction ports on tubes. The size of the ICUs in these groups is variable. The larger units are more likely to use PCT over the smaller units. Regarding subglottic suction ports on ETT and tracheostomy tubes, the size of the ICU does not necessarily dictate their use. We propose that all ICUs review their policy on the use of PCT and subglottic suction-assisted tubes to help improve surgical complications, cost, VAP rates and ICU stays.

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P329

Is the post-critical care environment safe for tracheostomy patients?

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Introduction Over 5,000 tracheostomies are performed in the UK per year [1]. The 4th National Audit Project identified significant morbidity and mortality associated with tracheostomy care [1]. The National Tracheostomy Safety Project (NTSP) 2013 manual highlighted the need for: local policy; an appropriate care environment; immediate availability of emergency equipment; trained staff and local training programmes; and bed-head sign and emergency algorithms for tracheostomy patients [2]. Following these guidelines, we asked: how are adult tracheostomy patients managed post discharge from the intensive care/high dependence unit (ICU/HDU) throughout the UK?
Methods In November 2013, 200 adult ICU/HDUs throughout the UK were contacted to take part in a telephone survey. Data were collected on tracheostomy weaning, post-ICU/HDU care, safety guidelines, emergency protocols and training for clinicians and nurses.
Results Out of the 200 adult ICU/HDUs contacted, 134 took part in the survey. Out of these, 44% have a tracheostomy weaning protocol, 69% initiate weaning whilst the patient is mechanically ventilated, and 92% use a speaking valve in their weaning process. Also, 87% allow tracheostomy patients to have oral nutritional intake and in 59% of these the decision involves speech and language therapy. Post ICU/HDU, 67% of units discharge to specialised wards, 22% to nonspecialised wards, 4% to dedicated step-down units and 6% do not step down their tracheostomy patients. A critical care outreach team reviews the patients in 73% of the hospitals surveyed. Furthermore, only 11% of the hospitals have a consultant lead tracheostomy ward round and 17% have a tracheostomy multidisciplinary team (MDT). Also within these hospitals, 57% have their own tracheostomy safety guidelines and 70% have emergency tracheostomy management protocols. On the wards: 34% have tracheostomy bed-head information signs, 93% have emergency bed-side tracheostomy equipment, 89% have a tracheostomy training programme, and 50% have a MDT approach to decannulation.
Conclusion There is a wide variation in post-ICU/HDU management of tracheostomy patients throughout the UK. Although there are well established UK national guidelines for the management of tracheostomy patients, outside the ICU/HDU environment there is a lack of full implementation of the NTSP recommendations, increasing the risk of tracheostomy-related morbidity and mortality.

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P330

Survey on the use of chlorhexidine and toothpaste as part of oral care in UK ICUs

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Introduction Ventilator-associated pneumonia (VAP) is the most common nosocomial infection among ventilated patients and is associated with increased mortality and morbidity [1]. Oral chlorhexidine has been used to decontaminate the airway in critically ill patients, as studies suggest a risk reduction in VAP [2]. Chlorhexidine reacts with soaps in toothpaste to form inactive insoluble salts [3]. A minimum delay of 30 minutes between tooth brushing and the subsequent application of chlorhexidine is therefore recommended [4].
Methods A telephone questionnaire was conducted on all ICUs in the UK to assess current oral decontamination procedures with regards to chlorhexidine use and the timing of tooth brushing with toothpaste.
Results Sixty-five per cent of ICUs in the UK responded to our survey (n = 157). Ninety-seven per cent (n = 152) used chlorhexidine and 96% (n = 150) used it as part of a ventilator care bundle. Forty-six per cent (n = 70) used a gel, 32% (n = 48) used a mouthwash and 23% (n = 34) used both preparations. The frequency of chlorhexidine application varied between ICUs; 15 (9.9%) applied 4-hourly, 91 (59.9%) 6-hourly, 20 (13.2%) 8-hourly, 19 (12.5%) 12-hourly and seven (4.6%) applied at variable times. Ninety-seven per cent (n = 152) brushed patient's teeth; 86% (n = 130) used toothpaste, 3% (n = 5) used chlorhexidine gel and 11% (n = 17) used both. Ninety-seven per cent (n = 147) of ICUs using chlorhexidine also brushed patient's teeth with toothpaste. Forty-eight per cent (n = 70) administered chlorhexidine within 30 minutes of toothpaste application (Table 1).

Table 1 (abstract P330). Timing difference between toothpaste and chlorhexidine (minutes)

Minutes	Number of ICUs (%)
>30	74 (50.3%)
<30	32 (21.8%)
Nil	38 (25.9%)
Variable	3 (2.0%)

Conclusion Chlorhexidine is being used too soon after the application of toothpaste in 48% of ICUs in the UK. This results in attenuation of its effect and may remove its beneficial risk reduction in VAP. Awareness of this interaction should be emphasised.

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P331

Effect of subglottic secretion drainage for preventing ventilator-associated pneumonia

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Introduction We aimed to assess the effect of continuous drainage of subglottic secretion in the prevention of ventilator-associated pneumonia (VAP) in patients requiring prolonged mechanical ventilation for more than 48 hours in the ICU as a prospective, randomized, controlled study.
Methods Our study was performed with a document from the ethics committee and written informed consent from the relatives of patients between April 2011 and February 2012 in our 14-bed ICU. Fifty-four patients whose mechanical ventilation requirements were expected to be longer than 72 hours were included in our study. Patients were randomly divided into two groups. These were formed as the group using a conventional intubation tube (Group C) and the group using an intubation tube allowing aspiration of subglottic secretions (Group S). In Group S, continuous subglottic aspiration occurred under constant pressure with a special device. In both groups, the cuff pressure was maintained at a constant pressure of 20 to 30 using a digital cuff pressure device [1].
Results In Group C, VAP was developed in 10 (35.7%) of 28 patients. In group S, VAP was developed in five (21.7%) of 23 patients. In both groups when compared according to the development of VAP, no

statistically significant differences were detected ($P = 0.276$). However, in the first 5 days the development of VAP was significantly higher in Group C (respectively, 4.3% vs. 25%, $P = 0.046$). The growth rate of VAP (VAP number/ventilator-day × 1,000) in Group C was 17.48, while in Group S it was 11.62. Between the groups there were no statistically significant difference according to ICU mortality, length of ICU stay and length of hospital stay ($P \geq 0.05$).

Conclusion This prospective randomized controlled study demonstrated that the incidence of VAP (especially early development of the VAP) with continuous aspiration of subglottic secretions without creating any undesirable clinical damage in the airways was significantly reduced.

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P332

Survey of the use and practicalities of subglottic suction drainage in the UK

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Introduction Subglottic secretion drainage (SSD) has been shown to reduce the incidence of ventilator-associated pneumonia (VAP) [1]. We reviewed current UK practice and practicalities surrounding implementation of SSD using a survey.

Methods We constructed a survey of 10 questions using SurveyMonkey and circulated it via an email link to the Linkmen of the UK Intensive Care Society. Responses were received between August and November 2013.

Results We had 77 responses. The majority were from doctors (88%) and the rest from nurses. Of respondents, 63% worked in district general hospitals, 28% in teaching hospitals and the rest in specialist units. Overall, 54% of respondents worked in units using SSD. From these responses, the types of patients receiving SSD are summarised in Table 1. One hundred per cent of units used intermittent SSD. Seventy-one per cent of respondents reported that SSD tubes were stored only on their ICU, with 26% reporting availability in acute areas and the rest hospital wide. Twenty-eight per cent of respondents indicated it was unit policy to reintubate patients to facilitate SSD. More than 90% of units had a ventilator care bundle and regularly measured cuff pressures. Overall, 83% of those surveyed thought SSD was beneficial in the prevention of VAP.

Table 1 (abstract P332). SSD in specific patient groups (more than one per responder)

Patients	Number
All	23
Tube >72 hours	6
Tracheostomy	13
Selected	7

Conclusion Despite specific recommendations from the UK Department of Health [2], only about one-half of respondents work in ICUs where SSD has been adopted. Most studies show benefit in patients expected to be ventilated for greater than 72 hours [1], but most units used SSD in all intubated patients. The reintubation rate to facilitate SSD was also reasonably high, despite a lack of evidence to support this practice. In the vast majority of hospitals, SSD endotracheal tubes are stored only on the ICU and so the need for reintubation may result from a lack of available appropriate tubes at the point of first intubation.

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P333

Intravenous perfluorocarbons increased oxygen delivery/consumption in ARDS in swine

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Introduction Emulsified perfluorocarbons (PFC) are synthetic hydrocarbons that can carry 50 times more oxygen than human plasma. Their properties may be advantageous in applications requiring preservation of tissue viability in oxygen-deprived states, which makes them a potential candidate for combat and civilian pre-hospital resuscitation. Our hypothesis was that an intravenous dose of PFC increases vital organ tissue oxygenation, improves survival and reduces or prevents the development of ventilator-associated ARDS. Here we report data from the second part (ARDS only) of a multiphase swine study to investigate the benefits of PFC in treating hemorrhagic shock and preventing ARDS.

Methods Anesthetized Yorkshire swine were randomized ($n = 6$/group) to receive a bolus of the PFC Oxycyte™ either 45 minutes before (PFC-B) or after (PFC-A) induction of ARDS or nothing as a control (NON). ARDS was induced via intravenous oleic acid infusion (time 0 (T0)) over 30 minutes. Animals were monitored for physiological and hematological parameters. They were euthanized at T180 minutes and a full necropsy and histopathological analysis was performed.

Results Survival was 100% in the NON group, 80% in the PFC-A group and 20% in the PFC-B group. Mean arterial pressure (MAP) and mean pulmonary artery pressure (MPAP) were significantly increased during infusion of PFC and during ARDS in the PFC-B group, while cardiac output (CO) was significantly reduced. In the PFC-A group it was observed that MAP and MPAP increased and CO decreased during ARDS induction, but not during PFC infusion. Those changes were significant in comparison with the NON group. Oxygen delivery and consumption in the PFC-A group were significantly increased. Histopathological analysis is currently being performed. Interim analysis showed a trend to reduced alveolar damage in PFC-A animals.

Conclusion Administration of PFC before induction of ARDS was detrimental, while giving PFC after ARDS improved oxygen delivery and increased oxygen consumption. Although survival in this group was lower than in the NON control group (80% vs. 100%, not significant), a reduction in alveolar damage was observed. This might improve long-term outcome after ARDS. Based on these data we will continue to the final phase of this project and evaluate the capacity of PFC to prevent ARDS in combination with HS.

P334

Prevention of pneumothorax using venovenous ECMO in acute respiratory distress syndrome with emphysematous/cystic changes in the lung

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Introduction Venovenous extracorporeal membrane oxygenation (VV ECMO) is a treatment option for acute respiratory distress syndrome (ARDS) to minimize ventilator-induced lung injury including life-threatening pneumothorax. The purpose of our study was to investigate the safety and efficacy of VV ECMO for preventing pneumothorax in ARDS patients who were complicated with emphysematous/cystic changes in the lung.

Methods We have retrospectively analyzed data of ARDS patients complicated with emphysematous/cystic changes in the lung who were admitted to our ICU from 2006 through 2012. We divided the subjects into two groups, patients treated with VV ECMO (ECMO group), and those treated only by conventional ventilator management (non-ECMO group). Correlations between age, sex, underlying disease, PaO_2/FIO_2 ratio on admission, duration of ICU stay, survival and incidence of pneumothorax were evaluated.

Results Forty-one patients were included in this study (ECMO and non-ECMO group, 21 and 20 patients, respectively). There were no significant differences between ECMO and non-ECMO groups as regards age, sex, underlying disease, PaO_2/FIO_2 ratio, duration of ICU stay, and survival. In the ECMO group, the mean duration of ECMO use was 17 ± 13 days, and bleeding due to anticoagulation was observed in five patients. The mean airway pressure in the ECMO group was significantly lower than in the non-ECMO group (12 ± 6 cmH_2O, 22 ± 6 cmH_2O, respectively; P <0.0001). The incidence of pneumothorax was also significantly lower in the ECMO group than the non-ECMO group (10%, 45%, respectively; P = 0.015). In Kaplan–Meier analysis, the proportion of pneumothorax-free patients was significantly higher in the ECMO group (P = 0.014). In multivariate analysis, conventional ventilator management, presence of interstitial pneumonia and the duration of intubation were the independent risk factors of pneumothorax (hazard ratio (HR), 18.0, P = 0.010; HR 33.3, P = 0.025; HR 1.05, P = 0.041, respectively).
Conclusion Although the survival rate was not statistically different, the use of ECMO for ARDS patients complicated with emphysematous/cystic changes in the lung markedly reduced the incidence of pneumothorax.

P335

Injurious ventilation has an age-dependent affect on the pulmonary renin–angiotensin system in LPS-challenged rats

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Introduction The underlying molecular mechanisms for the association between aging and a higher susceptibility to develop ARDS are poorly understood. The pulmonary renin–angiotensin system (RAS), with a lung-protective (angiotensin-converting enzyme (ACE)2–angiotensin (Ang)-1,7–Mas receptor) axis and a lung-injurious (ACE–Ang II–Ang II receptor (AT1)) axis, has been implicated in the pathogenesis of ARDS and changes with age. We hypothesized that injurious ventilation has an age-dependent effect on the pulmonary RAS in LPS-challenged rats that is associated with increased lung injury.
Methods Infant (~1/2 month), juvenile (~1 month), adult (~4 months) and older (~19 months) Wistar rats were challenged with intratracheal LPS and injurious ventilation using tidal volumes of 15 ml/kg for 4 hours. Lung injury was assessed by wet-to-dry ratio and changes in P/F ratio. Levels of inflammatory mediators were measured in bronchoalveolar lavage fluid; mRNA expression of key genes of the pulmonary RAS was determined in lung homogenates.
Results LPS-challenged and ventilated older rats showed higher mortality, larger change in wet-to-dry ratio and larger decline in P/F ratio, compared with other age groups. Increases in neutrophil influx and inflammatory mediators were age dependent, with higher levels with increasing age. Compared with controls, ventilated LPS-challenged rats showed a decrease in mRNA expression of ACE, ACE2, AT-1 and Mas receptor in all age groups, except for infants. The relative decrease in the mRNA expression of the Mas receptor was most extensive in older rats, thereby shifting the balance towards the lung injurious axis in this age group.
Conclusion The effects of injurious ventilation on lung injury are age dependent in a model of LPS-challenged rats, which is associated with a more pronounced imbalance of the pulmonary RAS at the expense of the lung-protective axis with increasing age.

P336

Role of Th1 and Th17 imbalance in acute lung injury mice

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Introduction Acute lung injury (ALI) is characterized by an excessive inflammatory response. Several recent clinical observations have shown that severe H1N1 influenza with ARDS is characterized by early secretion of Th17 (IL-6, IL-8, IL-9, IL-17) and Th1 (TNFα, IL-15, IL-12p70) cytokines [1,2]. However, the exact role of T-helper cells (Th) in the ALI model remains unknown. We hypothesized that there might be Th imbalance within the lung in the early phase of LPS-induced ALI. This study was to assess the role of lung Th polarization response in ALI mice.
Methods C57BL/6 mice were randomly divided into two groups: control group and ALI group. ALI animals received 2 mg/kg LPS. Lung wet weight/body weight (LW/BW) was recorded to assess lung injury. The pathological changes were examined under an optical microscope. The mRNA expression levels of T-bet, GATA-3 and RORγt were determined by quantitative real-time reverse transcriptase-polymerase chain reaction. Meanwhile, levels of IL-6, IFNγ, IL-4 and IL-17 in lung homogenates were assessed by enzyme-linked immunosorbent assay.
Results The increase in LW/BW was induced in ALI mice. Histologically, widespread alveolar wall thickening caused by edema, severe hemorrhage in the interstitium and alveolus, and marked and diffuse interstitial infiltration with inflammatory cells were observed in the ALI group. Meanwhile, the levels of IL-6 in lung tissue were significantly enhanced in the LPS-induced ALI mice. The mRNA expression of T-bet and RORγt was upregulated in ALI mice at 24 hours and 48 hours relative to normal mice (P <0.05 vs. Con). There was no significant difference in the expression of GATA-3 among groups at 24 hours and 48 hours. Meanwhile, the levels of IFNγ, IL-17 and IL-6 in lung tissue were significantly enhanced at 24 hours and 48 hours in the LPS-induced ALI mice. In addition, the levels of IL-4 in lung tissue were significantly enhanced at 48 hours in the LPS-induced ALI mice. The expression of T-bet mRNA and RORγt mRNA had a strong correlation with the IL-6 concentration. However, there was no significant correlation of GATA-3 with the IL-6 concentration. In addition, there was a significant correlation of IFNγ, IL-4 and IL-17 with the IL-6 level in LPS-induced ALI at 24 hours and 48 hours.
Conclusion ALI provokes Th1 and Th17 polarization response. Th1 and Th17 may participate in the early inflammatory response to ALI.
Acknowledgements Supported by the Research Project CPSFG 2013M542578, JSPSFG 1301005A, SYS201251 and 2013NJZS50.
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P337

Comparison of CD80 level on dendritic cells in acute lung injury mice

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Introduction Dendritic cells (DC) may play an important role in acute lung injury (ALI) [1]. CD80 is the crucial co-stimulatory molecule that is expressed on the surface of DCs. However, little is known about the expression of CD80. The purpose of this study was to observe the expression of CD80 on circulating, lung and splenic dendritic cells (DC) in ALI mice.
Methods Twelve C57BL/6 mice were randomly divided into two groups: control group and ALI group. Blood, lungs and spleens were harvested at 6 hours after LPS or PBS administration. The level of CD80 on DC was assessed by flow cytometry (FCM). The IL-6 level in the lung was measured by enzyme-linked immunosorbent assay. Lung wet weight/body weight (LW/BW) was recorded to assess lung injury. Meanwhile, pathological changes were examined under an optical microscope.
Results LPS-ALI resulted in a significant increase in lung W/D ratio. Histologically, widespread alveolar wall thickening caused by edema, severe hemorrhage in the interstitium and alveolus, and marked and diffuse interstitial infiltration with inflammatory cells were observed in the ALI group. Meanwhile, the levels of IL-6 in lung tissue were significantly enhanced in the LPS-induced ALI mice. FCM analysis showed that the level of CD80 on circulating DC in control group was (3.3 ± 1.5)%, CD80 expression on lung DC was (3.6 ± 1.2)%, and expression of CD80 on splenic DC was (9.0 ± 3.6)%, which was

significantly higher than that on circulating DC and lung DC (P <0.05). In the ALI mouse, the level of CD80 on peripheral blood DC was (5.1 ± 2.1)%; the CD80 level on lung DC was (9.6 ± 2.50)%, which was significantly higher than that on peripheral blood DC (P <0.05); and the level of CD80 on splenic DC was (25.2 ± 4.7)%, which was significantly higher than CD80 levels on the peripheral blood and lung DC (P <0.05). The CD80 level on lung and splenic DC in ALI mice was significantly higher than that on lung and splenic DC in control mice (P <0.05 vs. Con).

Conclusion There is a dynamic characteristic in the expression of CD80 on DC populations in normal and ALI mice. Elevated expression of CD80 on DC seems to play an important role in the pathogenesis of ALI.

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P338

Five-year single-centre review of ARDS patients receiving high-frequency oscillatory ventilation

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Introduction Two recent RCTs (OSCAR and OSCILLATE [1,2]) showed that high-frequency oscillatory ventilation (HFOV) had no positive impact on mortality. We present our experience over 5 years.

Methods Adult ARDS patients who received HFOV from 2008 to 2012 were included. Demographics, illness severity and outcomes were collected retrospectively.

Results A total of 118 patients were included; 56.8% were male, mean age was 54.8 years. RRT use was 45% during admission. Vasoactive agent use and neuromuscular blockade infusion rate was 81.9 and 29.7% pre HFOV respectively. The 28-day and 6-month mortality was 61.9 and 70.3%. A total of 60.1% had less than 48 hours conventional ventilation (CV) pre HFOV. The 6-month mortality was 64.8% for this group. Patients who had over 48 hours CV pre HFOV had a 6-month mortality of 76.6%. See Table 1.

Conclusion Mortality rates were higher than in recent trials [1,2]. Our patients represent a more critically unwell group with lower PF ratios pre HFOV and high vasoactive and RRT use. HFOV may still have a role in the treatment of these very sick patients with treatment refractory to conventional ventilation.

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P339

Blocking angiotensin type 1 receptor modulates Th1-mediated and Th17-mediated responses in lipopolysaccharide-induced acute lung injury mice

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Introduction Losartan, an antagonist of angiotensin II (Ang II) type 1 receptor, is a potential therapeutic drug for acute lung injury (ALI). Recent reports suggest that losartan inhibits T-helper (Th)-1 immune response and ultimately attenuates inflammation in several angiotensin II-mediated inflammatory diseases [1,2]. However, the possible protective mechanisms of losartan in ALI remain poorly understood. This study was to assess the effect of losartan on the lung Th polarization response in ALI.

Methods C57BL/6 mice were randomly divided into three groups: control group, ALI group and ALI + losartan group. ALI animals received 2 mg/kg LPS; ALI + losartan animals received 2 mg/kg LPS and 15 mg/kg losartan 30 minute before intratracheal injection of LPS. The pathological changes were examined under an optical microscope. The mRNA expression levels of T-bet, GATA-3 and RORγt were determined by quantitative real-time reverse transcriptase-polymerase chain reaction.

Results The increase in LW/BW induced by LPS was partly prevented by pretreated with losartan. Histologically, losartan effectively attenuated the LPS-induced lung hemorrhage, and leukocyte cell infiltration in the interstitium and alveolus. Meanwhile, the levels of IL-6 in lung tissue were significantly enhanced in the LPS-induced ALI mice. With pretreatment of ALI mice with losartan, the level of IL-6 in lungs markedly decreased. The mRNA expression of T-bet and RORγt was upregulated in ALI mice at 24 hours and 48 hours relative to normal mice (P <0.05 vs. Con). There was no significant difference in the expression of GATA-3 among groups at 24 hours and 48 hours. Of note, pretreatment of ALI mice with losartan resulted in significantly reduced mRNA expression of T-bet at 24 hours and 48 hours and RORγt mRNA expression at 48 hours (P <0.05 vs. ALI). Meanwhile, the levels of IFNγ, IL-4, IL-17 and IL-6 in lung tissue were significantly enhanced at 24 hours and 48 hours in the LPS-induced ALI mice. In addition, both IFNγ and IL-17 in lung tissue at 24 hours and 48 hours decreased significantly in losartan-pretreated mice compared with the ALI mice. With pretreatment of ALI mice with losartan, the level of IL-4 in lungs was not changed.

Conclusion Ang II-induced Th1 and Th17 polarization response could upregulate inflammatory response and induce lung injury, and losartan may be a promising substance for clinical use in LPS-induced ALI.

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Table 1 (abstract P338).

		OSCAR		OSCILLATE	
	Hull	**HFOV**	**Control**	**HFOV**	**Control**
Mean APACHE II	22.0	21.8	21.7	29	29
Mean Vt (ml/kg predicted)	8.6	8.7	8.3	7.2	7.1
PaO_2:FiO_2 (mmHg)	81.5	113	113	121	114
Vasoactive agents (%)	81.9	43.5 (day 1)	44.6 (day 1)	67	63
Hospital mortality (%)	66.1	50.1	48.4	46.9	35.2

P340

Echocardiographic guidance for Avalon Elite dual-lumen catheter implantation

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Introduction Venovenous ECMO is a therapeutic option in patients with severe ARDS. The dual-lumen catheter (Avalon Elite; Maquet Medical) offers excellent oxygenation and decarboxylation through a single insertion site and facilitates patient mobilization as it avoids femoral access. As incorrect placement of the catheter might result in perforation and cardiac tamponade, fluoroscopy guidance is advocated in the literature. Transporting an unstable patient for fluoroscopy, however, can endanger the patient.
Methods We report a retrospective analysis of out-of-center ECMO implantation in patients with severe ARDS. Our center provides a 24/7 service for out-of-hospital ECMO implantation with a team consisting of two intensive care physicians and a perfusionist. In all patients, ECMO therapy was initiated in a non-ECMO center prior to transportation to our hospital. Implantation of a dual-lumen catheter was first choice in all patients and was guided echocardiographically.
Results Between January 2011 and November 2013, a total of 56 patients (average age 53.3 years) underwent out-of-center venovenous ECMO implantation. In 52 cases (94.6%), a dual-lumen catheter could be implanted successfully using echocardiographic guidance. Either 31 Fr (65.0%) or 27 Fr (35.0%) Avalon Elite catheters were employed. No patient developed any major or even fatal complications related to ECMO implantation. In three out of 56 patients, poor imaging quality or technical issues hampered the implantation of a dual-lumen catheter and a femoral approach had to be made. Concerning short-term survival, 81.0% of all patients could be dismissed from the ICU.
Conclusion Echocardiographic guidance for out-of-center Avalon Elite catheter implantation is a safe and efficient option when performed by an experienced team.

P341

Lower airway sampling greatly increases detection of respiratory viruses in critically ill patients: the COURSE study

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Introduction The prevalence of viral respiratory infections in critically ill patients on the ICU and the diagnostic potential of tracheal aspirate sampling are unknown. For this study, the prevalence of respiratory viruses was investigated in intubated patients by simultaneous sampling of nasopharynx and tracheal aspirate.
Methods During March and April 2013, consecutive acutely admitted, intubated patients were included in three ICUs in the Netherlands, regardless of diagnosis at admission. Daily sampling of the nasopharynx (NP) with flocked swab and tracheal aspirate (TA) was performed until successful weaning from mechanical ventilation or death. Admission samples were tested via multiplex RT-PCR for influenza A and B, parainfluenza, RSV, human metapneumovirus, bocavirus, coronavirus, rhinovirus, enterovirus, parechovirus and adenoviruses. Of the influenza-positive patients, subsequent daily samples were tested for influenza. Results of viral diagnostics performed by routine care were collected, and compared with results found in this study.
Results As part of an ongoing observational study (COURSE study), 128 patients were included, of which 35 were virus-positive (27%). Of these, 13 patients were positive in both NP and TA, eight only in NP, and 14 only in TA. Thereby, 40% of the viruses would have been missed if only NP was performed in this study group. In eight out of 12 coronavirus-positive patients, only the TA sample was virus-positive, with negative NP. In subsequent daily samples of influenza-positive patients, viral loads were higher in TA compared with NP, up to 2 log viral copies. Duration of positivity of influenza in daily samples was up to two times longer in TA samples than in NP samples. Of all 35 virus-positive patients, 10 had received viral diagnostics via routine care.
Conclusion The prevalence of respiratory viruses in this unselected patient population is high. Forty percent would have been missed if only NP was sampled. Thereby, TA sampling adds to the detection of respiratory viruses in critically ill patients. Accuracy and implications of these results needs to be investigated further.

P342

Risk factors for multi-resistant organisms in sepsis

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Introduction The increasing prevalence of infections by multi-resistant organisms (MDR) has increased over the last decades, with implications not only in the overall level of therapeutic success, but also in the selective pressure exerted by the use of broad-spectrum antibiotics to defeat increasingly resistant agents, thereby creating a vicious cycle [1,2]. The aim of this study is to describe risk factors associated with infection by MDR organisms among septic patients.
Methods A retrospective cohort study including all adult patients with microbiological documented sepsis, admitted to the emergency room of a tertiary care, university hospital between 1 July 2011 and 30 June 2012.
Results During the study period, 162 patients were admitted to the emergency room with severe sepsis; 79 (49%) had microbiological documentation, and were included in this study. The mean (SD) age was 71 (15) years; 62% were men. Forty patients (51%) had an infection by a MDR organism. Risk factors associated with infection by a MDR organism were the presence of any comorbidity (OR = 3.542, $P = 0.022$), diabetes mellitus (OR = 4.500, $P = 0.006$), Karnofsky performance status (KPS) <70% (OR = 3.882, $P = 0.005$), the presence of modifiers of etiology (OR = 5,040, $P = 0.010$), chronic wounds (OR = 5.371, $P = 0.040$), healthcare-associated infections (OR = 3.325, $P = 0.026$) and hospital-acquired infections (OR = 5.225, $P = 0.016$). The multivariate model retained as independent variables associated with infection by a MDR organism: the presence of diabetes mellitus (adjusted OR = 4.1,95% CI: 1.4 to 12.6) and the need for assistance in daily activities (KPS <70%, adjusted OR = 3.6, 95% CI: 1.3 to 9.7).
Conclusion The presence of diabetes and decreased functional capacity should be considered risk factors for infection by a MDR organism and should be taken into consideration in the empirical therapy prescription.
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P343

Infections from MDR strains (*K. pneumoniae*, *P. aeruginosa*, *A. Baumannii* complex) in a multivalent ICU

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Introduction The infection incidences from MDR strains in our ICU are in accordance with the results of respective studies in other ICUs of our country. Our aim is to identify potential risk factors for the development of MDR infection in ICU patients.
Methods The sample consisted of 882 patients, admitted to our ICU from 1 January 2010 until 30 June 2013. The factors studied were: age, gender, length of stay in the ICU, origin of patient (for example, home or transferred from another institution), APACHE II score, adjusted mortality score, previous colonization with MDR, prior use of antimicrobial agents, duration of ventilator use, immunosuppression, diabetes, hypoproteinemia and presence of central venous catheter (CVC). Bivariable analyses were conducted to determine the association

between potential risk factors and development of MDR infection. Categorical variables were compared using the Fisher test. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to evaluate the strength of any association. Continuous variables were compared using the Student *t* test or the Wilcoxon test where appropriate. Multivariable analysis was performed using multiple logistic regression. Variables with $P < 0.20$ in bivariable analyses were considered for inclusion in a multivariable model.

Results Out of 882 patients, 135 (15.3%) developed MDR infection. The following factors showed statistical significant difference ($P << 0.01$): length of stay in the ICU, origin of patient, APACHE II score, previous colonization, previous use of carbapenems, duration of mechanical ventilation, immunosuppression, diabetes mellitus, hypoproteinemia and the presence of CVC. The multivariant analysis showed statistically significant correlations for the following independent risk factors: previous use of carbapenems (OR = 632.64, $P << 0.01$), origin of patient (OR = 19.60, $P = 0.014$), presence of CVC (OR = 14.19, $P = 0.015$), previous colonization (OR = 4.71, $P = 0.037$) and duration of ventilator use (OR = 1.10, $P = 0.029$).

Conclusion The analysis showed a very strong correlation between prior use of carbapenems and development of MDR infection. Other significant factors are presence of CVC, origin of patient, previous colonization and duration of ventilator use. The identification of the above factors and the effort for their restriction redound to the reduction of the MDR infections and, consequently, to the reduction of the morbidity and the mortality of the patients hospitalized in ICUs.

P344

Clostridium difficile infection in ICU patients

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Introduction *Clostridium difficile* infection is becoming more common worldwide. Critically ill patients are at particularly high risk for this disease due to multiple risk factors in this population. Accurate diagnosis is essential for patient management, infection control and epidemiology. There are a variety of methods to detect the presence of toxigenic *C. difficile* in stools [1,2]. The aim of this study was to evaluate the incidence of *C. difficile* infection in our ICU. Laboratory results of *C. difficile* toxin detection performed by the methods available in our institution are presented.

Methods During the last year, all stool specimens received in the microbiology department from patients hospitalized in the 30-bed, multidisciplinary ICU of a tertiary-care hospital were evaluated. Specimens were ordered by physicians in the presence of clinical features compatible with *C. difficile*-associated infection. Each specimen was subjected to diagnostic tests for *C. difficile* infection including toxin enzyme immunoassays for *C. difficile* toxins A and B detection (DUO Toxin A&B; VEDA.LAB, France), and glutamate dehydrogenase (GDH) for cell wall antigen detection (C. DIFF Quik Chek Complete®; USA).

Results During the study period, 335 stool specimens were evaluated. Results obtained with the two-stage immunoassay tests are shown in Figure 1. All infected patients were treated with metronidazole or vancomycin. Following a course of therapy, 2% of the infected patients had recurrence or relapse. The crude mortality rate was 17%.

Conclusion GDH antigen was positive in 12% of the stool specimens received from ICU patients with suspected *C. difficile*-associated infections. The majority of these specimens (51.4%) produce both *C. difficile* toxins A and B, whereas toxin B is produced in 31.4% and toxin A in the remaining 17.2%.

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P345

Retrospective observational analysis of the infective risk of arterial lines in a general ICU

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Introduction This study aims to describe the infective morbidity of arterial line catheters in a general ICU.

Methods All ICU admissions for the year 2012 were listed on the WardWatcher database. All cases in which arterial line tip samples returned any growth were reviewed in conjunction with the medical, nursing and daily chart recordings. Data were collected on the organisms grown and antimicrobial sensitivities. A qualitative decision of clinical relevance was established based on necessitated change in patient management, signs of local site infection or evidence of bacteraemia with the same organism.

Results During 2012 there were 416 ICU admissions, representing a total of 2,440 ITU-days and 1,994 arterial line-days. A total of 48 arterial line tips suspected of being infected were sent for culture.

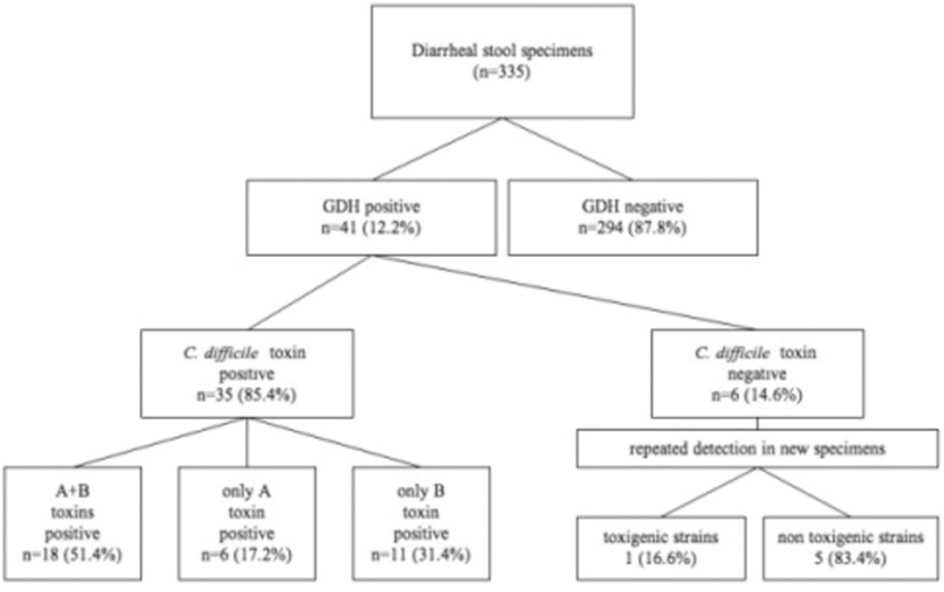

Figure 1 (abstract P344). Illustration of the tests performed for detection of *C. difficile*.

Thirty-seven arterial lines returned no growth (77.08%). Seven cultures grew organisms likely to be contaminants (14.58%). Four cultures grew significant organisms (yield of 8.33%). There were two cases with documented clinical signs of catheter-related local infection (CRLI) at the arterial line puncture site. In one case of CRLI the primary source of infection was felt to be remote from the arterial line. The second represented a local infection with organisms that are typically skin commensals. Of the four cultures likely to represent invasive pathogens, three had clinical suspicion that the primary source was a site remote from the arterial line. In two of these cases this was confirmed by growing the same organism at an alternative site more likely to be the source of infection.

Conclusion These results suggest that CRLI rates for arterial lines are low at 1.003 per 1,000 arterial line-days. However, there is a significant bacterial colonisation rate of the arterial lines sampled. Three arterial lines (6.25%) grew organisms that could represent an important potential source of ongoing bacteraemia. There is evidence to suggest that the risk of infection and colonisation of arterial lines may be similar to that of central lines [1]. Further prospective work is needed to assess the impact of catheter care bundles on colonisation and infection rates of arterial lines in the ICU.

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P346

Reducing CR-BSI in a general ICU

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Introduction Central venous catheters (CVCs) are essential for the delivery of medications and fluids in the ICU patient; however, they carry a substantial infection risk. Evidence from a collaborative, cohort study suggests bundled interventions can provide a sustained decrease in infection [1].

Methods Since December 2009, data have been collected daily on the number of patients with one or more CVC. All positive blood cultures are reviewed monthly against predefined criteria to judge whether these are genuine bacteraemic episodes and thus classified as laboratory-confirmed bloodstream infections. A monthly rate for CR-BSI per 1,000 dwell-days is calculated from these data. Since July 2010, a number of interventions aimed at reducing CR-BSI have been introduced to the ICU.

Results Data are presented on 15,644 CVC dwell-days over 47 months. Table 1 presents data for three full years and one part year* (January to November 2013). Despite an increase in bed-days per year, there has been a sustained reduction in infection rates and a reduction in dwell-days.

Table 1 (abstract P346). Catheter infection rates, APACHE score and bed-days 2010 to 2014

Year	Total CVC dwell-days	CR-BSI annually	CR-BSI/ 1,000 dwell-days	APACHE II (mean)	Bed-days	Dwell-days/ bed-days
2010	4,037	6	1.5	15.8	5,870	0.69
2011	3,942	2	0.5	16.3	5,967	0.66
2012	3,822	3	0.8	15.9	6,117	0.62
2013*	3,863	1	0.3	16.0	6,059	0.64

Conclusion CR-BSI rates of 1.5/1,000 dwell-days in the first year were similar to the post-intervention rate of 1.4 in the Pronovost study [1]. Subsequent rates have reduced, suggesting we are outperforming the secular trend [2]. The proportion of dwell-days to bed-days was reduced, which may suggest a reduction in duration and/or quantity of CVC placements.

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P347

Risk factors of candidemia in postoperative ICU patients: a prospective study

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Introduction The prediction for and the mortality of patients with candidemia are highly adverse. The aim of this study was to identify the risk factors for the development of candidemia in postoperative patients.

Methods From 1 July 2010 to 30 June 2013 all postoperative patients (n = 588) admitted to the multivalent ICU of our hospital were enrolled in this study. We recorded the age, sex, length of stay in the ICU, APACHE II score upon admission to the ICU, adjusted mortality score, underlying conditions, recent operations, invasive therapeutic procedures and prior usage of antimicrobial agents. Initial bivariable statistical comparisons were conducted using the χ^2 test for categorical data and the Student t test or Wilcoxon test for continuous data. Relative risks (RRs) and their 95% confidence intervals (CIs) were calculated. Statistical significance was set at P <0.05. To identify patient characteristics associated with candidemia we used multivariable logistic regression. In the multivariant analysis we also included the independent risk factors reported in recent medical literature. Results of the logistic regression analysis are reported as adjusted odds ratio (OR) with 95% CI.

Results Out of 588 patients, 30 (5.1%) developed candidemia (frequency: 12 per 1,000 days of hospitalization). The mortality of patients with candidemia was 66.7% (20/30). The monovariant analysis showed statistical significant difference in the following factors: immunosuppression (P = 0.0005), diabetes mellitus (P = 0.0005), hypoproteinemia (P = 0.0005), the presence of central venous catheter (P = 0.0005), the coexistence of bacteremia and the prior use of antimicrobial agents (P = 0.0005), length of stay in the ICU >5 days (P = 0.004) and the type of intervention (P = 0.001). As independent risk factors from the multivariant analysis were found the following: immunosuppression (exp(B) = 218.37, 95% CI = 11.76 to 4,053.72, P = 0.0005), hypoproteinemia (exp(B) = 25.69, 95% CI = 2.82 to 296.8, P = 0.009), presence of central venous catheter (exp(B) = 13.79, 95% CI = 1.86 to 102.51, P = 0.01) and the coexistence of bacteremia in combination with prior use of antimicrobial agents (exp(B) = 404.94, 95% CI = 11.61 to 14190.41, P = 0.001).

Conclusion Early candidemia identification, prompt collaboration of intensivists with biopathologists and immediate initiation of the proper antifungal treatment is of great significance. The concurrent understanding of the predisposing risk factors constitutes a significant supportive tool for the prediction of such infections.

P348

Escherichia coli infection in Polish neonatology ICUs in 2009 to 2012

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Introduction The aim of our study was the analysis of the epidemiology of infections caused by ECO in Polish NICUs and their resistance to antibiotics, with particular reference to their impact on the safety of infants with very low birth weight, and their relationship to the care of women who are pregnant and in labour. The routes of transmission of ECO strains were also evaluated.

Methods Continuous prospective infection surveillance was conducted in 2009 to 2012 in five NICUs and included 1,768 newborns whose birth weight was lower than 1,500 g.

Results The incidence of ECO infections was 5.4% and 2.0/1,000 patient-days. The occurrence of ECO infections depended significantly on the NICU and ranged from 3.9 to 17.9%. Multivariate analysis that took into account the combined effect of demographic data (gender, gestational

age and birth weight) and place of birth (NICUs, where the baby was born) showed that only the place of hospitalisation had a significant effect on the ECO infection risk. The highest levels of resistance among all ECO isolates were observed against ampicillin (88.8%) and amoxicillin/clavulanic acid (62.2%). ECO isolates showed very different pulsotypes and dominant epidemic clones were not detected. Cluster analysis based on PFGE of the 90 isolates showed 71 unique types, some of which were less than 70% similar, suggesting a genotypically variable population. Isolates that have identical pulsotypes usually were derived from the same patient (as in the case of 11 isolates) or were isolated from different patients of the same NICU in the same period of time (in the case of seven isolates). The location of the NICU and the site of the isolation did not appear to have a correlation in the cluster analysis

Conclusion Unfortunately, the presented data indicate that antibiotic prophylaxis in the presence of symptoms such as chorioamnionitis and PROM did not help to reduce the risk of ECO infection in the group of examined infants. In addition, multivariate analysis demonstrated only one significant risk factor for ECO infection among infants with a birth weight <1,500 g; that is, the impact of the NICU. Epidemiology of ECO infections clearly indicated that observed cases of infections have no connection with the horizontal transmission (thus no proof of a link between the observed ECO infections with possible negligence in hand hygiene or excessive congestion on NICUs). This is confirmed by the fact that no epidemic clones were observed (DEC-2011/01/D/N27/00104).

P349

Infection control as a nonpharmacologic strategy for the prevention of healthcare-associated infections in a Ukrainian hospital

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Introduction Healthcare-associated infections (HAI) in ICU patients are related to intubation, mechanical ventilation, and central venous and/or urinary catheters. The incidence of HAI is too high, and antibiotic strategies suffer from resistance to the common classes of antibacterial agents [1].

Methods A complex program including staff teaching on the basic approaches of hand hygiene, microbiological passport of the ICU departments, and detection of the sources of the pathogens polluting the treatment area of the ICU was implemented at the Lugansk Regional Clinical Hospital. The incidence of the HAI was studied in polytrauma patients in 1999 to 2003 (before the implementation of the program) and in 2008 to 2012 (after its implementation).

Results Before the implementation of the infection control program, the incidence of respiratory tract infections in polytrauma patients staying in ICUs was 57.4% of patients. Urinary infections occurred in 51.9% of patients. Surgical site infections were found in 32.8% of the patients. Combination of the infections was detected in 33.8% of patients. The incidence of the multiple-drug-resistant bacterial colonies was 5.8%.

In contrast, recent data obtained after the implementation of the program of the infection control showed that the respiratory infections occurred in 29.3% of the patients, catheter-related urinary tract infections were detected in 32.8%, and surgical site infections were detected in 8.6% of the polytrauma patients. On the other hand, the incidence of the multiple-drug-resistant bacterial colonies increased significantly up to 14.2% (P <0.001). Other types of HAI changed nonsignificantly.

Conclusion In the era of the total antibacterial resistance, the education strategies and organization approaches (for example, infection control, antibiotic susceptibility, hand hygiene, and so forth) become more potent and effective than pharmacology innovations. Polytrauma patients, as one of the most severe categories suffering from the HAI, demand a high level of compliance of the infection control approaches from the side of doctors as well as staff of and visitors to ICUs.

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P350

Surveillance for nosocomial pathogens in our ICU

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Introduction The use of contact precautions is recommended to reduce the transmission of these pathogens. However, there is little research regarding the relationship between the rate of patients with culture-positive findings for *Acinetobacter baumannii* and the consumption of hand disinfectant. The objective of this study was therefore to evaluate trends in nosocomial bacterial detection, including *A. baumannii*, and the use of hand disinfectant in our ICU.

Methods A single-center, retrospective, observational study was carried out. The results of all cultures (sputum, urine, blood, and so forth) were used to examine trends in the detection of microbiology in our ICU over a 4-year period from April 2009 through March 2013. The rate of culture-positive patients, frequency of use of hand disinfectant and the antimicrobial use density (AUD) values were investigated for the described periods and compared between the early period group (April 2009 to March 2011) and the late period group (April 2011 to March 2013).

Results We encountered 3,302 patients in our ICU during this period. No patients with culture-positive findings for multidrug-resistant *A. baumannii* were identified in this study. The rates of patients with culture-positive findings for multidrug-resistant *Pseudomonas aeruginosa* (0‰ vs. 0.05‰ per 1,000 patient-days, P = 0.99) and *P. aeruginosa* (6.96‰ vs. 7.21‰ per 1,000 patient-days, P = 0.7) were not significantly different between the early period group and the late period group. The rates of patients with culture-positive findings for MRSA (6.96‰ vs. 8.94‰ per 1,000 patient-days, P <0.05) and *A. baumannii* (4.98‰ vs. 6.51‰ per 1,000 patient-days, P <0.05) were significantly higher in the late period group than in the early period group. The frequency of use of hand disinfectant (99.5 ml/patient-day vs. 85 ml/patient-day, P <0.05) was significantly lower in the late period group. The AUD values for fluoroquinolones (34 vs. 31.1 defined daily doses/1,000 bed-days, P = 0.69), third-generation cephalosporins (23.5 vs. 38.4 defined daily doses/1,000 bed-days, P = 0.55) and glycopeptides (34.9 vs. 35.9 defined daily doses/1,000 bed-days, P = 0.66) were not significantly different between the early period group and the late period group. However, the AUD values for carbapenems were significantly higher in the early period group (40.6 vs. 71.8 defined daily doses/1,000 bed-days, P < 0.05).

Conclusion Improving compliance with hand hygiene and appropriate use of carbapenems is important for decreasing the rate of patients with culture-positive findings for MRSA and *A. baumannii*.

P351

Comparison of multidrug-resistant Acinetobacter and non-Acinetobacter infections in terms of outcome in critically ill patients

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Introduction Acinetobacter infections have increased and gained attention because of the organism's prolonged environmental survival and propensity to develop antimicrobial drug resistance [1,2]. We performed a retrospective, matched cohort investigation at a tertiary care hospital in a tier II city hospital of India to examine morbidity and mortality outcome of patients with multidrug-resistant (MDR) Acinetobacter (AB) infection compared with patients with MDR non-Acinetobacter (non-AB) infections.

Methods Patient records from the last 3 years from 2011 through 2013 were studied (n = 104) to examine outcomes of hospitalized patients in terms of number of organ dysfunctions, ICU length of stay, hospital length of stay and mortality in patients infected with MDR AB infection compared with the patients with MDR non-AB infection.

Table 1 (abstract P351).

Outcome evaluated	MDR AB	MDR non-AB	*P* value	*F* value
Mean length of stay after index day	8.488889	6.101695	0.029299	4.886684
Mean ICU stay after index day	5.311111	0.864407	1.73×10^{-11}	57.30083

Results MDR AB-infected patients (*n* = 45, 43%) had greater number of organ dysfunctions, and higher mean lengths of hospital stay (8.4 days vs. 6.1 days) and ICU stay (5.3 days vs. 0.8 days) after the index day than MDR non-AB infection (*n* = 59, 57%) (Table 1). In-hospital mortality rates for patients with MDR AB infections (42%) were higher than for MDR non-AB infection (10%). *F* critical = 3.934253.
Conclusion We demonstrated in patients infected with MDR strains of any organism that patients infected with Acinetobacter have greater number of organ dysfunction, longer lengths of stay in both the hospital and the ICU as well as increased mortality than patients infected with non-Acinetobacter infection when we controlled for severity of illness.
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P352

Candida in the respiratory tract secretions of critically ill patients and the impact of antifungal treatment: a randomized placebo-controlled pilot trial (CANTREAT study)

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Introduction Candida spp. are frequently recovered from endotracheal secretions in critically ill patients suspected of having ventilator-associated pneumonia. Observational studies reported an association with worse clinical outcomes [1] but the effect of antifungal therapy in these patients remains unclear. We designed this pilot study to assess the feasibility of a larger trial and to evaluate inflammatory profiles and clinical outcomes in these patients.
Methods We conducted a double-blind, placebo-controlled, multi-center, pilot randomized trial of antifungal therapy in critically ill patients with a clinical suspicion of ventilator-associated pneumonia with positive airway secretion specimens for Candida spp. We also included an observational group without Candida spp. in their airway secretions. We measured the recruitment rate, inflammatory profiles over time and clinical outcomes.
Results We recruited 60 patients into the randomized trial; 29 patients into the observational study. Recruitment was halted before the end of the study because of difficulty in recruiting patients. Markers of inflammation and all clinical outcomes were comparable between placebo and antifungal treatment groups at baseline and overtime. At baseline, TNFα levels were higher in the VAP with Candida compared with the observational group (mean ± SD) (21.8 ± 23.1 vs. 12.4 ± 9.3 pg/ml, *P* = 0.02) and these patients had lower response to the LPS stimulation test (854.8 ± 855.2 vs. 1,559.4 ± 1,290.6 pg/ml, *P* = 0.01).
Conclusion Given the difficulty recruiting patients and the lack of signal in clinical or inflammatory outcomes, this study does not provide evidence to support a larger trial examining the efficacy of empiric antifungal treatment in patients with a clinical suspicion of ventilator-associated pneumonia and Candida in the endotracheal secretions. The presence of Candida in the lung may be associated with persistent inflammation and immunosuppression.
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P353

Retrospective analysis of respiratory isolates post out-of-hospital cardiac arrest to establish choices in empirical antibiotic cover

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Introduction We analysed positive respiratory isolates for antibiotic resistance in our out-of-hospital cardiac arrest (OOHCA) population to establish adequacy of current empirical regimes. Pneumonia commonly complicates OOHCA, with studies suggesting a prevalence up to 48% [1].
Methods Patients admitted to the ICU between May 2007 and September 2013 who underwent therapeutic hypothermia post OOHCA were included in this study. Demographics and antibiotic resistance were collected from an electronic database.
Results A total of 160 patients were admitted to the ICU post OOHCA. In total, 37.5% (60/160) had no respiratory sample sent within 72 hours of admission and were excluded. Forty per cent (40/100) grew a clinically important isolate. Gram-negative bacteria (GNB) were most frequently isolated (42.5%, 17/40) followed by Gram-positive bacteria (32.5%, 13/40) and mixed bacterial growth (25%, 10/40). *S. aureus* (*n* = 14) isolates were often resistant to penicillin (92.8%, 13/14 isolates tested) but maintained macrolide (erythromycin 92.8%, 13/14), clindamycin (92.8%, 13/14) and vancomycin (100%, 13/13) sensitivity, if tested. *S. pneumoniae* isolates (*n* = 8) maintained penicillin (87.5%, 7/8), levofloxacin (100%, 6/6), erythromycin (87.5%, 7/8) and vancomycin (100%, 6/6) sensitivity. The most commonly isolated GNB, *H. influenzae*, maintained high-level sensitivity to amoxicillin (81.8%, 9/11) and co-amoxiclav (90.9%, 10/11). Other isolated GNB, however, demonstrated variable resistance to co-amoxiclav (69.2%, 9/13). Isolates were 100% sensitive to pipericillin–tazobactam (17/17), amikacin (12/12) and meropenem (16/16). The British Thoracic Society suggests co-amoxiclav and clarithromycin for first-line treatment of severe community-acquired pneumonia [2]. Based on this, 77.5% (31/40) of our patients would have received adequate cover. If pipericillin–tazobactam replaced co-amoxiclav, 95% (38/40) of our patients would have been treated with appropriate antibiotics.
Conclusion Respiratory samples post OOHCA frequently grow potentially pathogenic bacteria but current antibiotic guidelines fail to provide adequate cover in this population.
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P354

Pharmacokinetics of antituberculosis drugs in critically ill patients with tuberculosis and acute respiratory failure

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Introduction The purpose of this study was to describe the pharmacokinetics of antituberculosis drugs, isoniazid (INH), rifampicin (RIF) and pyrazinamide (PZA), in eight critically ill patients with tuberculosis and acute respiratory failure.
Methods We analyzed plasma concentrations of RIF, INH and PZA. Blood samples were obtained at steady state. Plasma concentrations were determined with HPLC. A population pharmacokinetic approach using a nonlinear mixed-effect model was implemented [1]. Interindividual variability in PK parameters was ascribed to an exponential model according to the equation: $\theta j = \theta p \times \exp(nj)$, where θj is the estimate for a pharmacokinetic parameter in the jth patient, θp is the typical population PK parameter value (ka, CL/F, V/F), and *n* is a random variable from a normal distribution with zero mean and variance ω^2. Residual variability was estimated using additive and additive-proportional error models; $Cij = Cj + \varepsilon add$ and $Cij = Cj(1 + \varepsilon p) + \varepsilon add$, where Cij and Cj are observed–predicted concentrations for the

Table 1 (abstract P354). Mean population parameters of antituberculosis drugs

Parameter	RIF	INH	PZA
ka	0.459	3.58	1.41
CL/F	6.69	2.74	1.56
V/F	105	42.3	33.4
ωka	0.645	38.7	0.98
ωCL/F	0.391	65.6	0.23
ωV/F	0.469	46.8	0.38
ε	0.441	0.235	0.089

jth patient at time i, respectively, and ε is the error, a random variable with a normal distribution with zero mean and variance σ^2. Bayesian estimates were obtained and the pharmacokinetic parameters Cmax, Tmax and AUC0–24 hours were calculated.

Results Cmax of PZA was above the recommended concentration (>20 mg/l). For RIF the Cmax was below the recommended level (>8 mg/l), and the Cmax of INH was below the recommended levels (>3 mg/l). See Table 1.

Conclusion Large interindividual pharmacokinetic variability and concentrations below the recommended levels for RIF and ISO. We need to monitor drugs and to re-evaluate the doses.

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P355

Eight-year study of the *Staphylococcus epidermidis* resistance profile against glycopeptides, oxazolidinones and glycylcyclines in an ICU of a Greek tertiary hospital

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Introduction *Staphylococcus epidermidis* (SE) is the most often isolated species of coagulase-negative staphylococci, which are recognized as one of the main causes of ICU infections [1]. In this study we aimed to study the resistance profile of SE clinical isolates against last-line antibiotics (vancomycin (VA), teicoplanin (TEC), linezolid (LZ) and daptomycin (DA)) for treating CNS infections, during an 8-year period.

Methods From January 2005 until December 2012 we examined 518 nonduplicated SE isolates recovered from blood cultures of 421 patients hospitalized in a surgical ICU of our hospital. Species identification and susceptibility testing were performed using the automated VITEK II system (Biomerieux). Additionally we used the E-test method (Biomerieux, ABI-Biodisk) in order to confirm some isolation resistances against TEC and LZ found by the VITEK II system and to estimate the MIC levels of DA and VA. Mueller–Hinton agar adjusted to contain physiologic levels of free calcium ions (50 μg/ml) was used when testing DA susceptibility. Isolates with MIC >4 mg/l were considered resistant to TEC and LZ and those with MIC <1 mg/l and MIC <4 mg/l susceptible to DA and VA, respectively.

Results The percentage resistance rate of the examined SE isolates is shown in Table 1. Methicillin resistance was observed with an overall prevalence of approximately 84.6%. All of the resistant isolates to TEC and LZ were also resistant to methicillin. The MIC values of VA were lower than 2 mg/l (Table 1).

Conclusion The examined SE isolates present a scattered resistance to TEC and they show a remarkable continuing increase of resistance to LZ. These findings enforced the necessity to take the appropriate measures in the ICU environment and during the clinical practice to limit the dissemination and the amplification of these resistances. DA and VA possess an excellent *in vitro* activity against SE isolates and they could be very good alternative solutions for treating ICU infections caused by this species.

Table 1 (abstract P355).

	2005 (*n* = 77)	2006 (*n* = 76)	2007 (*n* = 79)	2008 (*n* = 89)	2009 (*n* = 92)	2010 (*n* = 93)	2011 (*n* = 46)	2012 (*n* = 59)
VA	0	0	0	0	0	0	0	0
TEC	1.3	2.6	0	0	0	1.1	0	0
LZ	0	0	1.4	1.2	6.8	12.6	23.1	27.1
DA	Not tested	Not tested	Not tested	0	0	0	0	0

Reference

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P356

Vancomycin-resistant enterococci: eradication using vancomycin?

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Introduction Patient-to-patient transmission enables vancomycin-resistant enterococci (VRE) outbreaks. Outbreak management is expensive and time consuming, and therefore the possibility of VRE eradication is desirable. Since vancomycin is scarcely absorbed in the gastrointestinal tract, treatment with vancomycin *per os* may result in very high gastrointestinal concentrations (many times the minimum inhibiting concentration (MIC)). The purpose of this study is to measure *in vivo* gastrointestinal concentrations of vancomycin in patients that are treated with a standard dose orally, and to investigate *in vitro* whether vancomycin is able to kill VRE at concentrations up to 2,000 times the MIC.

Methods The faecal vancomycin concentration was measured in eight patients who suffered a *Clostridium difficile* infection and were treated with 4×500 mg vancomycin orally per day. *In vitro*, a (1:2) dilution series of vancomycin (range 6,250 to 0.4 μg/ml) was created and 1 ml vancomycin solution was then added to 1 ml standardized inoculum. One vancomycin-susceptible enterococcus isolate (VSE, MIC = 3 μg/ml) and two VRE isolates (MIC = 16 μg/ml) were studied. After 1, 7 and 14 days incubation at 35°C, growth was defined as macroscopic visible turbidity. To test for surviving bacteria, all inocula were cultured to sheep blood agar plates, which were read after 24-hour incubation at 35°C. E-tests to measure MIC were performed on relevant samples. The *in vitro* experiment was performed twice.

Results The faecal vancomycin concentration in patients treated orally with vancomycin was 8,000 μg/ml on average. VSE growth at day 14 was detected at up to 1.5 μg/ml vancomycin, whereas VRE growth was detected at up to 98 μg/ml. The MIC of these VRE species growing at 98 μg/ml vancomycin was increased (≥256 μg/ml). For both VSE and VRE, surviving bacteria were detected at very high concentrations of vancomycin (>98 μg/ml): the MIC of these survivors was not increased.

Conclusion Oral treatment with vancomycin results in extremely high faecal concentrations. At these high concentrations, VRE bacteria are killed *in vitro*; however, a minority of the VRE is able to survive. Vancomycin thus seems unsuitable for eradication. However, high concentrations of vancomycin dramatically reduce the bacterial VRE load. Therefore oral treatment with vancomycin may help to terminate VRE outbreaks: a dramatic reduction in bacterial load of the colonised patient will minimise the risk of patient-to-patient transmission.

P357

Audit of bacteraemia management in a university hospital ICU

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Introduction The optimal duration of antibiotic treatment in critically ill patients remains a subject of debate. In our multidisciplinary ICU, a short course of antibiotic monotherapy (5 to 7 days) is generally used as

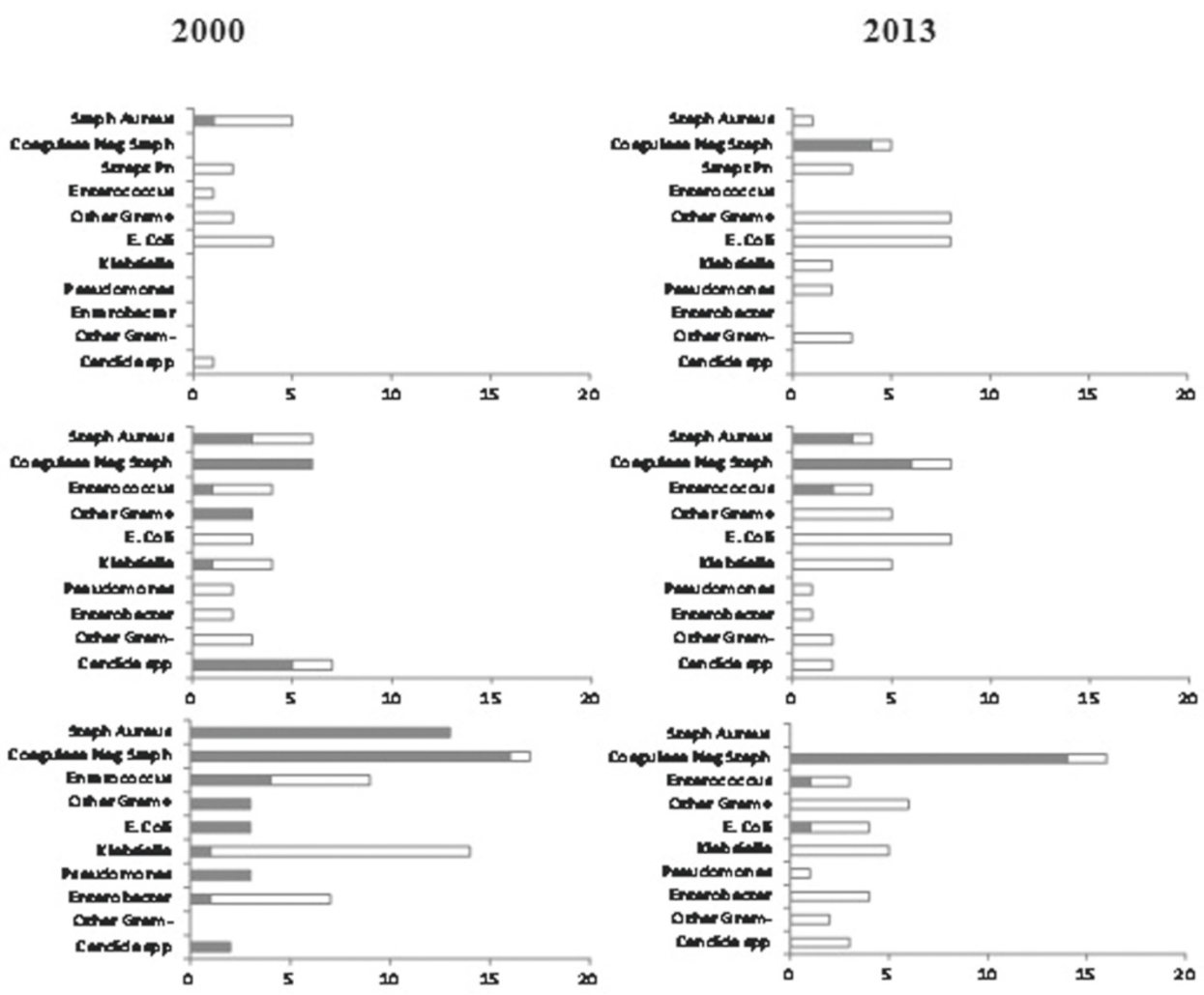

Figure 1 (abstract P357). Microorganisms isolated in each bacteraemia group. Left panel, 2000; right panel, 2013. Top panel, community-acquired bacteraemia; Middle panel, hospital-acquired bacteraemia; lower panel, ICU-acquired bacteraemia. Shaded areas represent numbers of methicillin-resistant strains for *S. aureus* and coagulase-negative staphylococci; vancomycin-resistant strains for Enterococcus spp.; multidrug-resistant strains for Gram-negative pathogens; and fluconazole-resistant strains for Candida spp.

a strategy to treat bacteraemia, unless specifically indicated otherwise (for example, endocarditis, osteomyelitis). We aimed to determine the impact of this strategy on antibiotic resistance patterns and patient outcomes compared with a similar exercise we conducted in 2000 [1].

Methods We conducted a retrospective study of all patients with bacteraemia or fungaemia (community-acquired, hospital-acquired, and ICU-acquired) treated in our university hospital ICU over a 6-month period (December 2012 to May 2013). We compared this against data from blood culture-positive patients admitted between February and July 2000. Information was collected on bacteraemia episodes, causative pathogens, antimicrobial resistance patterns, antibiotic use and duration, and patient outcomes. Notably, our ICU admits many immunosuppressed patients (for example, haemoncology).

Results Table 1 presents demographics and incidence of bacteraemia. Antimicrobial resistance remained low in the 2013 cohort with few multi-resistant Gram-negative organisms, few fungaemia episodes and a marked decrease in methicillin-resistant *Staphylococcus aureus* (MRSA) (Figure 1). The number of relapses and breakthrough bacteraemias remained low.

Conclusion A strategy of short-course antibiotic monotherapy is associated with low breakthrough and relapse rates and a low rate of antibiotic resistance.

Table 1 (abstract P357). Demographics and incidence of bacteraemia

Variable	2000 cohort	2013 cohort
Total ICU population	713	1,318
Patients with bacteraemia	91	87
Episodes of bacteraemia	102	113
Community-acquired bacteraemia	13	37
Hospital-acquired bacteraemia	28	39
ICU-acquired bacteraemia	60	37
Hospital mortality	45%	32%
Monotherapy treatment (%); duration median (IQR)		
Community-acquired bacteraemia	57%; 6 (5 to 6)	65% 5 (3 to 5)
Hospital-acquired bacteraemia	78%; 6 (5 to 8)	63%; 5 (4 to 7)
ICU-acquired bacteraemia	80%; 5 (5 to 7)	62%; 4 (3 to 6)

Reference

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P358

Sepsis: impact of timely and appropriate empirical antibiotic therapy on mortality

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Introduction The administration of timely and appropriate antibiotic therapy is a well-known prognostic factor among severe sepsis patients [1-4]. The purpose of this study is to describe the magnitude of the impact of early and appropriate empirical antibiotic therapy on hospital mortality.
Methods A retrospective cohort study including all adult patients with sepsis admitted to the emergency room of a tertiary care, university hospital between 1 July 2011 and 30 June 2012.
Results A total of 1,219 patients were admitted to the emergency room during the study period, of which 162 (13%) had severe sepsis. Forty (25%) patients had withheld therapeutic decisions and were excluded from the current analysis; 20 additional patients transferred from other acute healthcare facilities were excluded due to missing or inaccurate data, leaving 102 patients to be included with a hospital mortality rate of 45%. The median time to antibiotics administration was 36 minutes (IQR 0 to 174), 59 (58%) patients had antibiotic administered within the first hour after sepsis recognition; 60 (59%) had positive microbiology, 74% with appropriate empiric antibiotic therapy. An association was found for hospital mortality with: heart failure (OR = 4.297; $P = 0.037$), decreased functional status (Karnofsky performance status <70%) (OR = 2.368; $P = 0.034$) and SOFA score (OR per point = 1.415; $P < 0.001$). Two multivariate models with hospital mortality as the dependent variable were built using alternative severity scores: one with SAPS II that was retained in the final model (adjusted OR = 1.068, 95% CI = 1.020 to 1.119) along with heart failure (adjusted OR = 5.859, 95% CI = 0.996 to 34.474); and another with SOFA score that was also retained in the final model (adjusted OR = 1.659, 95% CI = 1.227 to 2.242) along with heart failure (adjusted OR = 12.636, 95% CI = 1.423 to 112.229).
Conclusion Contrarily to what has been described previously, early and appropriate empirical antibiotic therapy was not associated with better prognosis. The most probable explanation is the higher compliance found with the current recommendations, reinforcing the need for period audits and feedback to the team.
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P359

Safety and efficacy of amphotericin B inhalation for Candida spp. in the respiratory tract of critically ill patients

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Introduction Candida spp. are increasingly isolated in the critically ill, but the clinical significance hereof is hard to establish [1]. Candida spp. colonization has been suggested as a risk factor for ventilator-associated pneumonia (VAP) [2]. The efficacy and safety of inhalational amphotericin B (AB) is unknown [3]. The hypothesis was that inhalational AB deoxycholate is a safe and effective treatment for Candida spp. colonization of the respiratory tract and thereby prevents VAP and prolonged need for mechanical ventilation.
Methods All patients admitted to the ICU from December 2010 to 2011 with positive Candida spp. cultures of the respiratory tract and requiring mechanical ventilation >48 hours were included. AB treatment was decided by attending intensivists. The colonization index was calculated to determine the effect of AB. The clinical pulmonary infection score (CPIS) and the lung injury score (LIS) were calculated to determine pulmonary effects of AB.
Results Fifty-five of 181 patients had been treated with AB. The AB decreased indicators of Candida spp. load but increased the duration of mechanical ventilation as compared with nontreated patients, associated with a higher CPIS and LIS, even in those with similar degree and duration of colonization and thus probably Candida spp. load at baseline ($P < 0.001$) (Figure 1). There was no difference in occurrence of VAP or mortality.
Conclusion AB deoxycholate treatment is effective for the treatment of Candida spp. colonization of the respiratory tract in critically ill patients. However, patients are mechanically ventilated for longer.
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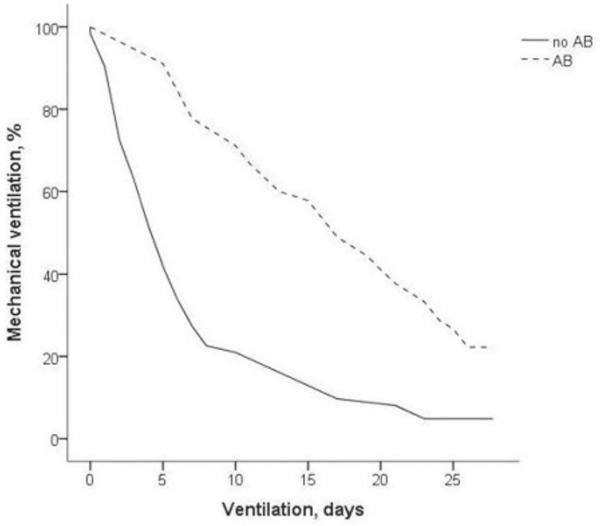

Figure 1 (abstract P359). Duration of mechanical ventilation grouped by amphotericin B.

P360

Inhaled tobramycin for the treatment of nosocomial pneumonia in sepsis

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Introduction Nosocomial pneumonia (NP) is frequently caused by multiresistant Gram-negative bacteria. The inhaled antibiotics provide us with a new treatment modality for NP in sepsis. The aim of this study was to estimate the efficacy of inhaled tobramycin (IT) as an adjunct to systemic antibiotics in the treatment of NP in sepsis.
Methods Fifty ICU ventilated septic patients with NP were enrolled in the study (all male, 55.3 ± 7.3 years old; primary reason for ICU stay – intraabdominal infections (78%), mediastinitis (13%), other (9%)). Diagnosis of NP was made according to the standard clinical and CPIS criteria. Associations of multiresistant Gram-negative bacteria were detected in bronchoalveolar lavage (BAL) of all patients. Seventy-two percent of bacteria were sensitive to tobramycin. Patients were randomized into two groups: IT (group 1, $n = 25$), addition of IT to systemic antibiotics (carbapenems, aminoglycosides, protected penicillins); and no IT (group 2, $n = 25$), shift of systemic antibiotics according to sensitivity. Groups were comparable in APACHE II and CPIS scores. IT (Bramitob) was administered 300 mg twice daily via nebulizer. The data were statistically analyzed by STATISTICA 7.0 (M, σ, Newman–Keuls test; $P < 0.05$).
Results Administration of IT as an adjunct to systemic antibiotics was associated with a decrease of systemic inflammation and acute respiratory insufficiency signs 2.3 ± 1.2 days after the treatment onset (vs. 6.3 ± 1.5 days in group 2, $P = 0.03$). The decrease of microbial titer to 10^3 to 10^4 CFU/ml was detected in both groups by days 5 to 7, but it

was reliable in 80% of the patients of group 1 (P <0.02). It is noteworthy that 21% of group 1 patients were *in vitro* resistant to tobramycin, but it was clinically effective, probably due to a local superconcentration. Treatment with IT was associated with an increase of sensitivity of microbes to antibiotics they were prior resistant to (32% of patients). This is probably due to IT effects on biolayers. De-escalation of antibiotic therapy was possible in group 1 by day 5 in 42% of patients. The treatment with IT made it possible to wean 40% of patients by day 5.3 ± 1.8 after treatment cessation (vs. 35% and 11.2 ± 1.3 days in group 2, P = 0.02). Hearing loss and tinnitus was detected only in three patients of group 1. There were no cases of bronchospasm. The mortality was 12% (n = 3) in group 1 and 16% (n = 4) in group 2 (P >0.05), and was not related to a progression of NP [1].

Conclusion Administration of IT as an adjunct to systemic antibiotics is efficient in treatment of NP caused by multiresistant Gram-negative bacteria in sepsis.

Reference

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P361

Sternal wound infections in cardiac surgery: effects of vancomycin prophylaxis

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Introduction Appropriate antibiotic prophylaxis plays a crucial role in preventing sternal wound infection after cardiac surgery [1]. In institutions with high prevalence of methicillin-resistant *Staphylococci* species, vancomycin prophylaxis is recommended either as a monotherapy or as an adjuvant agent [2]. In our study, we assessed sternal wound infection rates before and after the introduction of a vancomycin prophylaxis protocol.

Methods Twenty-six of a total 227 consecutive cardiac surgical patients, between July and December 2012, developed sternal wound infection (Group A). All of the patients received a standard empirical antibiotic prophylaxis. From January to July 2013, 308 patients underwent cardiac surgery (Group B). In this group, we applied a more restricted antibiotic protocol, considering the resistance patterns and the results of microbiological tests of group A. We also evaluated the results of MIC susceptibility testing of five antibiotics: oxacillin, linezolide, daptomycin, teicoplanin and vancomycin. In the new protocol the first vancomycin dose was given 1 hour before sternal incision followed by three additional doses (48 hours duration).

Results In group A, 26 patients (11.45%) developed sternal wound infection. Twenty out of 26 patients had staphylococcal infections characterized by high prevalence of oxacillin resistance while six patients had Gram-negative infections. In the vancomycin prophylaxis group (group B) we observed a significant reduction in the incidence of sternal wound infection rate (P <0.01). Among 308 patients, six patients (1.94%) developed sternal wound infections, two of them caused by coagulase-negative oxacillin-resistant staphylococci while in four patients Gram-negative microorganisms were cultured. Mortality in infected patients was 0% in both groups.

Conclusion Appropriate antibiotic prophylaxis in cardiac surgery patients is of paramount importance in preventing sternal wound infections, resulting in dramatic reduction of postoperative morbidity and in significant economic benefits.

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P362

Retrospective analysis of the clinical utility of blood cultures taken surrounding intensive care admission

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Critical Care 2014, **18(Suppl 1):**P362 (doi: 10.1186/cc13552)

Introduction This study aimed to establish clinical utility of blood cultures taken surrounding ICU admission. Blood culture cost in terms of resources and false results is well established and unnecessary cultures can cause patient harm.

Methods All ICU admissions in 2011 were listed retrospectively. Notes were reviewed for those with blood cultures taken during, or within 24 hours prior to or following, ICU admission. Data collected for positive blood cultures included organism, antimicrobial sensitivity, culture timing with respect to ICU admission and antibiotic therapy before and after positive blood culture. Qualitative decisions were made regarding clinical utility of each positive blood culture. Results were deemed useful if management changed – starting, changing or stopping antibiotics or altering antibiotic duration. Confirmatory results or those not altering treatment were not deemed useful. Statistical analysis was performed using the chi-squared test.

Results During 2011 and 2012, there were 450 ICU admissions. In total, 698 blood cultures were taken during, or within 24 hours prior to or following, ICU admission. A total of 135 blood cultures were taken in the 24 hours prior to ICU admission. Of these, 26 grew significant organisms (19.3%). Nine of these cultures were deemed clinically useful (6.7%). A total of 542 blood cultures were taken during ICU admission. Thirty-three of these yielded significant results (6.1%) but only nine (1.7%) were deemed clinically useful. A total of 102 cultures were taken in the first 24 hours of the ICU, of which 17 were positive (16.7%) and six were useful (5.9%). Fifty-three were taken over the next 24 hours, of which two were positive and two were useful (3.8%). Forty-four cultures were taken over the following 24 hours, of which two were positive (4.5%) and one was useful (2.3%). A total of 343 cultures were taken subsequent to this in the ICU, of which 12 were positive (3.5%) and three were deemed useful (0.9%). Of 22 blood cultures taken in the 24 hours post ICU, one was positive but deemed useful (4.5% yield).

Conclusion These results demonstrate overall low clinical utility of blood cultures but specifically that utility of ICU cultures is significantly lower than pre ICU (1.7% vs. 6.7%; P = 0.0001). The yield of positive blood cultures and their clinical utility also decrease during ICU stay. This may reflect appropriate empirical antibiotics and lower bacteraemia burden in later illness. Given the low clinical yield and a lack of established sensitive or specific triggers [1], we suggest further work in an ICU setting to maximise utility whilst minimising harm.

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P363

Employing quality improvement methodology in sepsis: an electronic sepsis order set further improves compliance with the Surviving Sepsis Campaign 3-hour bundle

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Critical Care 2014, **18(Suppl 1):**P363 (doi: 10.1186/cc13553)

Introduction The Surviving Sepsis Campaign (SSC) has developed guidelines to promote evidence-based management for patients with severe sepsis [1]. Improvements in bundle compliance have been demonstrated over time, but compliance remains below 40%. Sepsis has been studied in acute and critical care environments, but little research has focused on the management in level 1 wards. An initial audit of patients with sepsis who were referred to the GSTT critical care outreach team revealed very low overall compliance to the SSC 3-hour bundle. A novel quality improvement campaign was instituted with the aim of improving bundle compliance.

Methods A retrospective cohort study in a university hospital was performed. Patients on level 1 wards with severe sepsis registered in the adult critical care response team (CCRT) database in November 2012 were identified (Cohort A). Physiological observation, track and trigger scores, compliance with the 3-hour bundle elements (measured lactate, blood cultures before antibiotics, fluid challenge, early antibiotics), antimicrobial stewardship and 28-day mortality were recorded. Following this, a quality improvement project was initiated: central to this was an electronic 'SEPSIS' order set, containing appropriate investigations and a step-by-step management guide for use on level 1 wards. A 'viral' print and social media campaign were also undertaken. Compliance to the SSC early care bundle was re-examined

in two cohorts of patients in July 2013; patients that were referred to the CCRT as before (Cohort B) and also patients who had the electronic order set activated (Cohort C).
Results The mean age of all patients studied (n = 79) was 66.5 years. Fifty-three per cent of the patients were male. Thirty-one per cent were in septic shock at the time of sepsis identification. Overall SSC bundle compliance was 6.60% (Cohort A), 24% (Cohort B) and 45.5% (Cohort C). Improvements in other bundle parameters were also seen, including blood culture (54%, 72%, 91%), antibiotic administration (50%, 69%,76%) and fluid administration in septic shock (50%, 42%, 75%) in Cohort A, Cohort B and Cohort C respectively.
Conclusion Baseline compliance with the SSC 3-hour bundle on level 1 wards was very low. An electronic sepsis order set was associated with marked improvement. Novel quality improvement methodology may be important to achieve optimal compliance with evidence-based guidelines and an electronic sepsis order set is recommended.
Reference
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P364

Acute kidney injury in cardiorenal syndrome type 1: a meta-analysis

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Critical Care 2014, **18(Suppl 1):**P364 (doi: 10.1186/cc13554)

Introduction Cardiorenal syndrome type 1 (CRS-1) reflects an abrupt worsening in cardiac function leading to acute kidney injury (AKI). Acute cardiac conditions contributing to CRS-1 include acute heart failure (AHF), acute coronary syndrome (ACS) and cardiac surgery (CS). The objective of this study was to evaluate the epidemiology of AKI in CRS-1.
Methods This is a systematic review and meta-analysis. AKI defined by the RIFLE definition and its modifications AKIN and KDIGO is grouped as AKIRIFLE. Similarly, AKI defined by variations of worsening renal failure is grouped as AKIWRF. Incidence of AKI is reported by the different definitions of AKI. In addition, we report on mortality and length of intensive care and hospital stay (LOSICU and LOShosp) for AKIRIFLE. Data are reported as percentage, risk ratio (RR), and mean difference (MD).
Results Our literature search yielded 316 potential papers, of which 57 were included (20 papers on AHF, 15 ACS and 22 CS). A risk of bias analysis showed a low risk for selection bias in 55% of the studies and prospective data collection in 45%. AKIRIFLE was used in 33 studies (RIFLE in 22, AKIN in 14, KDIGO in four), AKIWRF, with six variants, in 24 studies and use of RRT (AKIRRT) in 20 studies. The incidence of AKI in CRS-1 patients defined by AKIRIFLE and AKIWRF was similar (22.5%, respectively 22.4%, P = 0.401), and greater than AKIRRT (2.6%, both P <0.001). AKIRIFLE occurred more frequently in AHF patients compared with ACS and CS patients (55.0% vs. 14.9% vs. 19.3%; P = 0.009 respectively P = 0.001, P = NS for ACS vs. CS). This was similar when defined by AKIWRF. AKIRRT was evenly distributed among CRS-1 subtypes (AHF 4.3%, ACS, 1.7%, and CS 3.1%, P = 0.611). Despite predominant low severity of AKIRIFLE (stage 1: 16.9%, stage 2: 3.7%, and stage 3: 3.6%), AKIRIFLE was associated with increased mortality (RR = 5.4), LOSICU (MD 1.7 days), and LOShosp (MD 4.4 days), and increasing AKIRIFLE severity was associated with increase in these three outcomes in all CRS-1 patients as well as in the three subgroups. The impact of AKIRIFLE on mortality was greatest in CS patients (AHF RR = 2.8, ACS RR = 3.5, and CS RR = 9.1). Not surprisingly, AKIWRF had similar impact on outcomes, but AKIRRT had greater impact compared with AKIRIFLE (mortality RR = 9.16, LOSICU MD = 10.6 days, and LOShosp, MD = 20.2 days).
Conclusion Almost one-quarter of patients with an acute cardiac condition had AKI, and RRT was used in approximately 3%. AKI was associated with significant worse outcomes. AHF patients experienced the highest incidence of AKI, but the impact on mortality was greatest in CS patients.

P365

Early detection of postoperative acute kidney injury by Doppler renal resistive index in major lung and cardiac operations

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Introduction Lung and cardiac operations cause significant changes in the fluid balance, and thus have a high incidence of development of postoperative acute kidney injury (AKI). The renal resistive index (RRI) calculated by the pattern of the renal artery flow is an indicator of renal artery flow. In this research work, we aimed to evaluate the efficiency of the RRI on the early prediction of postoperative kidney injury in major lung and cardiac operations.
Methods Twenty-two patients who have undergone lung or cardiac surgery were included in the study. After the kidneys were localized by ultrasonography, the best regions of blood flow were detected using color Doppler and then the arterial waveforms of these regions were obtained and optimized by Doppler. The measurements taken from three different regions were averaged. The RRI was calculated at the preoperative and postoperative first and 24th hours respectively.
Results A significant correlation was established between RRI and postoperative creatinine levels (P <0.01). RRI values reached their highest point at the postoperative first day whereas the creatinine levels reached their highest level at the postoperative third day. Although there was no correlation between postoperative creatinine level and duration of staying in hospital, a significant relationship was detected between duration of staying in ICU and the creatinine levels (P <0.01). When the cases were divided into two groups as RRI is less (n = 13) and larger (n = 9) than 0.7, significant differences were present with regard to age and creatinine levels.
Conclusion The RRI, which is used to evaluate renal arterial flow, is directly related with increasing renal vascular resistance in the case of AKI. The usefulness of RRI for prediction of AKI was shown both clinically following a renal allograft and experimentally in the acute tubular necrosis modeling [1,2]. Also in septic patients this was asserted, as RRI is a better marker than cystatin C, which is one of the popular markers of recent times for prediction of development of AKI [3]. Our results show that RRI could be a simple, non-invasive and useful technique for early diagnosis of AKI in patients undergoing major operations such as lung and cardiac surgeries.
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P366

Renal resistive index at ICU admission and its change after 24 hours predict acute kidney injury in sepsis

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Introduction The renal resistive index (RI) measured by Doppler ultrasound reflects the changes in renal microvascular resistance. It was recently shown that the RI measured at ICU admission was associated with development of AKI and with persistent AKI on day 3 after admission. The aim of this study was to investigate whether change of RI after the first 24 ICU hours has an additional predictive value for the development of AKI.
Methods This non-interventional study included adult patients with sepsis admitted to a medical ICU. Patients with renal transplant and those in terminal renal failure were excluded. The RI was measured within 2 hours from admission and 24 ± 2 hours after ICU admission. Occurrence of AKI within the first 5 days was classified according to the AKI Network criteria. There was no intervention guide by RI measurements, nor were the results known to the attending physicians.
Results There were 52 patients included in the study. At admission, eight patients had AKI stage 2 or 3 and it was persistent in five patients

on day 3. Within the first 5 days a total of 17 patients had AKI stage 2 or 3. The RI at admission was associated with APACHE II score, hypotension at admission, baseline serum lactate and history of type II diabetes treated with insulin. Patients who developed AKI stage 2 or 3 had significantly higher RI on admission (0.79 vs. 0.67, $P = 0.021$). A cutoff value of 0.72 best differentiated patients with AKI 2 or 3. Raise of RI by ≥0.05 during the first 24 hours was associated with the development of AKI stage 2 or 3 ($P = 0.034$). Patients with persistent AKI on day 3 had higher RI values on admission, and those who recovered lowered their RIs by >0.05. In multivariate analysis, admission RI and raise of RI by ≥0.05 were independently associated with development of AKI stage 2 or 3 and ICU mortality. Best sensitivity for AKI was achieved when both criteria were used: elevated RI at admission (>0.72) and raise of RI by ≥0.05 at 24 hours post admission.

Conclusion The renal RI measured at admission and its dynamics after the first 24 ICU hours are predictive of the development of AKI and ICU mortality. Further studies are needed to confirm these results.

P367

Acute kidney injury and cardiac surgery: impact of fluid balance on AKI classification and prognosis

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Introduction We assessed the effect of fluid balance (FB) on acute kidney injury (AKI) classification/prognosis in cardiac surgical patients by comparing patients classified with AKI, before and after adjusting the creatinine (used to classify AKI) for FB. Fluid accumulation is associated with negative outcomes including development of AKI in critically ill patients [1]. Cardiac surgical patients commonly receive large volumes of fluid postoperatively and could be at risk for the harmful effects of fluid accumulation. Furthermore, fluid accumulation may influence serum creatinine concentration and mask AKI [2].

Methods We performed a retrospective analysis of prospectively collected data on all cardiac surgical patients admitted to St Vincent's Hospital ICU, Melbourne, Australia from 1 July 2004 to 30 June 2012. AKI Network creatinine criteria were used to classify AKI in the usual method and then using FB-adjusted creatinine (FB at 18 hours and an assumption that total body water is 60% of weight involved). FB (total i.v. input minus (total urine output + chest drain losses)) was calculated for 18 hours post surgery as most patients were in the ICU for this period.

Results Patients classified with AKI increased from 27.7% to 37.2% ($n = 2,171$) after adjusting creatinine for FB. Patients were categorised into four groups based on presence or absence of AKI before and after adjustment for FB: group A, no AKI before or after adjustment for FB; group B, no AKI before/AKI after; group C, AKI before/no AKI after; and group D, AKI before and after. Group B ($n = 209$) had an in-hospital mortality rate similar to patients in group D ($n = 599$) (3.4% vs. 4.3%, $P = 0.53$) and greater than those in group A ($n = 1,333$) (3.4% vs. 1.6%, $P = 0.07$). Group B also had an ICU mortality rate similar to patients in group D (2.9% vs. 2.7%, $P = 0.88$) and significantly greater than those in group A (2.9% vs. 0.7%, $P = 0.003$). The need for renal replacement therapy (RRT) in group B was also high as for patients in group D (7.7% vs. 12.4%, $P = 0.06$) and was significantly greater than those in group A (7.7% vs. 1.6%, $P < 0.001$). Thus, hospital and ICU mortality and use of RRT in patients classified with AKI only after adjustment for FB were similar to patients with AKI before and after adjustment for FB and were notably higher than those of patients without AKI.

Conclusion Lack of adjustment for FB post cardiac surgery may mask the presence of AKI that is associated with increased risk for death and RRT, which could hinder optimal treatment.

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P368

Acute kidney injury of all severity is associated with extended hospitalization after critical illness

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Introduction Acute kidney injury (AKI) complicates over 50% of ICU admissions and is associated with significantly increased mortality, length of stay, and costs across a broad spectrum of conditions [1].

Methods We performed a single-centre, retrospective analysis of AKI diagnosis in patients with ICU admissions of 5 days or more who survived to hospital discharge between 2009 and 2011. We examined the relationship between hospital length of stay, AKI diagnosis, demographics and clinical characteristics in a multivariable Cox-hazard analysis.

Results We identified 700 cases, with a 66% incidence of AKI. The AKI was associated with older age, greater initial illness severity and longer ICU and hospital length of stay in univariate analysis (Table 1). In Cox-hazard analysis, only AKI category and ICU length of stay were significantly associated with lower probability of discharge over time (Figure 1). AKI-1 was associated with a hazard ratio for hospital discharge of 0.66 (0.55 to 0.79), AKI-2 with 0.55 (0.42 to 0.71) and AKI-3 with 0.54 (0.44 to 0.66).

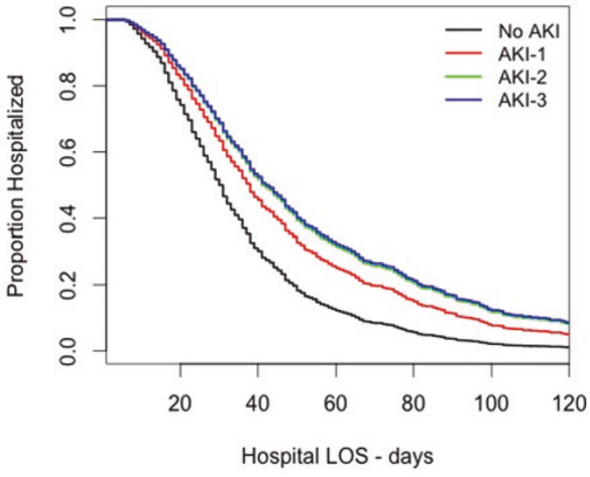

Figure 1 (abstract P368). Cox-hazard prediction of AKI class on hospitalization (ICU LOS fixed at median).

Table 1 (abstract P368). Patient characteristics by AKI

	No AKI	AKI	*P* value
Age	46 (32 to 60)	51 (37 to 64)	<0.001
SAPS-2	35 (27 to 42)	41 (32 to 49)	<0.001
ICU LOS	8 (6 to 12)	12 (7 to 18)	<0.001
Hospital LOS	27 (17 to 42)	41 (28 to 72)	<0.001

Data presented as median (IQR).

Conclusion AKI was a significant predictor of remaining in hospital at all levels of AKI severity even after allowing for longer ICU stay. Even mild AKI is associated with extended recovery from critical illness and healthcare costs even after ICU discharge.

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P369

Early acute kidney injury in nonsepsis, noncardiac surgical patients admitted to a general surgical ICU

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Introduction Perioperative AKI is a significant factor determining morbidity/mortality in surgical patients. We sought to determine the prevalence and risk factors of early AKI (within 72 hours of ICU admission) in nonsepsis, noncardiac surgical patients admitted to the general surgical ICU.
Methods This prospective observational study was done in 600 nonsepsis, noncardiac surgical patients admitted to the 14-bed general surgical ICU of Siriraj Hospital. The following data were collected: patient demographic data, ASA, comorbidity, type and urgency of surgery, type of anesthesia, preoperative and the first 72 hours laboratory data, amount of bleeding, type/amount of fluid and blood replacement, average intraoperative and the first 72 hours MAP, and severity score. Outcome as ventilator-hours, ICU length of stay and ICU mortality were also determined. Risk factors were identified by multiple logistic regression. AKI was defined and classified according to the AKIN criteria using adjusted serum creatinine (Cr) [1].
Results In total, 41.7% of the study patients developed AKI (AKIN-I 31.0%, AKIN-II 10%, AKIN-III 4.8%) and 4.8% received RRT. The following factors were different between AKI and non-AKI patients: baseline expected GFR <60 ml/minute/1.73 m^2, baseline serum Cr and baseline serum albumin, major abdominal surgery, vascular surgery, combined regional and general anesthesia, APACHE II score, receiving 6% 130/0.4 hydroxyethyl starch (HES) >20 ml/kg/day, 4% gelatin >20 ml/kg/day, crystalloid >30 ml/kg/day and positive fluid balance in the first 48 hours. Multiple logistic regression showed that independent risk factors of AKI included: baseline eGFR <60 ml/minute/1.73 m^2 (OR = 1.53; 95% CI, 1.08 to 1.27, P = 0.02), baseline serum albumin <2 mg/dl (OR = 1.75; 95% CI, 1.01 to 3.06, P = 0.049), admitting hemoglobin <8 g/dl (OR = 2.41; 95% CI, 1.14 to 5.11, P = 0.02), receiving 6% 130/0.4 HES >20 ml/kg/day (OR = 2.02; 95% CI, 1.09 to 3.76, P = 0.03), receiving crystalloid >30 ml/kg/day (OR = 3.15; 95% CI, 1.53 to 6.48, P = 0.01), vascular surgery (OR = 1.67; 95% CI, 1.05 to 2.64, P = 0.03), and major abdominal surgery (OR = 1.68; 95% CI, 1.11 to 2.55, P = 0.01). AKI patients had higher ventilator-hours (P = 0.02) and ICU length of stay (P = 0.04).
Conclusion The prevalence of early AKI in nonsepsis, noncardiac patients admitted to the general surgical ICU was 41.7%. Surgical patients with risk factors should be carefully cared for to prevent the development of AKI. Receiving 6% 130/0.4 HES >20 ml/kg/day and crystalloid >30 ml/kg/day increased the risk of early AKI in nonsepsis, noncardiac surgical patients.
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P370

Impact of kidney function calculation formulae on predicting early adverse renal events in cardiac surgery

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Introduction The Cockcroft–Gault (CG) equation and the four-variable Modification of Diet in Renal Disease (MDRD) formula are the most commonly used methods to provide estimation of kidney function. The newly developed Mayo Clinic quadratic equation (MCQE) is another alternative. The scope of this study is to investigate the prognostic value of the above algorithms as prediction models for development of acute renal injury (AKI) and early renal dialysis (RD) in cardiac surgery patients during the postoperative ICU stay.
Methods A retrospective single-centre study of 528 consecutive patients admitted to the ICU, who underwent elective cardiac surgery under extracorporeal circulation from July 2012 to November 2013. Patients undergoing urgent or emergent surgery were excluded prior to the study. Preoperative estimation of renal function was obtained using CG, MDRD and MCQE equations. The predictive capacity of these formulae was tested and compared in relation to AKI and RD incidence by constructing receiver operating characteristic curves for each of the models.
Results The mean age of the cohort was 64.7 ± 0.45 years and the mean value of estimated kidney function from MCQE, MRDR and CG formulae was 83.7 ± 1.03 ml/minute/1.73 m^2, 69.03 ± 0.82 ml/minute/1.73 m^2 and 75.3 ± 1.18 ml/minute/1.73 m^2 respectively. AKI was identified in 75 (14.2%) patients, whereas early RD was necessary in 16 (3%) patients. All of the three variables showed a good predictive value for estimating AKI and RD after cardiac surgery. The area under the curve values for the early RD group was 0.887, 0.867 and 0.804, respectively and for the AKI group was 0.701, 0.651 and 0.691, respectively.
Conclusion On the basis of our findings, all of the above algorithms seem to be accurate in predicting AKI and RD incidence in the early ICU postoperative period after elective cardiac surgery. Nevertheless, the MCQE equation more accurately classified individuals compared with MDRD and CG formulae. Our results extend knowledge from previous studies [1,2]. Further investigations should be performed to determine whether these costless formulae could be used as an additional validated predictor in this group of patients and hence whether they could be incorporated into clinical practice.
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P371

Fluid accumulation increases the risk of AKI progression and death in critically ill patients with early AKI

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Introduction Fluid therapy is a cornerstone in the management of patients with evolving acute kidney injury (AKI). Despite the wide availability of advanced hemodynamic monitoring to guide therapy, there are few data on how to manage hemodynamics optimally once early AKI has occurred. Our aim was to investigate the association between cumulative fluid balance (FB)/fluid administration and outcome (progression to AKI III and hospital mortality) in critically ill patients with early AKI, and its interaction with other hemodynamic parameters.
Methods A retrospective analysis (2-year period) of all patients admitted to an adult ICU with AKI (defined by KDIGO criteria) who had hemodynamic monitoring within 12 hours of AKI I. We recorded FB, urinary output (UO), fluid administered and hemodynamic parameters including mean arterial pressure (MAP) on the day of AKI I and in the following 72 hours. Logistic regression was employed to determine independent predictors of outcome.
Results A total of 210 patients (median age 70 years; 138 male) had hemodynamic monitoring within 12 hours of AKI I. In total, 41.5% progressed to AKI III and 43.3% died. Patients with fluid overload after the diagnosis of AKI I (FB >1 l/day; n = 85) had a higher rate of progression to AKI III (63.5 vs. 23.3%, respectively; P <0.001) and in-hospital mortality (43.5 vs. 24.8%, respectively; P = 0.004) compared with patients with FB <1 l/day. There was no difference in the other parameters (demographics, comorbidities, severity scores, hemodynamic parameters on day of AKI I, vasopressor use), with the exception of MAP on the day of AKI I (71 vs. 74 mmHg, respectively; P = 0.01). In multivariate analysis after adjustment for demographics, severity scores, comorbidities and hemodynamic parameters on the day of AKI I, a higher FB was associated with an increased risk of progression to AKI III and death (odds ratio (OR) per each 1 l/day increase 2.8; P <0.001) and death (OR 1.6; P = 0.001). Similarly, a higher amount of fluid administered was associated with an increased risk of AKI progression (OR per each 1 l/day increase 1.8; P = 0.011), even with adjustment for UO. There were no significant interactions between the risk of progression/death and other hemodynamic parameters. With the exception of MAP, improvements in other hemodynamic

parameters in the days after AKI I diagnosis did not have a significant impact on outcome.
Conclusion In critically ill patients with early AKI, a positive fluid balance, induced by excessive fluid administration, is associated with an increased risk of AKI progression and death.

P372

Postoperative acute kidney injury in patients with gynecologic malignancies

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Introduction Postoperative acute kidney injury (AKI) is an important cause of mortality and morbidity among surgical patients. Less is known about the occurrence of AKI after operations for gynecologic malignancies. The aim of this study was to determine the incidence of AKI in patients who underwent surgery for gynecologic malignancies and to compare patients with and without postoperative AKI.
Methods A total of 1,000 patients were enrolled retrospectively from January 2007 through March 2013. Patients under 18 years of age, those with chronic kidney disease and patients who died within the first week after surgery were excluded. AKI was defined according to the KDIGO 2012 Clinical Practice Guideline for Acute Kidney Injury. Perioperative variables of patients were collected from medical charts.
Results The mean age was 55.4 ± 12.4 years. The incidence of postoperative AKI was 8.8%, stage 1 occurred in 5.9%, stage 2 in 2.4% and stage 3 in 0.5% of the patients. Patients who had AKI were significantly older (57.9 ± 12.8 vs. 55.1 ± 12.3 years, $P = 0.046$), had higher body mass index (30.1 ± 7.1 vs. 28.6 ± 6.4, $P = 0.031$), higher preoperative C-reactive protein (CRP) levels (157.8 ± 121.5 vs. 76.6 ± 81.1 mg/dl, $P = 0.037$) and more frequently had history of distant organ metastasis (13.3 vs. 7.8%, $P = 0.022$) when compared with those who did not have AKI. When compared with patients who did not develop AKI postoperatively, longer operation times (149.1 ± 62.5 vs. 123.8 ± 56.6 minutes, $P = 0.001$), intraoperative usage of higher amounts of erythrocyte suspension (279.5 ± 616.7 vs. 128.3 ± 296.1 ml, $P = 0.001$) and fresh frozen plasma (165.9 ± 284.8 vs. 94.1 ± 185.9 ml, $P = 0.001$) were seen in those who developed AKI.
Conclusion Our results demonstrate that AKI occurs in 8.8% of the patients following surgery for gynecologic malignancies. Patients who had AKI were older, had higher body mass index with higher preoperative CRP levels, more frequent distant organ metastasis and longer operation times and higher amounts of blood transfused intraoperatively.

P373

Acute kidney injury after elective adult cardiac surgery

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Introduction Acute kidney injury (AKI) is a significant complication following cardiac surgery associated with an increase in morbidity, hospital stay and mortality. Although the estimated incidence of AKI following cardiac surgery is 30%, few studies have identified the incidence of AKI following cardiac surgery as defined by the Kidney Disease: Improving Global Outcomes (KDIGO) group [1]. We conducted a prospective observational study at our institution to identify the incidence and staging of AKI according to the KDIGO definition. We also aim to identify the factors that predispose adult patients to developing AKI post cardiac surgery.
Methods A prospective analysis was performed on 103 adult patients admitted to ICU post-cardiac surgery from September to October 2013. Data for perioperative risk factors and renal biochemical markers were collected up to the sixth postoperative day and are expressed as mean (SD).
Results Ordered logistic regression was used to analyse the data. Thirty-three per cent of cardiac surgery patients at our institution developed AKI. Factors such as poor left ventricular (LV) function, low preoperative haematocrit and low preoperative glomerular filtration rate (GFR) were significant risk factors ($P = 0.03$, $P = 0.04$ and $P < 0.01$ respectively) for developing postoperative AKI following cardiac surgery. See Table 1.

Table 1 (abstract P373). Results

Age (years)	66 (13.8)
Male	69
Female	34
No AKI	69
KDIGO 1	22
KDIGO 2	6
KDIGO 3	6

Conclusion Our results suggest that we should focus on LV function and GFR as predictors for developing AKI following cardiac surgery. Strategies to increase preoperative haematocrit should be investigated to reduce in the incidence and severity of postoperative AKI.
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P374

Incidence and outcomes of contrast-induced nephropathy in adult ICU patients

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Critical Care 2014, **18(Suppl 1):**P374 (doi: 10.1186/cc13564)

Introduction Critically ill patients cared for in ICUs often require radiological investigation using iodinated contrast agents. Contrast-induced nephropathy (CIN) – a form of acute kidney injury (AKI) – is a complication following the use of such contrast. Although CIN has been thoroughly studied in some populations (for example, those undergoing coronary angiography), it has not been investigated in large numbers of ICU patients [1].
Methods We conducted a single-centre retrospective review of the electronic patient records of general adult ICU patients who received iodinated contrast over a 3-year period (2009 to 2011). Our review identified evidence of CIN or AKI post scan (assessed using CIN and KDIGO criteria); and clinical outcomes post scan (renal replacement therapy (RRT), ICU length of stay, mortality). Patients were excluded if: they had received pre-scan RRT; they did not have pre/post-scan creatinine measurements. Univariate analyses investigated the relationship between CIN or AKI and ICU outcomes (use of RRT post scan, ICU mortality and ICU length of stay), using chi-squared tests for categorical outcomes and nonparametric tests for continuous outcomes.
Results A total of 479 scans involving 331 patients were included. In total, 303 (63%) scans involved males, median age 61 (IQR 46 to 71) years, 119 (25%) diabetic, with median pre-scan eGFR of 85 (38 to 113) ml/minute/1.73 m^2. Scans occurred a median of 2.9 (0.8 to 8.8) days from admission. A total of 266 (56%) scans were associated with CIN (grade 0, $n = 167$; grade 1, $n = 39$; grade 2, $n = 60$). Clinical outcomes were significantly worse in patients developing higher grades of CIN (increased use of RRT post scan, $P = 0.02$; increased ICU length of stay, $P = 0.04$; increased ICU mortality, $P = 0.01$). Ninety-five (20%) scans were associated with AKI (stage 1, $n = 45$; stage 2, $n = 13$; stage 3, $n = 37$). Clinical outcomes were again significantly worse in patients developing AKI (increased use of RRT post scan, $P < 0.001$; increased ICU mortality $P = 0.01$).
Conclusion Renal impairment/injury is common in adult ICU patients undergoing investigations using iodinated contrast and the incidence varies depending upon the classification used. Whichever classification is used, patients developing CIN/AKI following contrast administration have poorer clinical outcomes than patients who do not.
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P375

Human acute kidney injury is associated with a proinflammatory phenotype

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Critical Care 2014, **18(Suppl 1):**P375 (doi: 10.1186/cc13565)

Introduction Animal research suggests that acute kidney injury (AKI) is an inflammatory condition [1]. Our aim was to describe the immune phenotype in human AKI.
Methods We enrolled patients with: AKI grade II/III (defined by KDIGO criteria) and systemic inflammatory response syndrome (SIRS) without sepsis; SIRS without AKI; and AKI II/III without SIRS. A healthy control population was used for baseline comparison. Serial blood samples were taken on days 0, 2 and 7. Cells were separated using Percoll gradients and phenotyped using flow cytometry.
Results The results from 24 day 0 samples identified statistically significant differences between SIRS, AKI, AKI + SIRS and healthy controls amongst: $CD8^+$ cytotoxic T cells, $CD45^-CD25^{+++}$ regulatory T cells, and $CD45^-CD25^{++}$ cytokine secreting non-T-regulatory cells (Table 1). The percentage of CD69-positive neutrophils was significantly increased across all three groups relative to controls, with little variation between AKI, SIRS and AKI + SIRS patients.

Table 1 (abstract P375).

	AKI + SIRS	AKI no SIRS	SIRS alone	Control
% $CD8^+$ cytotoxic T cells	23.3	16.7	11.6	31.1
% Fr. II T-regulatory cells	4.1	2.7	1.6	1.2
% Fr. III cytokine T cell	11.5	21.2	13.9	8.0
% $CD69^+$ neutrophils	83.9	69.7	65.5	7.35

Conclusion Human AKI is associated with a proinflammatory phenotype.
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P376

Risk factors for the development of contrast-induced nephropathy in ICU patients

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Introduction Critically ill patients cared for in ICUs often require radiological investigation using iodinated contrast agents. Contrast-induced nephropathy (CIN) – a form of acute kidney injury (AKI) – is a complication following the use of such contrast. Although CIN has been thoroughly studied in some populations (for example, those undergoing coronary angiography), it has not been investigated in large numbers of ICU patients [1].
Methods We conducted a single-centre retrospective review of the electronic patient records of general adult ICU patients who received iodinated contrast over a 3-year period (2009 to 2011). Our review identified: patient demographics; ICU admission details (specialty, time of admission, elective/emergency admission); physiological status pre scan (evidence of shock, eGFR, urine output); volume of iodinated contrast; and evidence of CIN or AKI post scan (assessed using CIN and KDIGO criteria). Patients were excluded if they had pre-scan renal replacement therapy. Analyses investigated the risk factors for CIN or AKI using chi-squared tests for categorical variables and nonparametric tests for continuous variables (as no continuous variable was normally distributed, even with log transformation).
Results In total, 479 scans involving 331 patients were included. A total of 266 (56%) scans were associated with CIN. Significant risk factors for the development of CIN included male gender ($P = 0.02$), reduced pre-scan GFR ($P < 0.001$), and decreasing time from admission to scan ($P = 0.03$). Ninety-five (20%) scans were associated with the development of AKI. Significant risk factors for AKI again included male gender ($P = 0.009$), reduced pre-scan eGFR ($P < 0.001$), and decreasing time from admission to scan ($P = 0.003$), but also included emergency admission to ICU ($P = 0.03$), pre-scan shock ($P < 0.001$), and pre-scan oliguria ($P < 0.001$).
Conclusion Male gender, reduced pre-scan eGFR and decreasing time from admission to scan are risk factors for the development of both CIN and AKI. The association with time from admission to scan may reflect inadequate patient optimisation prior to contrast administration; this hypothesis is supported by the risk factors significantly associated with AKI alone (emergency admission to ICU and pre-scan shock). Given the adverse clinical outcomes associated with the development of CIN/AKI, these findings necessitate a review of current practice.
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P377

Test characteristics of acute kidney injury biomarkers in animal models of sepsis

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Introduction Approximately 50% of acute kidney injury (AKI) is associated with sepsis. Neutrophil gelatinase-associated lipocalin (NGAL) and cystatin C are the two most widely used biomarkers for AKI. However, these two markers are also affected by the systemic inflammatory response, and their diagnostic value in sepsis-induced AKI is disputed [1,2]. Unlike clinical AKI, animal models can be used to explore single etiology. The purpose of this study is to examine the relationship between inflammatory mediators and biomarkers for AKI in a sepsis model in rats.
Methods Sepsis was induced by cecal ligation and puncture (CLP) in 60 adult SD rats and then observed for AKI and survival. Blood and urine samples were collected at baseline, and 18, 22, and 48 hours after CLP. AKI severity was assessed by RIFLE criteria (creatinine only). The associations between plasma IL-6 and plasma NGAL, plasma cystatin C, urine NGAL and urine cystatin C were analyzed. The area under the receiver-operator characteristic curves (AUC) was used to evaluate the diagnostic capability between severe AKI (RIFLE-I or RIFLE-F) and no AKI (includes RIFLE-R) for different biomarkers.
Results The changes of plasma NGAL, plasma cystatin C, urine NGAL and urine cystatin C with time were similar to the changes of plasma IL-6. However, only plasma NGAL levels were closely correlated with levels of plasma IL-6 ($R^2 = 0.36$, $P < 0.05$). The analysis for plasma cystatin C, urine NGAL and urine cystatin C at 22 hours for severe AKI showed AUCs of 0.78, 0.71 and 0.75 respectively (all $P < 0.05$), and the AUC for plasma NGAL was 0.62 ($P = 0.11$). There were no significant differences in plasma NGAL at 22 hours between severe AKI and no AKI (2,143.32 vs. 2,077.02 U/ml, $P = 0.21$).
Conclusion In this animal model of CLP sepsis, plasma NGAL levels were affected by the systemic inflammatory response, and did not discriminate for AKI. Urine NGAL, plasma cystatin C and urine cystatin C were able to differentiate severe AKI from no AKI in CLP sepsis.
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P378

Perioperative measurement of urinary oxygen tension as a tool in the prevention of acute kidney injury?

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Critical Care 2014, **18(Suppl 1):**P378 (doi: 10.1186/cc13568)

Introduction Acute kidney injury (AKI) remains a common complication after cardiopulmonary bypass (CPB) and can be diagnosed by

serum creatinine [1]. However, serum creatinine is an insensitive and nonspecific biomarker [2]. This study was designed to investigate whether a correlation exists between urinary oxygen tension (UOT) and early markers of AKI. The aim was to evaluate whether UOT could provide warning signs of an insufficient renal oxygen supply, which can lead to postoperative AKI.

Methods Fourteen subjects undergoing cardiac surgery with CPB were included in this prospective clinical pilot study. UOT was measured perioperatively in all patients, both in the operating room (before, during and after CPB) and in the ICU. Biomarkers of AKI in blood and urine were measured preoperatively and postoperatively at 3, 6, 12 and 24 hours after the initiation of CPB. These included serum creatinine and the early urinary biomarkers kidney injury molecule-1 (KIM-1), neutrophil gelatinase-associated lipocalin (NGAL) and cystatin C. Student's *t* tests and Mann–Whitney tests were used to compare continuous variables.

Results There was a significant decrease in UOT between the start of CPB (138.44 ± 22.19 mmHg) and the lowest UOT during CPB (107.70 ± 23.28 mmHg) ($P = 0.001$). Dividing the subjects into two groups according to the Acute Kidney Injury Network (AKIN) classification, no significant differences were found in mean UOTs between the group of patients with a normal kidney function ($n = 7$) and the group with AKIN stage 1 or 2 ($n = 7$). For KIM-1, a significant difference between the two groups was found at 3 hours ($P = 0.041$) after the initiation of CPB. Further, for NGAL a significant increase in biomarker concentrations compared with the preoperative value was observed in the group with an AKIN stage 1 or 2 at all different postoperative time points (3 hours ($P = 0.013$), 6 hours ($P = 0.003$), 12 hours ($P = 0.009$) and 24 hours ($P = 0.003$)). On the contrary, there were no significant increased urinary NGAL levels measured in the group with the normal kidney function.

Conclusion This pilot study was not able to demonstrate any association between perioperatively measured UOT and markers of postoperative AKI. Additional laboratory and clinical studies will be necessary to further define the relationship between the UOT and new biomarkers of AKI.

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P379

Postoperative acute kidney injury can be predicted by the novel biomarkers insulin-like growth factor-binding protein 7/tissue inhibitor of metalloproteinases-2 as early as 6 hours after surgery

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Introduction Acute kidney injury (AKI) in surgical critically ill patients is an independent risk factor for early mortality. Two novel urine biomarkers, insulin-like growth factor-binding protein 7 (IGFBP7) and tissue inhibitor of metalloproteinases-2 (TIMP-2), may help to detect clinically silent episodes of AKI in the golden hours prior to irreversible damage of the kidney. We evaluated the early predictive value of these biomarkers for AKI, moderate and severe AKI, early requirement of renal replacement therapy (RRT), and ICU mortality, with a cutoff value of IGFBP7/TIMP-2 >0.3.

Methods Four to six hours after admission to the surgical ICU, urine biomarkers were prospectively evaluated in all patients with present exposures and susceptibilities for AKI according to the KDIGO recommendation. The incidence and severity of AKI (KDIGO 2012) and requirement of RRT were assessed over 48 hours after admission. In addition, ICU mortality and variables such a norepinephrine dose, mean arterial pressure, hemoglobin level, cumulative fluid balance and urine production were noted at the time of biomarker evaluation (4 to 6 hours) and for the first 24 hours after admission.

Results A total of 120 patients were included in the study. The area under the curve (AUC) for IGFBP7/TIMP2 >0.3 was 0.83 for early detection of AKI, 0.86 for moderate and severe AKI, 0.86 for RRT in the first 48 hours after admission and 0.86 for ICU mortality. Patients with IGFBP7/TIMP-2 >0.3 had a higher risk (odds ratio 11.7) for development of AKI compared with patients with IGFBP7/TIMP-2 ≤0.3. The norepinephrine dose, mean arterial pressure, fluid balance and urine output in the first 6 hours after admission were significantly different for patients with low and high risk for AKI. The negative predictive value (NPV) of 0.41 for urine output <1 ml/kg/hour over the first 6 hours after admission was significantly lower if compared with NPV of 0.86 for GFBP7/TIMP-2 ≤0.3 for exclusion of AKI. Similarly NPV of urine output <1 ml/kg/hour of 0.89 for moderate and severe AKI (stage 2 and 3) was lower than the NPV of 1.00 for GFBP7/TIMP-2 ≤0.3.

Conclusion The novel urine biomarkers IGFBP7 and TIMP-2 enable early risk stratification of surgical ICU patients at risk for development of AKI. The predictive values of biomarkers were better for early prediction than clinical parameters such as urine output within the first 6 hours after admission to ICU.

P380

Urine TIMP2 × IGFBP7 increases 24 hours before severe AKI

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Introduction We recently reported a 728-patient multicenter study (Sapphire) where a biomarker combination of tissue inhibitor of metalloproteinases-2 (TIMP-2) and insulin-like growth factor binding protein 7 (IGFBP7) were validated for risk stratification for moderate or severe acute kidney injury (AKI) KDIGO stage 2 and 3 [1].

Methods We subsequently selected two clinical cutoff values for the TIMP2 × IGFBP7 combination from the Sapphire dataset, one (0.3) with high sensitivity (89%) (specificity = 50%) and one (2.0) with high specificity (95%) (sensitivity = 42%) for the development of AKI KDIGO stage 2 and 3 within 12 hours of study enrolment. We examined the timing of change in TIMP2 × IGFBP7 relative to change in creatinine using the sign test.

Results TIMP2 × IGFBP7 results were available for 178 patients who developed AKI stage 2 or 3. The median TIMP2 × IGFBP7 result was significantly greater than the cutoff value of 0.3 from 24 hours before to 24 hours after AKI 2 or 3 ($P < 0.01$) (Figure 1). Conversely, median serum creatinine was not different from baseline prior to development of AKI 2 or 3.

Conclusion The TIMP2 × IGFBP7 biomarker combination identifies patients who ultimately develop moderate or severe AKI 24 hours earlier than serum creatinine.

Reference

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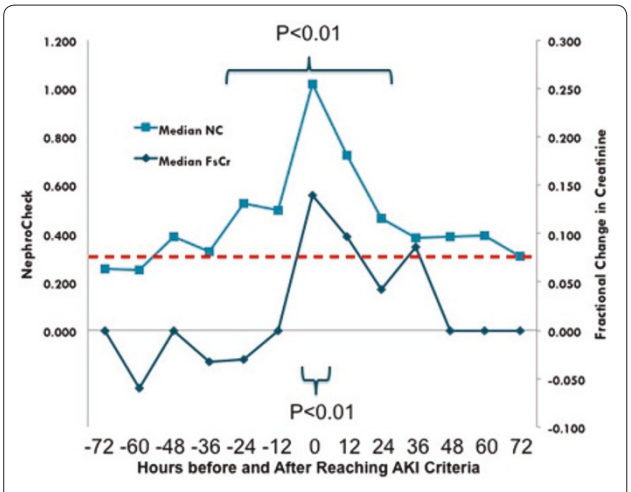

Figure 1 (abstract P380). NC, Nephrocheck (TIMP2 × IGFBP7); Cr, creatinine.

P381

Urinary tissue inhibitor of metalloproteinases-2 and insulin-like growth factor-binding protein 7 as early biomarkers of acute kidney injury and renal recovery following cardiac surgery

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Introduction Difficulties in prediction and early identification of acute kidney injury (AKI) have hindered the ability to develop preventive and therapeutic measures for this syndrome. We tested the hypothesis that a urine test measuring insulin-like growth factor-binding protein 7 (IGFBP7) and tissue inhibitor of metalloproteinases-2 (TIMP-2), both inducers of G_1 cell cycle arrest, a key mechanism implicated in AKI, could predict AKI in cardiac surgery patients.
Methods We studied 50 patients at high risk for AKI undergoing cardiac surgery with cardiopulmonary bypass. Serial urine samples were analyzed for [TIMP-2] × [IGFBP7] concentrations. The primary outcome measure was AKI as defined by international consensus criteria following surgery. Furthermore, we investigated whether urine [TIMP-2] × [IGFBP7] could predict renal recovery from AKI prior to hospital discharge.
Results Twenty-six patients (52%) developed AKI. Diagnosis based on serum creatinine and/or oliguria did not occur until 1 to 3 days after cardiopulmonary bypass. In contrast, urine concentration of [TIMP-2] × [IGFBP7] rose from a mean of 0.49 (0.24) at baseline to 1.51 (0.57) 4 hours after cardiopulmonary bypass in patients who developed AKI. The maximum urinary [TIMP-2] × [IGFBP7] concentration achieved in the first 24 hours following surgery (composite time point) demonstrated an area under the receiver-operating characteristic curve of 0.84. Sensitivity was 0.92, and specificity was 0.81 for a cutoff value of 0.50. The decline in urinary [TIMP-2] × [IGFBP7] values was the strongest predictor for renal recovery.
Conclusion Urinary [TIMP-2] × [IGFBP7] serves as a sensitive and specific biomarker to predict AKI early after cardiac surgery and to predict renal recovery.

P382

Urine microscopy score combined with albumin creatinine ratio score improves prediction of future acute kidney injury (AKI) and worsening AKI

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Critical Care 2014, **18(Suppl 1):**P382 (doi: 10.1186/cc13572)

Introduction Patients with AKI have a high morbidity and mortality. Diagnosis of AKI may be improved by examination of the urinary sediment with microscopy and by measurement of urine albumin. A urine microscopy score (UMS; 0 to 4 points) of renal tubular epithelial cells and granular casts has previously been developed to aid diagnosis. We have devised a urine albumin:creatinine ratio score (ACRS; 0 to 4 points) and have combined this with the UMS with the aim of stratifying the risk of developing future AKI or worsening AKI (UMS-ACRS; 0 to 8 points). The aims were to compare UMS-ACRS in critically ill patients with and without AKI at ICU admission, and to determine whether a high UMS-ACRS can predict if critically ill patients develop AKI or worsening AKI.
Methods Investigators were blinded to diagnosis prior to urine collection. Microscopy was performed on centrifuged urine obtained from 227 consecutive critically ill patients in a general ICU on day 1 of admission. Five photographs were taken and the mean UMS was calculated. An independent reviewer scored the photographs. The urine albumin:creatinine ratio was calculated and the ACRS determined. The UMS was then combined with the ACRS.
Results Mean UMS-ACRS ± SD was higher (2.66 ± 1.57) in patients with AKI on ICU admission (n = 106) compared with those without AKI (mean UMS-ACRS = 2.40 ± 1.03; n = 120), unpaired t test P = 0.14. Patients who developed AKI or worsening AKI (n = 58) had a mean score of 2.79 ± 1.21 versus 2.30 ± 1.14 in those who never developed AKI or improved (n = 150), P = 0.006. UMS-ACRS score >2 on admission had a sensitivity of 0.89 for identifying progressive AKI. UMS-ACRS score of 5 to 8 on admission had a positive predictive value for worsening AKI of 60%, a negative predictive value of 69% and a likelihood ratio 3.1 for developing AKI or worsening AKI.
Conclusion The mean UMS-ACRS is higher in patients with AKI. Combining UMS with ACRS improves prediction and stratification of which patients will develop AKI, or progressive AKI, after ICU admission. Clinical implications are that urine microscopy and ACR calculation are safe, inexpensive, non-invasive and may improve prediction of AKI in critically ill patients, potentially leading to earlier intervention and improved outcomes.

P383

Resveratrol ameliorates apoptosis induced by contrast medium ioxitalamate in HK-2 human renal proximal tubule cells *in vitro*

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Introduction Computed tomography with contrast medium is a common diagnostic tool in emergency and critical medicine. Contrast-induced nephropathy (CIN) is one of the leading causes of hospital-acquired acute kidney injury. Focus on renal tubule protection may be a hope to improve the effectiveness of current strategies.
Methods We used HK-2 human renal proximal tubule cells to evaluate the therapeutic potential of resveratrol, a polyphenol phytoalexin

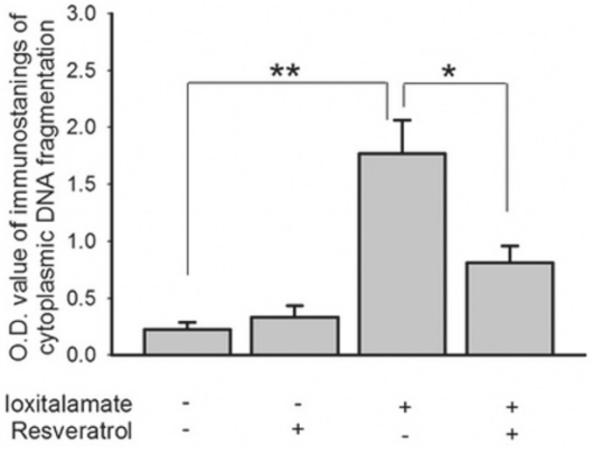

Figure 1 (abstract P383). Immunostaining of cytoplasmic DNA fragmentation in HK-2 cells.

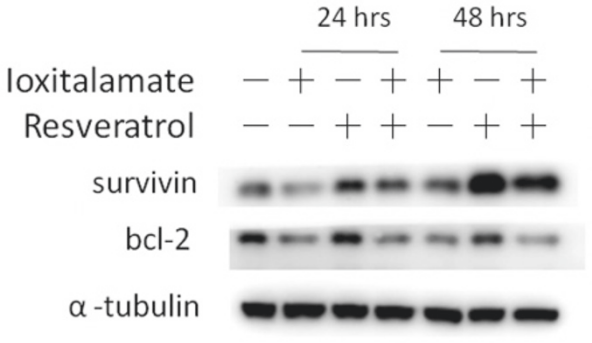

Figure 2 (abstract P383). Upregulated survivin expression by resveratrol.

produced naturally by several plants, for contrast ioxitalamate-induced toxicity *in vitro*. Cytotoxicity was determined by MTT assay. Patterns of cell death were observed by flow cytometry. Cytoplasmic DNA fragmentation was examined by ELISA. Western blots were used to analyze the expression of related proteins.
Results In a 48-hour administration, ioxitalamate elicited cytotoxicity on HK-2 cells. Annexin V^+ cells were significantly increased after 30 mg/ml ioxitalamate exposure. A decrease in bcl-2 expression explained the ioxitalamate-induced apoptosis. Co-treatment with resveratrol ameliorated the cytotoxicity induced by ioxitalamate. Resveratrol at 12.5 μM decreased ioxitalamate-induced DNA fragmentation through upregulated expression of survivin. See Figures 1 and 2.
Conclusion Resveratrol ameliorated apoptosis induced by contrast medium ioxitalamate in human renal proximal tubule cells. Investigations using animal models will be conducted in the future.

P384

Erythropoietin and Protection of Renal function in Cardiac Surgery (EPRICS) trial

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Introduction To date, there are no known methods for preventing acute kidney injury after cardiac surgery. Increasing evidence suggests that erythropoietin (EPO) has renal anti-apoptotic and tissue protective effects [1], and in animal models a single high dose of EPO has been shown to ameliorate reperfusion injury after ischemia [2]. However, recent human studies have shown conflicting results. We aimed to study the effect of a single high dose of EPO preoperatively on renal function after coronary artery bypass grafting (CABG) in patients with preoperative impaired renal function.
Methods This single-centre, randomized, double-blind, placebo-controlled study included 75 patients scheduled for CABG with preexisting renal impairment (estimated glomerular filtration rate based on p-cystatin C <60 ml/minute and >15 ml/minute). The patients either received a single high dose of EPO (400 IU/kg) or placebo preoperatively. The primary endpoint was renal protection evaluated by p-cystatin C at the third postoperative day compared with the preoperative values. Incidence of acute kidney injury and other renal biomarker changes were among secondary endpoints.
Results There was no significant difference on the third postoperative day for p-cystatin C levels (2.1 ± 0.8 mg/l for the study group and 1.9 ± 0.5 mg/l for the control group, $P = 0.51$). There were no significant differences in other renal biomarkers or measures between the groups (p-NGAL, p-creatinine, p-urea, and estimated glomerular filtration rate). There were no other differences in outcome variables between the groups.
Conclusion Intravenous administration of a single high dose (400 IU/kg) of EPO did not have a renal protective effect in patients with reduced kidney function undergoing coronary artery bypass surgery.
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P385

Estimated GFR versus creatinine clearance for evaluation of recovery from acute kidney injury

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Introduction The aim of this study is to quantify the impact of using eGFR instead of measured creatinine clearance (Clcr) on the evaluation of recovery from acute kidney injury (AKI).
Methods From a large RCT's database [1] we excluded patients with end-stage renal disease and kidney transplants. In the remaining 4,560 patients, 1,296 (28%) developed AKI (KDIGO criteria). After exclusion of ICU nonsurvivors ($n = 229$), patients on dialysis at ICU discharge ($n = 77$) and patients for whom Clcr on the last day of ICU was not available ($n = 206$), 784 patients were included in this analysis. We compared eGFR (MDRD equation) with measured Clcr (based on 24-hour urine collection and corrected for BSA) at ICU discharge for patient groups with different ICU stays. We also evaluated the impact of using the two GFR measurements on the estimation of complete recovery relative to baseline eGFR. Parameters were compared with the paired *t* test and McNemar's test.
Results Amongst the 784 patients with AKI, 456 (58%) reached stage 1, 143 (18%) stage 2 and 185 (24%) stage 3. Mean ± SD Clcr and eGFR at ICU discharge were respectively 54.5 ± 28 and 76 ± 55 ml/minute/1.73 m^2 ($P < 0.0001$). eGFR was not significantly different from Clcr in patients with ICU stay <7 days. In patients with ICU stay between 8 and 14 days, eGFR was significantly higher than Clcr (79 ± 51 vs. 48.5 ± 20, $P < 0.0001$) and the difference increased even further in patients with ICU stay over 14 days (102 ± 70 vs. 42.6 ± 20, $P < 0.0001$). The percentage of patients with complete recovery differed significantly when evaluated by eGFR (35.3%) or Clcr (28.7%) ($P = 0.007$). In patients with ICU stay >14 days, this difference increased to 56.4% by eGFR versus 14.1% by Clcr ($P < 0.0001$).
Conclusion Estimated GFR at ICU discharge is significantly higher than the measured Clcr in patients with prolonged ICU stay. This difference can be explained by loss of muscle mass with decreased creatinine production and results in an important overestimation of recovery.
Reference

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P386

Recovery from AKI by KDIGO criteria

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Introduction Data on recovery of AKI are mainly limited to persistent dialysis dependency in patients with dialysis-requiring AKI. The aim of this analysis is to evaluate recovery from different stages of AKI.
Methods In a large database ($n = 4,640$) of a previous RCT [1] we estimated renal recovery from AKI defined by KDIGO criteria (without urine output criteria). Patients with end-stage renal disease ($n = 56$), kidney transplantation ($n = 15$) or incomplete data ($n = 9$) were excluded. Patients were classified according to their maximal AKI stage (AKImax) during the ICU stay. Recovery was evaluated by AKI stage at hospital discharge. Complete recovery was defined as the absence of AKI, partial recovery as persistent AKI with a decrease in AKI stage compared with AKImax and no recovery as persistence of AKImax or worsening of AKI after ICU discharge. A persistent 0.3 mg/dl increase of Screat was also considered as no or partial recovery.
Results A total of 1,296 patients (28%) developed AKI. AKImax was stage 1 in 580 (45%) (416 with >50% increase of Screat), stage 2 in 207 (16%) and stage 3 in 509 (39%) (348 needing RRT). Mortality increased from 12 to 42% ($P < 0.0001$), hospital stay increased from 21 (14 to 37) to 34 (17 to 63) days ($P < 0.0001$) and complete recovery in survivors decreased from 82 to 53% ($P < 0.0001$) with increasing severity of AKI. In patients requiring RRT, 51% of survivors left the hospital without AKI whereas 16% remained dialysis dependent. Within the AKI 3 group, the need for RRT significantly increased mortality ($P = 0.0002$), but did not affect complete recovery in survivors (51% vs. 58%, $P = 0.16$). Patients with a '0.3 mg/dl increase of serum creatinine only' had a significantly higher mortality than patients without AKI in the ICU ($P = 0.0004$). They also had a worse kidney outcome at hospital discharge ($P = 0.006$).
Conclusion Increasing severity of AKI according to the KDIGO criteria is associated with increased mortality and decreased recovery of kidney function. The need for RRT significantly increases mortality but complete recovery in survivors of AKI 3 is not different with or without RRT. The 0.3 mg/dl criterion proves valid with regard to mortality and kidney outcome.
Reference

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P387

Incidence and outcomes of acute kidney injury following orthotopic lung transplant: a population-based cohort study

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Critical Care 2014, **18(Suppl 1):**P387 (doi: 10.1186/cc13577)

Introduction Acute kidney injury (AKI) is a serious complication following lung transplantation (LTx) [1-3]. We aimed to describe the incidence and outcomes associated with AKI following LTx.
Methods A retrospective population-based cohort study of all adult recipients of LTx at the University of Alberta between 1990 and 2011 was performed. The primary outcome was AKI, defined and classified according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria, in the first seven postoperative days. Secondary outcomes included risk factors, utilization of renal replacement therapy (RRT), occurrence of postoperative complications, mortality and kidney recovery.
Results Of 445 LTx recipients included, AKI occurred in 306 (68.8%), with severity classified as stage I in 38.9% (n = 173), stage II in 17.5% (n = 78) and stage III in 12.4% (n = 55). RRT was received by 36 (8.1%). Independent risk factors associated with AKI included longer duration of cardiopulmonary bypass (per minute, odds ratio (OR) 1.003; 95% CI, 1.001 to 1.006; P = 0.02), and mechanical ventilation (per hour (log-transformed), OR 5.30; 95% CI, 3.04 to 9.24; P <0.001), and use of cyclosporine (OR 2.03; 95% CI, 1.13 to 3.64; P = 0.02). In-hospital and 1-year mortality were significantly higher in those with AKI compared with no AKI (7.2% vs. 0%, adjusted P = 0.001; 14.4% vs. 5.0%, adjusted P = 0.02, respectively). At 3 months, those with AKI had greater sustained loss of kidney function compared with no AKI (estimated glomerular filtration rate (mean (SD)) 68.9 (25.7) vs. 75.3 (22.1) ml/minute/1.73 m^2, P = 0.01).
Conclusion By the KDIGO definition, AKI occurred in two-thirds of patients following LTx. AKI portended greater risk of death and loss of kidney function.
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P388

Fluid accumulation post cardiac surgery and risk for renal replacement therapy

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Introduction We assessed the impact of fluid accumulation on the development of acute kidney injury (AKI) and need for continuous renal replacement therapy in cardiac surgical patients. Fluid accumulation has been associated with negative outcomes including development of AKI in critically ill patients [1-3]. As cardiac surgical patients commonly receive large volumes of i.v. fluid within 24 hours of surgery, they could be at risk of the harmful effects of fluid accumulation.
Methods We performed a retrospective analysis of prospectively collected data on all patients admitted after cardiac surgery to St Vincent's Hospital ICU, Melbourne, Australia from 1 July 2004 to 30 June 2012 (n = 3,207). The fluid accumulation percentage (total urine and chest drain losses subtracted from total i.v. intake (l) /weight (kg) × 100) was calculated for 18 hours post surgery as most patients were in the ICU for this period. Acute Kidney Injury Network (AKIN) creatinine criteria were used to classify AKI using creatinine adjusted for fluid balance.
Results Renal replacement therapy was performed on 136 patients in this group (4.2%). The fluid accumulation percentage was associated with an 8% increase in odds for AKI (OR (CI), 1.08 (1.04 to 1.12)), and a 13% increase in odds for requiring renal replacement therapy (1.13 (1.05 to 1.21)) for each percent increase in fluid accumulation (l/kg%) after cardiac surgery, after adjusting for variables including APACHE score, cardiac failure, type of surgery, and inotrope use in multivariate analysis.
Conclusion In this relatively homogeneous patient group undergoing cardiac surgery, postoperative percent fluid accumulation at 18 hours was associated with AKI and need for renal replacement therapy. Whether there is residual confounding due to indication for fluid use or unmeasured risk factors requires further investigation in controlled trials.
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P389

Recovery of renal function after acute kidney injury requiring continuous renal replacement therapy

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Introduction Acute kidney injury (AKI) is increasingly common in critically ill patients and many patients with severe kidney injury require continuous renal replacement therapy (CRRT). However, little is known regarding the incidence rate and associated factors for developing chronic kidney disease after CRRT in AKI patients. This study aimed to investigate renal outcome and the factors associated with incomplete renal recovery in AKI patients who received CRRT.
Methods Between January 2011 and August 2013, 397 patients received CRRT in our ICU. Among them, patients who had normal renal function before AKI and were discharged without maintenance renal replacement therapy (RRT) were included in this study. We examined the incidence of incomplete renal recovery with estimated glomerular filtration rate (eGFR) <60 ml/minute/1.73 m^2 during follow-up. Factors that increased risk of incomplete renal recovery after AKI were investigated with multiple logistic regression.
Results Forty-one AKI patients were discharged without further RRT and followed up for a mean of 7 months. Sixteen (39.0%) of 41 patients incompletely recovered their renal function. Patients with incomplete renal recovery showed older age and longer duration of anuria compared with complete renal recovery patients (69.7 ± 7.0 vs. 54.8 ± 16.9 years, P = 0.002; 128.6 ± 192.1 vs. 26.9 ± 66.6 hours, P = 0.019). Multivariate analysis adjusting for sex, initial eGFR, hemoglobin level, diabetes mellitus and hypertension showed that old age and long duration of anuria were independent risk factors for incomplete renal recovery (OR = 1.143, 95% CI = 1.020 to 1.281, P = 0.021 and OR = 1.011, 95% CI = 1.001 to 1.032, P = 0.038, respectively).
Conclusion The renal outcome of severe AKI requiring CRRT was poor even in patients with previous normal renal function. Long-term monitoring of renal function is needed especially in severe AKI patients with old age and long duration of anuria.

P390

Relation between preoperative use of diuretics and renal replacement therapy after cardiac surgery: a propensity score analysis

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Critical Care 2014, **18(Suppl 1):**P390 (doi: 10.1186/cc13580)

Introduction The aim was to evaluate the relation between preoperative use of diuretics and renal replacement therapy (RRT) in postoperative patients of cardiac surgery.

Methods A prospective cohort of adult patients who underwent cardiac surgery in 11 institutions all over the Andalusia community from March 2008 to July 2012 was included in the ARIAM adult cardiac surgery project. Diuretic users prior to the intervention were pair-matched to nonusers on the basis of a propensity score based on demographics, comorbidities, medication and surgical data. We analysed differences in RRT in both groups.
Results The total cohort was composed of 7,276 patients with 63.91 ± 12.45 years and 61.1% male gender. Elective scheduled surgery was done in 85.9% of patients. Surgical risk assessed by the additive EuroSCORE was 5.86 ± 3.14 points and predicted mortality by the Logistic EuroSCORE was 8.10%. Mortality in the ICU was 7.6% and in-hospital mortality was 10.1% (8.1% missing data). Prior to surgery, 10.4% of patients had a creatinine level between 1.2 and 2 mg/dl, 1.1% between 2 and 2.3 mg/dl, 0.8% between 2.3 and 3.5 mg/dl and 0.3% above 3.5 mg/dl. In the nonmatched cohort, 180 patients (2.5%) needed RRT. RRT was needed in 3.5% of 3,771 patients with diuretics and in 1.4% of 3,505 patients not treated with them (P <0.001); 2.61 (1.87 to 3.65). After adjusting with logistic regression by additive EuroSCORE, SAPS 3, bypass time exceeding 120 minutes and prior renal dysfunction, the OR was 1.67 (1.15 to 2.45). When we analysed 3,426 matched patients according to the propensity score, RRT was needed in 3% of 1,713 patients with diuretics and in 1.6% of 1,713 not treated with them (P <0.009), 1.85 (1.16 to 2.94).
Conclusion Preoperative use of diuretics is associated with an increased risk of need for RRT.

P391

Continuous renal replacement therapy (CVVHD) for acute kidney injury in critical care: incidence and outcome across South West Wales

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Critical Care 2014, **18(Suppl 1):**P391 (doi: 10.1186/cc13581)

Introduction Renal replacement therapy in critical care is associated with increased mortality. It is not known for which patients RRT confers the most benefit, or who will recover function and remain dialysis independent on a long-term basis.
Methods All ICU patients receiving CVVHD (diffusive haemodialysis) for AKI were analysed in a retrospective cohort study of mixed non/surgical patients at a tertiary renal centre over a 2-year period (December 2011 to November 2013). Children <18 years, patients on intermittent haemodialysis or patients requiring plasma exchange were excluded from analysis.
Results A total of 2,297 patients were admitted to the ICU, of which 14% (319) required CRRT. Thirteen patients were excluded from analysis; n = 306, of which 58% were male. Causes of AKI included sepsis (37%), surgery (13%, of which 82% were emergency procedures) and vascular events (9%). Mean values for patients requiring RRT versus all ICU patients: age (65 vs. 62.5 years), APACHE II score (21.2 vs. 14.8), length of stay (13 vs. 8.2 days). Forty-seven per cent of patients received incident dialysis <24 hours of admission, with mean flow rates of 31 ml/kg/hour (2 l) in 39%. Mortality at hospital discharge was 56% for RRT versus 20% in all ICU patients admitted over the same time period.
Conclusion The reported incidence of AKI in critical care ranges from 20 to 50%, with the highest rates seen in sepsis [1]. Utilisation of CRRT for AKI is higher at our centre than the described 5% [2], potentially due to close collaboration between critical care and nephrology [3] or relatively lenient ICU admission criteria. Increasing mortality was seen with age, APACHE II score and delay in initiation of RRT. Prospective analysis is required to look at determining biomarkers for AKI and risk factors for mortality; dynamic monitoring of haemodynamic responders (↑MAP, ↓vasopressor requirement <24 hours), percentage creatinine decrease [4], severity-of-illness scores and urine output. Results of current RCTs are awaited, which may provide more information on mode of clearance, flow rates and early versus standard initiation of RRT to more accurately prognose patients' outcomes.
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P392

Renal replacement therapy in very elderly critical care patients

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Introduction The very elderly (>80 years) UK population is increasing and along with it there is an increased utilisation of critical care resources [1]. The use of chronological age as a bar to treatment is unethical, yet a discrepancy of opinion remains between the disinclined and the elderly advocate intensivist [2]. Acute kidney injury requiring dialysis is a frequent complication of critical illness and is associated with high morbidity and mortality. An increased risk is seen with age due to the high prevalence of risk factors and chronic kidney disease in the elderly [3].
Methods Very elderly patients admitted to our tertiary referral ITU were included in a 2-year (December 2011 to November 2013) retrospective cohort analysis. The outcome of those receiving RRT was reviewed.
Results There were 2,297 admissions to the ITU, of which 323 (14%) were classified as very elderly with a mean APACHE II score of 17.3. RRT was utilised in 12.4% (n = 40) of the very elderly patients with a mean APACHE II score of 25. Forty-five per cent of AKI was due to sepsis and 25% due to emergency surgery. ITU very elderly patient mortality was 30.1%, and in those who received RRT was 42% and 67% at ITU and hospital discharge respectively. Recovery of renal function was seen in 19 patients at ITU discharge, of these 11 survived to hospital discharge. Two patients required ongoing IHD in the community.
Conclusion Current predictions estimate that the very elderly UK population will almost double by 2030 [4]. The biggest uptake in acceptance of chronic RRT has been in the elderly [5], where no difference has been shown in health-related quality of life from the general dialysis population [6]. Our experience suggests that RRT has a role in the critically ill elderly patient, with 33% surviving to hospital discharge. The challenge is identifying those most likely to benefit from a cohort with multiple comorbidities, against the available resources, rising demand for critical care in an aging population and increasing expectations [7].
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P393

Preventing continuous renal replacement therapies (CRRT)-induced hypophosphatemia using a phosphate-containing CRRT solution in the setting of regional citrate anticoagulation

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Introduction Phosphate depletion is a known issue during continuous renal replacement therapies (CRRT) with an incidence of hypophosphatemia up to 80% when standard CRRT solutions are used. The aim was to evaluate the effects on serum phosphate and phosphorus supplementation needs of a regional citrate anticoagulation (RCA) protocol for CRRT combining the use of citrate with a phosphate-containing CRRT solution.
Methods In critically ill heart surgery patients undergoing CRRT for acute kidney injury, we adopted RCA in a CVVH or CVVHDF modality combining a commercially available citrate solution (18 mmol/l) with a phosphate-containing CRRT solution as dialysate and/or replacement fluid (HCO_3^- 30 mmol/l, phosphate 1.2). The prescribed CRRT dose,

corrected for predilution, was at least 25 ml/kg/hour with about 50 to 60% of dialysis dose given as phosphate-containing solution. By convention, hypophosphatemia was defined as follows: mild (<0.81 mmol/l), moderate (<0.61 mmol/l) and severe (<0.32 mmol/l).
Results Forty-eight patients were treated with RCA-CRRT for at least 72 hours (total running time 12,502 hours). Two-hundred and nineteen RCA-CVVH circuits were used with a mean filter life of 57.1 ± 41.7 hours (median 47, IQR 24 to 83). Acid–base status was adequately maintained without the need for additional interventions on RCA-CRRT parameters (pH 7.43 (7.40 to 7.47), bicarbonate 25.3 mmol/l (23.8 to 26.6), BE 0.9 (–0.7 to 2.4); median (IQR)). Serum phosphate was steadily maintained in a narrow range throughout RCA-CRRT days (1.2 mmol/l (0.97 to 1.45); median (IQR)). At some times during CRRT, only 10 out of 48 patients (20.8%) received a low amount of phosphate supplementation (D-fructose-1,6-diphosphate 1.05 ± 2.04 g/day) for mild (n = 7) to moderate (n = 3) hypophosphatemia. In particular, considering all patients, only 33 out of 513 serum phosphorus determinations met the criteria for mild (n = 24) to moderate (n = 9) hypophosphatemia. Severe hypophosphatemia was never observed.
Conclusion The use of a phosphate-containing CRRT solution, accounting for about 50 to 60% of the CRRT dose in the setting of RCA-CVVH or RCA-CVVHDF, allowed one to prevent CRRT-induced phosphate depletion in most of the patients, minimizing the need for phosphate supplementation and maintaining phosphorus levels in a near-normal range throughout CRRT days.

P394

Elimination rates of electrolytes, vitamins and trace elements during continuous renal replacement therapy with citrate CVVHD: influence of treatment dose

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Introduction During continuous renal replacement therapy (CRRT), relevant losses of nutritional substrates, vitamins and trace elements due to diffusive transport and elimination via the filter may occur. We investigated the amount of these losses with regard to treatment dose during a 72-hour treatment period.
Methods Forty-one patients with CRRT were investigated. Patients were treated with a citrate CVVHD with different standard doses resulting in a treatment dose range from 14 to 53 (median 27) ml/kg/hour. Losses were calculated from substrate concentrations in the dialysate × (dialysate + ultrafiltration) flow. During a 72-hour treatment period, each 24 hours were determined separately. Regression analysis was performed for the respective per-day losses related to treatment doses.
Results Regression analyses of ER for Ca^{2+}, Mg^{2+}, PO_4^{2-}, zinc, folic acid and vitamin B12 are shown in Table 1 as the median and interquartile range.

Table 1 (abstract P394). ER elimination rates

Parameter	Average daily ER	Day 1 R^2	Day 2 R^2	Day 3 R^2
Ca^{2+} (mmol/day)	97 (83 to 107)	0.2125	0.2448	0.2315
Mg^{2+} (mmol/day)	6 (3 to 9)	0.0247	0.0708	0.0733
PO_4^{2-} (mmol/day)	53 (40 to 69)	0.003	0.0556	0.0012
Zinc (µmol/day)	46 (27 to 73)	0.005	0.0527	0.0502
Folic acid (nmol/day)	268 (180 to 388)	0.0935	0.0031	0.0353
Vitamin B12 (pmol/day)	2,060 (1,690 to 2,558)	0.0009	0.0092	0.0152

Conclusion Only Ca^{2+} showed a correlation of ER and treatment dose. Mg^{2+}, PO_4^{2-} zinc, folic acid and vitamin B12 were eliminated without a correlation to treatment dose.

P395

Evaluation of functional differences between two anticoagulation methods used in continuous renal replacement therapy in critical patients

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Introduction The aim of this study is to analyze the functional alterations that may influence the final result when using citrate versus heparin anticoagulation in critically ill patients [1].
Methods We performed a retrospective and analytical study including patients exclusively submitted to citrate or heparin through years 2011 and 2012. Included were demographic data with SAPS II, SOFA, RIFLE scores and mortality rate. For functional analysis we consider the timing of the beginning, duration, loss of dose and loss of creatinine clearance. We analyzed dialitrauma, considering the variation of: potassium, total and ionized calcium, magnesium, sodium, phosphorus, pH, lactates, bicarbonate, platelets, albumin, creatinine and urea. Data are presented as the average and standard deviations. To access the influence of dose and clearance losses on mortality, we used logistic regression test.
Results The study included 44 patients in the citrate group versus 61 in the heparin group. We found no statistical significant differences for: age (P = 0.06); SAPS II (P = 0.28); SOFA (P = 0.19); the timing of beginning of the technique (P = 0.61), with 34.8% versus 47.5% of patients in R (RIFLE), 27.8% versus 18% in I (RIFLE) and 16% versus 21% in F (RIFLE); duration of the technique (P = 0.74) and length of stay. Although we noticed a greater loss of dose and absolute creatinine clearance in the citrate group, this had no statistical significance (P = 0.18 and P = 0.13). The mortality found for citrate and heparin groups was 60.4% and 39.4% respectively. The differences with statistical significance related to dialitrauma emerged in K^+ (P = 0.03), Ca^{2+} (P = 0.02), Na^+ (P = 0.004), platelets (P = 0.002), pH (P = 0.02) and bicarbonate (P = 0.0001). Logistic regression for mortality in the citrate versus heparin groups showed the following values: effective dose (ROC 0.435 vs. ROC 0.663), clearance (ROC 0.606 vs. ROC 0.663), SAPS II (ROC 0.482 vs. ROC 0.696), SOFA (ROC 0.713 vs. ROC 0.696) and RIFLE (ROC 0.695 vs. ROC 0.636).
Conclusion We may say that there are functional differences that must be taken into account. Despite not having statistical significance on this sample, losses of dose and creatinine clearance showed a direct relation with mortality.
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P396

Development of key performance indicators for renal replacement therapy in adult intensive care to guide safe and cost-effective therapy

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Introduction Renal replacement therapy (RRT) is common. We undertook to develop and report some key performance indicators (KPIs) to monitor our provision of this costly therapy. We utilised data already collected in an electronic clinical information system that records the care received by our patients. We reduced our prescribed RRT dose to 25 ml/kg/hour in December 2011 following an appraisal of the literature [1]. We assessed whether the KPIs informed us if our practice changed and such changes were sustained.
Methods We calculate the hourly effluent rate corrected for a patient's predicted body weight, and the lifespan of haemofilters. This takes less than 30 minutes each month. Statistical process control charts (SPCs) are used to assimilate the indicators over time.

Table 1 (abstract P396). KPI for renal replacement therapy 2013

	Jan 2013	Feb 2013	Mar 2013	Apr 2013	May 2013	Jun 2013	Jul 2013	Aug 2013	Sep 2013	Oct 2013	Nov 2013	Dec 2013
AICU-RBH no. of patients on CVVHD	**8**	**8**	**17**	**15**	**6**	**7**	**13**	**12**	**9**	**15**	**21**	
AICU-RBH no. of patient-days on CVVHD	61	73	98	86	65	85	44	77	112	119	137	
AICU-RBH filter started	32	30	52	47	34	50	26	60	71	62	74	
AICU-RBH hours of CVVHD	1,154	1,463	1,769	1,532	1,317	1,565	693	1,422	2,215	2,157	2,393	
AICU-RBH estimated no bags	544	602	763	689	636	695	294	629	995	952	1,054	
AICU-RBH fluid cost (£)	4,994	5,526	7,004	6,325	5,838	6,380	2,699	5,774	9,134	8,739	9,676	
AICU-RBH ml/kg/hour actual	39.90	28.17	29.10	30.53	33.93	31.52	31.25	29.90	30.40	32.55	32.36	
AICU-RBH ml/kg/hour 24 hours	32.46	23.44	22.23	23.60	29.32	24.43	21.34	23.93	25.25	25.38	24.01	
AICU-RBH percent on CVVHDF	0.79	0.84	0.75	0.67	0.84	0.77	0.66	0.77	0.82	0.76	0.73	
AICU-RBH average filter life (hours)	36.06	48.77	34.02	32.60	38.74	31.30	26.65	23.70	31.20	34.79	32.34	
AICU-RBH filter cost (£)	2,477	2,322	4,025	3,638	2,632	3,870	2,012	4,644	5,495	4,799	5,728	
AICU-RBH effluent bags cost (£)	680	753	954	861	795	869	368	786	1,244	1,190	1,318	
AICU-RBH total consumable (£)	3,157	3,075	4,979	4,499	3,427	4,739	2,380	5,430	6,739	5,989	7,045	
AICU-RBH total cost CVVHD (£)	**8,151**	**8,601**	**11,983**	**10,824**	**9,265**	**11,119**	**5,079**	**11,204**	**15,873**	**14,728**	**16,721**	
AICU-RBH average cost per patient (£)	1,019	1,075	705	722	1,544	1,588	391	934	1,764	982	796	
AICU-RBH average cost per patient day (£)	134	118	122	126	143	131	115	146	142	124	122	

Results A total of 736 patients received RRT during the study. Prior to the dose change, the mean set and delivered doses were 39 and 31 ml/kg/hour respectively. Thereafter the mean set and delivered doses were 33 and 26 ml/kg/hour respectively. Whilst higher than our guideline dose, they are significantly less than the doses prior to the change in practice (both P <0.001). The SPC indicates that the change in practice has been sustained. See Figure 1 and Table 1.

Conclusion The KPIs could be produced quickly and allowed monitoring of the reduction in RRT dosing, assuring us that it is in excess of 20 ml/kg/hour. The KPIs did not require additional data collection processes. We are developing similar indicators for other organ systems, therapies and processes.

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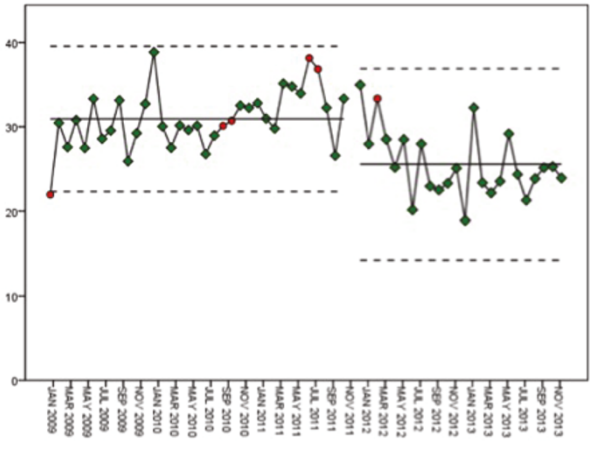

Figure 1 (abstract P396). Delivered dose of RRT each month.

P397

Effectiveness of sub-albumin protein leakage membrane EMIC2 in post-cardiac surgery rhabdomyolysis

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Introduction A high postoperative serum myoglobin (MyG) concentration predicts the incidence of acute kidney injury (AKI) and need for renal replacement therapy (RRT), as reported in several surgical settings. The incidence of such events in the ICU is reported to be 2 to 5% of all causes of AKI [1], but can even worsen in the case of cardiac surgery (40.3%) [1]. MyG is a small protein (17.8 kDa) that can be removed with RRT, typically in convection cases. New-generation membranes, removing sub-albumin protein molecular weight solutes, can be used in diffusive treatments (CVVHD) with the advantage of limiting albumin loss and easily combining with citrate anticoagulation, pivotal for cardio-surgical settings. We assessed the effectiveness of EMIC2 with citrate anticoagulation in AKI prevention of post-cardiac surgical patients.

Methods This is a case series of eight patients (mean age 62.7 years, five male, EuroSCORE log 15.61) in cardiac surgery on CPBP for 150 minutes

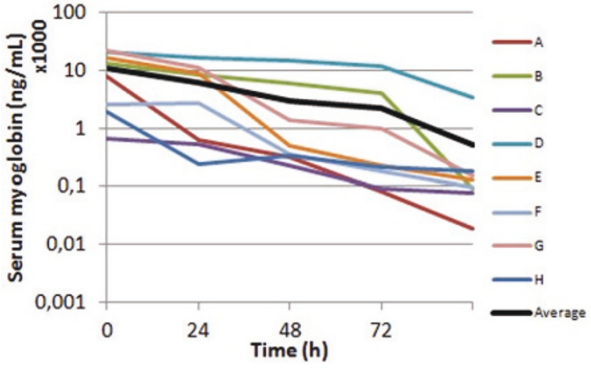

Figure 1 (abstract P397).

and mean aortic cross-clamping of 98 minutes (range 25 to 190). We measured MyG, procalcitonin (PCT), and creatinin (sCr) at ICU admission and, if serum MyG was higher than 600 mg/dl, the patient was treated with CVVHD-EMIC2–citrate anticoagulant within 12 hours of ICU admission for 72 hours and a dose of 2,000 ml/hour. Biochemical assays were obtained at 12, 24, and 72 hours and at ICU discharge.

Results The pretreatment MyG median value was 10,789 ng/ml; it significantly reduced on average 92.8% during CVVHD (see Figure 1) and it remained low at ICU discharge (median value 114 ng/ml). sCr remained stable (average time value equal to 0.94 mg/dl) during CVVHD; PCT also decreased over time with a reduction rate equal to 78% (from 5.35 ± 4.39 mg/dl to 1.23 ± 1.09 mg/dl at the end of CVVHD). Finally, six patients survived at 90 days.

Conclusion This small experience confirms that serum MyG is likely to increase in post-cardiac surgical high-risk patients and suggests a beneficial effect of CRRT treatments with EMIC2 membranes and citrate on serum MyG, potentially preventing AKI. Further larger assessment can be advised for confirmation.

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P398

Myoglobin removal of small-protein leakage membrane (EMIC2) in patients in the ICU: a case series

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Introduction Rhabdomyolysis is characterized by breakdown of striated muscle due to a great number of causes. Acute kidney injury (AKI) is a common complication as a consequence of high concentrations of circulating myoglobin (Mb). The AKI degree can vary but often requires dialysis, a condition which drastically worsens the ICU stay and prognosis. Since Mb overconcentration represents the cause of AKI, one of the therapy's aims should be its removal to prevent further kidney damage and to allow faster renal recovery. Both intermittent hemodialysis and high-volume CVVHF are poorly effective in removing Mb, while small-protein leakage membranes seem to be promising in this setting. The aim of our study was therefore to measure efficacy of Mb removal of a new high cutoff membrane (EMIC2; Fresenius, cutoff value 40 kDa) for continuous renal replacement therapies (CRRT) in the ICU setting.

Methods We report results of EMIC2-based treatments in seven patients (four male/three female) with different causes of rhabdomyolysis (trauma, sepsis, limb ischemia). Five patients had classic dialysis indications (persistent anuria) while in two patients treatment was prophylactically started. CRRT were delivered in CVVHD mode with the EMIC2 dialyzer and with loco-regional trisodium–citrate anticoagulation. Mb plasma levels were assessed each 12 hours while the removal rate, total body and dialyzer clearances were estimated by kinetic modeling as previously described [1]. Clinical data were also collected and both global and renal patient survival was reported.

Results The median Mb value at CRRT start was 6,971 ng/ml (range 4,679 to 48,011 ng/ml). CRRT were delivered with an average blood flow rate of 143 ± 45 ml/minute and a dialysate flow rate of 2,134 ± 1,334 ml/hour. These operating conditions allowed one to stop treatment on average after 75 ± 47 hours (median 54 hours) with a Mb reduction of 82.2% (range 99.4 to 44.4%). Overall median Mb removal per treatment was 59 mg (range 33 to 279 mg) mainly due to the first 24 hours of treatment (54 mg, range 20 to 187 mg). Only two patients had residual renal function that was in one case measured to account for only 7.45 mg Mb removal during the entire treatment. Six patients survived and recovered renal function with no dialysis need at present follow-up. One patient died during the ICU stay.

Conclusion Our data measured high performance of the EMIC2 membrane in Mb removal and confirm theoretical models indicating that CRRT with a high cutoff membrane can achieve major Mb removal within 24 hours with great superiority in comparison with all other available techniques.

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P399

Plasma filtration with dialysis (plasma diafiltration) in critically ill patients with acute liver failure

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Introduction Removing the middle molecular weight substances including cytokines and albumin-bound toxin could be effective for patients with acute liver failure (ALF). We have developed a new system, plasma filtration with dialysis (plasma diafiltration (PDF)) [1,2], and assessed its efficacy in multicenter analysis.

Methods A subgroup analysis of an observational study conducted in the ICUs of six hospitals. In PDF, simple plasma exchange is performed using a selective membrane plasma separator (Evaxclio EC-2A; Kawasumi Chemical Inc., Tokyo Japan), which has a sieving coefficient of 0.3 for albumin, while the dialysate flows outside the hollow fibers. The flow rate of the blood, dialysate, substitute and additional substitute was 80 to 100 ml/minute, 600 ml/hour, and 0 to 450 ml/hour according to the rate of water elimination and 150 ml/hour, respectively. As the substitute from the additional fluid line, we added 1,200 ml (150 ml/hour) of fresh frozen plasma followed by 50 ml of 25% albumin considering the loss of albumin by diffusion. As an anticoagulant, nafamostat mesilate (Torii Pharmaceutical Co. Ltd, Tokyo, Japan) was used at a rate of 15 to 25 mg/hour.

Results A multicenter study was underway from October 2005 to August 2011. We performed PDF on 65 patients with ALF (severe sepsis, 22; post operation, 15; fulminant hepatitis, 11; alcohol hepatitis, 3; graft versus host disease, 4; and others, 10). The serum total bilirubin, plasma PT-INR and the model for end-stage liver disease (MELD) score before the PDF procedure were 15.0 ± 8.15 mg/dl (average ± SD), 2.3 ± 1.5 and 35.8 ± 9.3, respectively. PDF was performed as 9.2 ± 13.2 sessions per patient and the overall 28-day survival rate was 68.5%. According to the severity of the MELD score, we stratified patients into three categories defined by the MELD score. The numbers of patients were 15 (23%) in score 20 to 29, 30 (46%) in score 30 to 39 and 19 (29%) in score over 40. The 28-day survival rates were 73.3%, 40% and 16%, respectively.

Conclusion PDF may be a useful blood purification therapy for ALF, but PDF should be performed below a MELD score of 30.

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P400

Efficacy of continuous plasma diafiltration therapy

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Introduction Acute liver failure (ALF) is a critical illness with high mortality. Plasma diafiltration (PDF) is a blood purification therapy in which simple plasma exchange is performed using a selective membrane plasma separator while the dialysate flows outside the hollow fibers. While several studies demonstrated that PDF therapy is a useful blood purification therapy for patients with ALF, PDF therapy is often difficult to employ in ALF patients complicated with multiple organ failure, especially in those with unstable hemodynamics. Furthermore, it is likely to re-occur immediately after PDF therapy. We developed continuous PDF (CPDF) as a new concept in PDF therapy, and assessed its efficacy and safety in ALF patients compared with conventional plasma exchange (PE) plus continuous hemodiafiltration (CHDF) therapy in this study.

Methods Ten ALF patients (gender: male/female = 6/4, age: 47 ± 14) employed CPDF therapy. The primary outcomes were altered liver function, measured by the model for end-stage liver disease (MELD) score, and total bilirubin and prothrombin time International

Normalized Ratio (PT-INR), 5 days after CPDF therapy. Secondary outcomes included Sequential Organ Failure Assessment (SOFA) scores, 5 days after CPDF therapy, and the survival rate 14 days after this therapy.
Results The MELD score (34.5 to 28.0; $P = 0.005$), total bilirubin (10.9 to 7.25 mg/dl; $P = 0.048$), PT-INR (1.89 to 1.31; $P = 0.084$), and SOFA score (10.0 to 7.5; $P < 0.039$) were improved 5 days after CPDF therapy. Nine patients were alive and one patient died due to acute pancreatitis, complicated by ALF. The efficacy of CPDF therapy for maintaining liver function and renal function was not inferior to PE plus CHDF therapy. Parameters of renal function such as the creatinine value were also improved 5 days after CPDF therapy. Circulation parameters such as mean arterial pressure and heart rate were maintained without inotropic and vasopressor support during the CPDF treatment period. The oxygenation index (PaO_2/FiO_2) as a measure of pulmonary function tended to increase after this treatment. We could employ this treatment without any adverse events, such as infections and unstable hemodynamics.
Conclusion In the present study, CPDF therapy safely supported liver function and generally improved the condition of critically ill patients with ALF.

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Hemodialysis with high cutoff membranes improves tissue perfusion in severe sepsis: preliminary data of the Sepsis in Florence sTudy (SIFT)

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Introduction It has been demonstrated that blood purification therapy performed by means of venovenous hemodialysis with high cutoff membranes (HCO-CVVHD) may modulate the host inflammatory response in septic patients with acute kidney injury (AKI), potentially limiting organ dysfunction. Improvement in hemodynamics and respiratory function has been described during HCO-CVVHD treatment [1]. The Sepsis in Florence sTudy (SIFT) has been designed to evaluate changes in inflammatory biomarkers and tissue oxygenation/perfusion indexes in septic ICU patients with AKI during HCO-CVVHD.
Methods Patients with microbiologically confirmed severe sepsis/septic shock and AKI (RIFLE criteria F or more) treated with HCO-CVVHD, started within 12 hours from the diagnosis, were prospectively included in the study. The cumulative vasopressor index (CVI), C-reactive protein levels (CRP), serum lactate concentration (Lac) and central venous oxygen saturation ($ScvO_2$) were measured before (T0h) and at 24 hours and 48 hours after HCO-CVVHD initiation. Data are expressed as the median (range). The Mann–Whitney U test was applied to detect differences in CVI, CRP, Lac and $ScvO_2$ at the three time points (statistical significance for $P < 0.05$).
Results In 16 ICUs, a total of 16 patients (six cardiac surgery, four abdominal surgery and six medical) met the inclusion criteria and were enrolled in the study. A significant reduction in CRP levels was observed over time: 263 (216 to 358) mg/dl at T0h to 153 (56 to 186) mg/dl at T48h ($P < 0.05$). $ScvO_2$ significantly increased from 45 (40 to 55)% at T0h to 75 (68 to 77)% at T48h ($P < 0.05$). Finally, serum lactate decreased from 5.1 (3.0 to 9.5) mmol/l at T0h to 1.6 (1.0 to 4.6) mmol/l at T48h ($P < 0.05$). Conversely, CVI did not significantly reduce over time (8.2 (4 to 9) at T0h vs. 4.5 (4 to 8) at T48h, $P > 0.05$).
Conclusion Our preliminary data show that patients with sepsis-related AKI may benefit from early treatment with HCO-CVVHD. The modulation of proinflammatory and anti-inflammatory mediators, as previously demonstrated [1], may improve microcirculation, tissue perfusion and cellular oxygenation. Although promising, our results must be confirmed at the end of the study with larger observations. Finally, a subgroup analysis is absolutely mandatory in order to explore different behaviors of tissue perfusion indexes in different populations of patients.
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P402

Pharmacodynamics and pharmacokinetics of ciprofloxacin during sustained low-efficiency dialysis

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Introduction Little information is available regarding ciprofloxacin pharmacokinetics and pharmacodynamics in sepsis patients receiving sustained low-efficiency dialysis (SLED). This study determined the pharmacokinetics and simulated pharmacodynamics of ciprofloxacin in ICU patients during SLED.
Methods This study was a prospective evaluation of ciprofloxacin pharmacokinetics in patients with sepsis and >18 years of age, urine output <200 ml/day and receiving SLED for at least 8 hours. Following informed consent, plasma samples were collected at baseline and 1, 2, 4, and 8 hours after a ciprofloxacin 400 mg dose i.v. during SLED and post-SLED therapy at the same times. Dialysate samples were collected at 4-hour intervals during SLED. Pharmacokinetic parameters were determined using WinNonlin and compared between the two periods. Simulated pharmacodynamic parameters were determined for *Pseudomonas aeruginosa* using MIC = 2.
Results A total of seven patients (four male, three female, age 56.9 ± 7.6, APACHE II 26.8 ± 2.4) were enrolled. Ciprofloxacin was cleared relatively rapidly with a half-life of 6.9 hours and a Ke of 0.108/hour during SLED compared with 11.9 hours and 0.057/hour post-SLED ($P < 0.05$). Simulated pharmacodynamics demonstrated inadequate coverage for *P. aeruginosa* during SLED with Cmax/MIC ratio 5.7 ± 1.2 and AUC/MIC 77.5 ± 22.3.
Conclusion Ciprofloxacin is rapidly cleared during SLED similar to clearance during normal renal function, which may result in adequate pharmacodynamic coverage for some pathogens.

P403

Pharmacokinetics of meropenem during continuous renal replacement therapy in critically ill patients

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Introduction Antibiotic dosing for patients with acute renal failure receiving continuous renal replacement therapy (CRRT) is a clinical challenge. The aim of this study was to investigate the pharmacokinetics of meropenem (M) during CRRT.
Methods A prospective and multicenter study was conducted at seven hospitals. Fifteen critically ill patients undergoing either continuous venovenous hemofiltration (CVVHF) or hemodiafiltration (CVVHDF) were included. Serum and ultrafiltrate (UF) levels of M were determined by liquid chromatography. Blood samples were drawn 24 hours after starting CRRT at 08:00 a.m., 09:00 a.m., 10:00 a.m., 01:00 p.m., 06:00 p.m., 20:00 p.m. and 08:00 a.m. of the following day. CRRT clearance (Cl), total amount of M in the UF (MUF), percentage of the dose extracted by CRRT (EF) and the AUC (ng/hour/ml) were calculated.
Results Nine patients were treated with CVVHDF and six with CVVHF. M (0.5 to 2 g) was administered every 6 to 12 h by i.v. infusion over 15 minutes. Data (mean and SD) concerning the dialysate flow rate (DF; ml/hour), blood flow rate (ml/minute) and the average UF rate (ml/kg/hour) for CRRT techniques are shown in Table 1. Pharmacokinetic

Table 1 (abstract P403). Parameters of CRRT techniques

	CVVHF ($n = 6$)	CVVHDF ($n = 9$)
DF rate		964/94
Blood flow rate	190/33	187/29
UF rate	37.7/5.7	29.8/15.6

Table 2 (abstract P403). Pharmacokinetic parameters for meropenem

	CVVHF	CVVHDF
AUC	357/188	433/369
M dose (g/day)	1.7/0.4	2.2/1.4
MUF (mg)	338/104	625/499
EF (%)	28/13	30/26
M Cl (l/hour)	1.2/0.7	1.7/1.5

parameters for M are depicted in Table 2. No differences in either EF or M Cl between the two CRRT techniques were observed.
Conclusion A significant removal of M by CVVHF/CVVHDF was observed. Dose adjustment is necessary in critically ill patients receiving CRRT.
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P404

Impact of ideal versus estimated body weight on haemofiltration dosing in critically ill patients with AKI

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Introduction Acute kidney injury (AKI) in the critically ill is an independent risk factor for adverse outcome [1]. Previously, it was suggested that high-volume haemofiltration (HVHF) may confer a mortality benefit and lead to a reduction in organ failure compared with standard ultrafiltration rates (UF) [2]. This was not confirmed by a recent investigation [3]. It has also not been determined whether ideal (IBW) or estimated/actual body weight (E/ABW) was used to calculate UF rates. We sought to determine what impact different weight calculations have on delivered UF rates.
Methods A retrospective single-centre study in a tertiary referral institution. Continuous venovenous haemodiafiltration (CVVHDF) was administered according to the patient's IBW. The delivered UF rate was then calculated both for IBW and E/ABW. The latter was based on measurements obtained at the time of ICU admission. We compared the highest predilution, postdilution and dialysate volume administered each day according to the different weight estimate measurements respectively. Student's *t* tests and chi-square tests were used for statistical analysis ($P < 0.05$).
Results Data from 33 patients receiving renal replacement therapy were analysed. Mean time (± SD) of treatment interruption was 1.4 ± 2.7 hours/day due to filter changes, transfers for CT scans and surgical procedures. Therefore, 94% of the prescribed dose was delivered. There was a mean of 2.3 filtration dose prescriptions per patient over the observation period (due to changing clinical conditions), with a total of 77 dose adaptations. Mean E/ABW was significantly higher than calculated IBW (76.3 kg vs. 61.4 kg), and thus a difference of 14.9 kg (95% CI = 9.2 to 20.6 kg). This resulted in a significant difference in mean filtration dose delivered of 33.1 ml/kg/hour for E/ABW versus 39.7 ml/kg/hour for IBW respectively ($P < 0.001$). As a consequence, in 29.6% (8/27) of cases where HVHDF (>35 ml/kg/hour) was prescribed, standard volume haemodiafiltration (SVHDF) (≤35 ml/kg/hour) was delivered. In 10% (5/50) of cases where SVHDF was prescribed, HVHDF was delivered ($P < 0.001$).
Conclusion We conclude that the delivered UF rate in our cohort of patients differed significantly depending on measured or calculated body weight. In almost one-third of cases where HVHDF was prescribed, SVHDF was delivered. As many interventions in the ICU are based on IBW and daily weighing of patients is not uniformly practiced, this makes comparison of data difficult.
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P405

ICU patients treated with RRT for AKI who have chronic kidney disease have better 1-year outcome compared with patients with better kidney function

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Introduction Chronic kidney disease (CKD) is a risk factor for developing acute kidney injury (AKI) with need for renal replacement therapy (RRT). AKI-RRT is associated with important short-term mortality, and recent data showed there is also important increased risk for 1-year mortality. The aim of this study is to evaluate variables associated with 1-year survival, and in particular the impact of baseline CKD in a cohort of AKI-RRT patients.
Methods A single-center observational study in a 50-bed ICU tertiary care hospital. During the study period August 2004 to December 2012, all consecutive adult AKI-RRT patients were included. Data were retrieved from the electronic ICU patient file, the electronic hospital patient file and the electronic ICU-RRT database. Long-term outcome data were collected by a telephone survey.
Results During the 9-year study period, a total of 1,291 AKI-RRT patients were included. Short-term mortality at day 30 was 47.2%; mortality at 1 year was 64.3%. Compared with nonsurvivors, 1-year survivors had similar age (65 vs. 67 years, $P = 0.077$), worse kidney function at baseline (eGFR 46 vs. 52 ml/minute/1.73 m^2, $P = 0.001$; CKD stage ≥3 65% vs. 58%, $P = 0.019$), a greater proportion was male (69.0% vs. 63.2%, $P = 0.048$), and more were admitted to the cardiac surgery ICU (39% vs. 46%, $P = 0.012$). They were less severely ill as illustrated by lower SAPS 2 score at ICU admission (52 vs. 69, $P < 0.001$), and at the time of initiation of RRT, and a lower SOFA score (9 vs. 11; $P < 0.001$). A smaller proportion was on mechanical ventilation (85.1% vs. 89.7%, $P = 0.042$) and on vasoactive drugs (45.7% vs. 63.9%, $P < 0.001$). Survivors had earlier initiation of RRT (2 vs. 3 days, $P = 0.034$), and more frequently intermittent RRT was used (84.8% vs. 63.2%; $P < 0.001$). When corrected for gender, age, severity of illness, and modality and timing of RRT, worse baseline kidney function, defined as CKD stage ≥3, remained associated with better 1-year survival (odds ratio 1.6, 95% CI: 1.1 to 2.2, $P = 0.011$).
Conclusion In ICU patients who had AKI-RRT, 1-year survival was associated with lower severity of illness. Surprisingly, worse kidney function or CKD stage ≥3 was also associated with long-term survival. This effect remained present after adjudication for relevant covariates.

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Long-term outcomes in acute kidney injury patients treated with renal replacement therapy who were alive at hospital discharge

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Introduction Acute kidney injury (AKI) treated with renal replacement therapy (RRT) in ICU patients is associated with high mortality, chronic kidney disease (CKD) (eGFR <60 ml/minute/1.73 m^2, or CKD stage ≥3) and end-stage kidney disease (ESKD). Data on long-term outcomes vary among studies due to differences in age, CKD, severity of illness, RRT modality and timing of initiation of RRT. Long-term patient and kidney outcomes in AKI-RRT patients were evaluated in this study.
Methods A retrospective study of all consecutive treated AKI-RRT patients in a 50-bed ICU academic hospital from August 2004 to December 2012. Data were retrieved from the electronic ICU, RRT and hospital patient files. Long-term outcomes data were obtained by a telephone survey.
Results During the study period 1,291 ICU patients were treated with RRT for AKI. Mortality was 47.2% at day 30 and 57.2% at hospital discharge. Mortality in hospital survivors showed an important increase until 3-year follow-up, and a moderate increase later (1 year: 14.4%, 2 years: 20%, 3 years: 35.7%, and 7 years: 39%). In-hospital survivors' Scr and eGFR at baseline were comparable to 1-year follow-up (1.4 vs.

1.4 mg/dl, $P = 0.162$, respectively 46 vs. 51 ml/minute/1.73 m^2) and we observed an increase of CKD stage in 36.0% of patients, a decrease in 36.3%, and stable CKD stage in 27.7%. A total 43.1% of patients with CKD stage <3 at baseline had an increase to CKD stage ≥3 at 1 year. A total 26.6% of patients with CKD stage ≥3 at baseline decreased to CKD stage <3. A total of 8.3% of hospital survivors developed ESKD. Patients with increase of CKD stage had similar age (67 vs. 64 years, $P = 0.145$), SAPS 2 (57 vs. 51, $P = 0.858$), and SOFA score (9 vs. 9, $P = 0.275$) compared with patients with stable or decreased CKD stage. There were no differences in type of ICU, modality of RRT, or number of patients treated with vasopressors (44% vs. 47%, $P = 0.617$) or invasive ventilation (84% vs. 81%, $P = 0.496$). However, these patients were more probably male (76.9% vs. 65.6%, P = 0.042), had lower Scr at baseline (1.1 vs. 1.7 mg/dl, $P < 0.001$) and at ICU admission (1.7 vs. 2.4 mg/dl, $P < 0.001$), and were started on RRT later (3 vs. 2 days, $P = 0.008$).

Conclusion The annual mortality in AKI-RRT hospital survivors is approximately 10% per year during the first 3 years of follow-up. One-third of patients had an increase of CKD stage at 1 year of follow-up and almost one-half of patients who had eGFR >60 ml/minute/1.73 m^2 developed CKD. Patients who had an increase of CKD had similar severity of illness, but lower Scr at baseline and at ICU admission, and had later initiation of RRT compared with patients who had stable or decreased CKD stage.

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Polymyxin B-immobilized fiber hemoperfusion therapy improves sepsis-related immunosuppression

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Introduction Sepsis-induced immunosuppression has long been considered a factor in the late mortality of sepsis patients, but little is known about the immunity of immunocompetent cells and the effect of polymyxin B-immobilized fiber hemoperfusion therapy (PMX-DHP) on sepsis-induced immunosuppression. The present study was designed to evaluate the effect of PMX-DHP on recovery from sepsis-related immunodeficiency.

Methods Patients with septic shock who were treated with PMX-DHP were enrolled in this study. Study 1: (1) numbers of peripheral lymphocytes and $CD4^+$ T cells, especially regulatory T cells (Tregs), and serum cytokine levels were examined to evaluate the effects of PMX-DHP in septic shock patients. (2) Peripheral blood mononuclear cells (PBMCs) in these patients were examined to evaluate inflammatory cytokine production before and after PMX-DHP. The obtained PBMCs were stimulated with interleukin (IL)-2 and IL-12, anti-CD3 antibody, or lipopolysaccharide for 24 hours, and tumor necrosis factor alpha and interferon-gamma (IFNγ) production in the culture supernatants was measured using enzyme-linked immunosorbent assay. Study 2: whole blood from patients with sepsis was incubated with a polymyxin B-immobilized filter (cut into small sizes) for small animals for 2 hours (PMX group), or were treated with 200 μg polymyxin B for 2 hours (PLB group), or were not treated (sepsis group). IFNγ production by PBMCs was compared among the three groups.

Results Study 1: (1) the number of $CD4^+$ T cells was lower and the percentage of Tregs in $CD4^+$ T cells was higher in septic shock patients compared with those without shock. A significant increase in the number of $CD4^+$ T cells, a significant decrease in the percentage of Tregs in the $CD4^+$ T-cell population, and a significant decrease in serum IL-10 levels were observed 24 hours after PMX-DHP in septic shock patients who survived compared with those who did not. (2) IFNγ production by PBMCs was significantly lower in patients with sepsis than in healthy volunteers. IFNγ production by IL-2-stimulated and IL-12-stimulated PBMCs significantly increased after PMX-DHP therapy. Study 2: IFNγ production by PBMCs in patients with sepsis increased significantly in the PMX and PLB groups compared with that in the sepsis group.

Conclusion PMX-DHP directly decreased the number and percentage of Tregs in peripheral blood circulating $CD4^+$ T cells in patients with septic shock. PMX-DHP improved IFNγ production by natural killer (NK)/NKT cells in patients with septic shock. Therefore, PMX-DHP could improve sepsis-related immunosuppression.

P408

Endotoxin activity assay and polymyxin B hemoperfusion use in a cohort of critically ill patients

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Introduction Endotoxin plays a crucial role in the pathogenesis of severe sepsis and septic shock (SS&SSh) [1]. The aim of this study is to analyze the impact of extracorporeal endotoxin removal with polymyxin B hemoperfusion (PMX-DHP) (Toraymyxin®).

Methods All patients admitted to our ICU between 1 April 2011 and 30 June 2013 who developed SS&SSh and underwent endotoxin activity assay (EAA) measurement were retrospectively evaluated.

Results During the study period, EAA was dosed in 100 patients. Eighty-one patients were affected by septic shock. The source of infection was identified in 70.4% of cases (45% abdominal) and the percentage of microbiologically confirmed episodes was 77% (81% Gram-negatives). The mortality rate was 49%. The mean EAA level was 0.66 ± 0.2, and in 66% of patients the value was higher than 0.6. No significant differences were found in terms of SAPS II ($P = 0.32$) and SOFA score ($P = 0.67$), according to EAA level (>/≤0.6). Patients with levels >0.6 presented a higher percentage of microbiologically confirmed infections (84% vs. 66%; $P = 0.09$). Thirty-two of 66 patients with EAA >0.6 were treated with Toraymyxin®. No complications leading to treatment interruption were recorded and a relevant decrease of cardiovascular SOFA score and lactate levels were observed 72 hours after treatment ($P = 0.05$ and $P = 0.06$, respectively). Source control and Toraymyxin® treatment resulted as the only modifiable factors improving the ICU survival rate (Table 1).

Table 1 (abstract P408). Multivariate analysis for ICU mortality risk factors

	P value	OR (95% CI)
SAPS II score	0.04	1.1 (1.01 to 1.1)
Septic shock	0.02	10.4 (1.5 to 71)
PMX-DHP	0.04	0.2 (0.1 to 0.9)
Source control	0.01	0.1 (0.03 to 0.5)

Conclusion EAA is a rapid and reliable method to identify patients who may be treated with polymyxin B hemoperfusion. Source control and extracorporeal endotoxin removal have appeared as two effective interventions that should be implemented in the early management of patients with SS&SSh.

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P409

Awakening and Breathing Coordination, Delirium Monitoring and Early Mobility bundle in adult ICU patients: a preliminary cost analysis

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Introduction We previously demonstrated a significant increase in the number of ventilator-free days and reduced the rate of delirium in ICU patients treated with the Awakening and Breathing Coordination, Delirium Monitoring and Early Mobility (ABCDE) bundle. This study investigated whether implementation of the ABCDE bundle was cost-effective at an academic medical center.

Methods A *post-hoc* cost-effectiveness study was done following the before–after ABCDE bundle implementation study. The bundle

consisted of the following components: daily spontaneous awakening trials (SATs); daily spontaneous breathing trials coordinated with the SATs; delirium monitoring; and early mobility. The study's primary endpoint was the cost-effectiveness of the ABCDE bundle in terms of the bundle's cost to prevent 1 day of mechanical ventilation (MV) or 1 day of delirium for all patients, as well as for a subgroup of non-MV patients. All cost-effectiveness ratios (CERs) were constructed from the hospital's cost perspective. The economic analyses were carried out in two steps. First, the mean cost per patient per hospital stay and total costs in the pre-ABCDE and post-ABCDE bundle periods were compared. Next, CERs of each respective primary endpoint were computed as incremental costs of implementing the bundle to prevent 1 day of MV and to prevent 1 day of delirium. $P < 0.05$ was considered statistically significant.

Results Data were analyzed from 146 and 150 patients in the pre-ABCDE and post-ABCDE groups respectively. There were mean decreases of 0.59 MV days and 0.83 delirium days between the pre and post bundle implementation. The mean costs (per patient per ICU stay) of implementing the bundle components were significantly higher in the post-ABCDE cohort versus the pre-ABCDE cohort ($191 vs. $92, $P < 0.0001$), with an additional increase in total costs ($8,930 vs. $8,624, $P = 0.0233$). Costs to prevent 1 day of MV and to prevent 1 day of delirium were $552 and $368 respectively. In the non-MV patients, the post-ABCDE bundle demonstrated fewer days of delirium than the pre-ABCDE cohort (0.8 vs. 1.13 days, $P < 0.05$) but had higher overall costs ($5,417 vs. $4,546, $P < 0.05$), resulting in a cost of $2,639 to prevent 1 day of delirium in a non-MV patient.

Conclusion Implementing the ABCDE bundle in adult ICU patients appears to be a feasible cost-effective strategy when considering costs of mechanical ventilation and ICU delirium.

P410

An assessment of long-term sleep quality using actigraphy in survivors of critical illness

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Introduction Recent studies have suggested that critical illness survivors experience long-term sleep disruption [1,2]. The Actigraph device is a sleep watch that has been shown to have equivalent accuracy to polysomnography and previously used during critical illness to show sleep disruption [3]. Our objective was to assess patients long-term sleep quality using the Actigraph device.

Methods Study patients were selected from a 24-bed multidisciplinary ICU. Thirteen patients who were ≥18 years old, stayed longer than 4 days in the ICU and did not have and acute brain injury were followed up at 2 months post hospital discharge. The Actigraph device was given to patients to take home and worn for 72 hours. Previously validated algorithms were used to analyze sleep and wake cycles [4]. Additionally, patient completed the Pittsburgh Sleep Quality Index (PQSI), as a measure of subjective sleep quality.

Results Sixty-two percent of patients at 2 months post hospital discharge reported poor sleep quality as per the PSQI. The Actigraph results showed patients' average total sleep time was 6.15 hours, with a sleep efficiency of 78%. The mean time to fall asleep was 12 minutes. Patients had an average of 11 awakenings per night and were awake for an average of 7 minutes during the awakenings. There were no associations found between patients' perceived sleep quality and total sleep, sleep efficiency or sleep disruptions. Patients' severity of illness, as measured by the APACHE II score, was statistically associated with lower total sleep time ($\beta = -12.6$, $P = 0.019$), reduced sleep efficiency ($\beta = -1.18$, $P = 0.042$) and higher number of sleep disruptions ($\beta = 0.64$, $P = 0.023$). The number of days ventilated or ICU and hospital length of stay were not statistically associated with the Actigraph sleep parameters.

Conclusion Survivors of critical illness have high levels of sleep dysfunction as measured by actigraphy. Patients' severity of illness while critically ill appears to increase the level of long-term sleep dysfunction experienced. There is discordance between objective and subjective measures of sleep quality, which has been shown previously [5]. Objective measures of sleep quality are needed on a larger number of patients to confirm these findings.

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P411

Study to assess whether staff are able to accurately assess sleep quality and quantity in intensive care patients

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Introduction Sleep deprivation is recognised as an important cause of morbidity after ICU admission, but most centres do not routinely assess their patients' sleep. Considering the invasive nature and costs associated with objective sleep measurements, they are unsuitable for routine use. Subjective measurements offer an easy-to-use and economical alternative, the most well validated of which is the Richards–Campbell Sleep Questionnaire (RCSQ). This can be used to derive an accurate estimation of the sleep efficiency index (SEI), a well-validated measure of sleep. However, there are several concerns regarding patients reporting their sleep quality and quantity using these questionnaires [1]. Additionally, they cannot be used to assess sleep in sedated or delirious patients. It has been suggested that one way to bypass the drawbacks of patients assessing their own sleep would be to utilise nursing staff [1]. Previous smaller scare studies have since agreed with this suggestion [2]. This study aimed to assess whether staff were able to use the RCSQ to accurately assess their patients' sleep.

Methods Fifty-nine patients consented to complete the RCSQ for each night of their ICU admission. Alongside this, the nurses who had cared for these patients were asked to assess their patients' sleep using the RCSQ. These were then matched with their patients' responses. The Bland–Altman method was applied to assess for agreement between patient and nurse SEIs in order to reveal whether nurses could accurately estimate their patients' night sleep. Additionally, Cronbach's alpha was derived to assess for internal consistency. Ethical approval was gained prior to the start of the study.

Results A total of 126 pairs or RCSQs were gathered. The mean difference between nurse and patient SEIs was −0.9, suggesting there is no significant trend regarding nurses overestimating or underestimating patients' SEIs. In total, 94.2% of nurses' estimations fell within the limits of agreement. The variability of the differences was consistent across the range of averages. Cronbach's alpha was 0.63 between nurse and patient scores, suggesting questionable reliability between the RCSQ pairs. See Figure 1.

Conclusion The data gathered here demonstrate that nurses are not able to accurately estimate their patients sleep using the RCSQ, and hence alternative methods of sleep monitoring should be developed for routine use.

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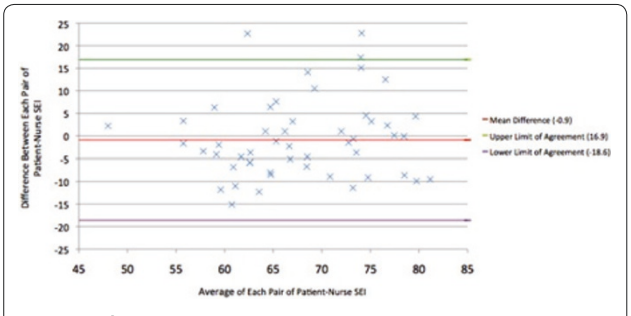

Figure 1 (abstract P411).

P412

Simplified versus standard EEG to measure the depth of sedation in mechanically ventilated ICU patients

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Introduction The accurate measure of sedation depth among mechanically ventilated ICU patients remains challenging. The Patient State Index (PSI) is a quantitative measure calculated using an algorithm derived from a simplified four-channel EEG. The aim of this study was to examine the value of the PSI to assess the level of sedation, and to verify its accuracy in comparison with the quantitative spectral analysis derived from a standard 19-channel EEG.
Methods Using the SEDLine four-channel simplified EEG system (Masimo Corporation, Irvine, CA, USA), which assessed depth of sedation through two frontal leads, we prospectively studied mechanically ventilated sedated ICU patients and examined whether the PSI was accurate to quantify the individual level of sedation. Pain stimuli were applied and changes in PSI were examined and compared with changes in electrical activity (% of delta power), measured by the frontal Fp2–Fp1 electrodes using a standard 19-channel EEG system (Viasys Neurocare, Madison, WI, USA). EEG recordings were performed simultaneously during 20 minutes, and the relationship between PSI and % of delta power was analyzed with the Pearson's correlation coefficient.
Results Ten consecutive patients (mean age 59 ± 12 years) were included. EEG recordings were performed on average 6 ± 6 days from ICU admission. Sedation consisted of propofol (seven patients), midazolam (two patients) or both (one patient). The median PSI was 54 (range 10 to 97), indicating large individual variations in PSI values. In contrast, the median delta power was 86.3% (range 55.2 to 99.4), indicating a deep sedation level. Pain stimuli were associated with a significant increase of PSI value from baseline 51 (range 16 to 96) to 68 (42 to 95) ($P = 0.009$). However, we found no correlation between the PSI and the % delta power, both at baseline ($R = 0.32$, $P = 0.37$) and after pain stimulation ($R = 0.17$, $P = 0.63$). The % delta power from frontal electrodes (Fp2–Fp1) was well correlated with that obtained from posterior electrodes (P4–Pz; $R = 0.42$, $P < 0.0001$), and remained unchanged after pain stimulation, indeed confirming a deep sedation level in our patient cohort.
Conclusion Using standard EEG in this small cohort of mechanically ventilated ICU patients, a deep sedation level was frequently observed. Our preliminary data suggest that simplified EEG with the SedLine system is less accurate than the standard 19-channel EEG to assess the depth of sedation in the ICU setting.

P413

Implementation of the Behavioural Pain Scale in sedated mechanically ventilated patients in a UK ICU

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Introduction Pain is a common problem in mechanically ventilated patients and assessing pain in the sedated patient is difficult, as patients are often unable to verbalise [1]. Behavioural pain assessment tools have been developed and validated for the assessment of pain in this patient group. A behavioural pain assessment tool was implemented as part of a wider ventilator-associated pneumonia (VAP) prevention programme within a large UK ICU.
Methods The Behavioural Pain Scale (BPS) [2] was selected and implemented into daily clinical practice supported by a tailored education programme and incorporation into the clinical information system (MetaVision). Questionnaires pre and post BPS implementation were used to assess nursing staff opinions on pain assessment and opioid infusion titration. Four months of data were compared pre and post implementation, examining aspects of patient sedation and analgesia exposure and ventilated patient outcome parameters.
Results In the pre-implementation and post-implementation questionnaire (response rate of 38% and 37% respectively of nurses surveyed), nursing staff reported they were significantly more confident in titrating opioids after implementation (3 (2; 3) and 3 (3; 4) respectively; $P < 0.01$), despite a lack of significant difference in their reported confidence to assess pain. Compliance was good, with a median daily documentation rate of 66% with the standard being once per 8-hour shift. Median BPS score rank was significantly higher on patient movement (2 (1; 2)) compared with at rest (1 (1; 2); $P < 0.001$) (1 = no pain, 2 = mild pain). No statistically significant difference was seen in the length of stay, duration of mechanical ventilation, VAP rate or median sedation exposure. Pre-implementation median opioid administration when looking at morphine (mg) equivalence was 455.8 (203.1; 1,174.8), and post implementation the median increased to 620.3 (218.1; 1,502); however, this did not reach statistical significance ($P = 0.235$). There was no statistically significant change in the prescribing of analgesic adjuncts. The sample size was underpowered to detect significant differences.
Conclusion The BPS was successfully implemented into routine nursing practice and significantly improved nurse confidence in opioid infusion titration. Analgesic use was not significantly different between evaluation periods, but the results indicate that further education on anticipating pain and treating pain pre-emptively with timely administration of opioids is needed.
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P414

Haemodynamic effects of clonidine in an ovine model of severe sepsis with septic acute kidney injury

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Introduction In sepsis, sympathetic nerve activity is increased, which helps maintain arterial pressure in the face of nitric oxide-induced vasodilatation. Accordingly, we investigated the haemodynamic effects of the centrally acting α-adrenoceptor agonist clonidine in an ovine model of severe sepsis.
Methods A prospective interventional blinded crossover study in 12 Merino ewes with cardiac and renal flow probes implanted to continuously measure cardiac output and renal blood flow. Arterial pressure was continuously monitored and blood and urine samples were taken. After 24 hours of control, sepsis was induced by an intravenous bolus and continuous infusion of live *Escherichia coli* for 32 hours. After 24 hours of sepsis, animals were randomly and blindly allocated to vehicle infusion or clonidine (1 μg/ml/kg/minute) for 8 hours. The *E. coli* infusion was then discontinued, gentamycin 150 mg given i.m. and the animals were followed for 16 hours during recovery. The animals that survived were crossed over to the alternative treatment 2 weeks later.
Results Complete data were collected on eight animals/group, three animals died/group. Hyperdynamic sepsis with hypotension and acute kidney injury of similar degree developed in the two groups. Haemodynamic and renal effects of clonidine are shown in Figure 1.
Conclusion In ovine hyperdynamic sepsis, clonidine transiently increased urine output without affecting creatinine clearance.

P415

Off-label use of clonidine for sedation in Dutch ICUs

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Introduction Clonidine is an α_2-agonist, licensed in most countries for treatment of hypertension. Other pharmacologic characteristics of α_2-agonists are sedation, hypnosis, anxiolysis, sympatholysis, and analgesia [1]. Because of these central nervous effects, clonidine can

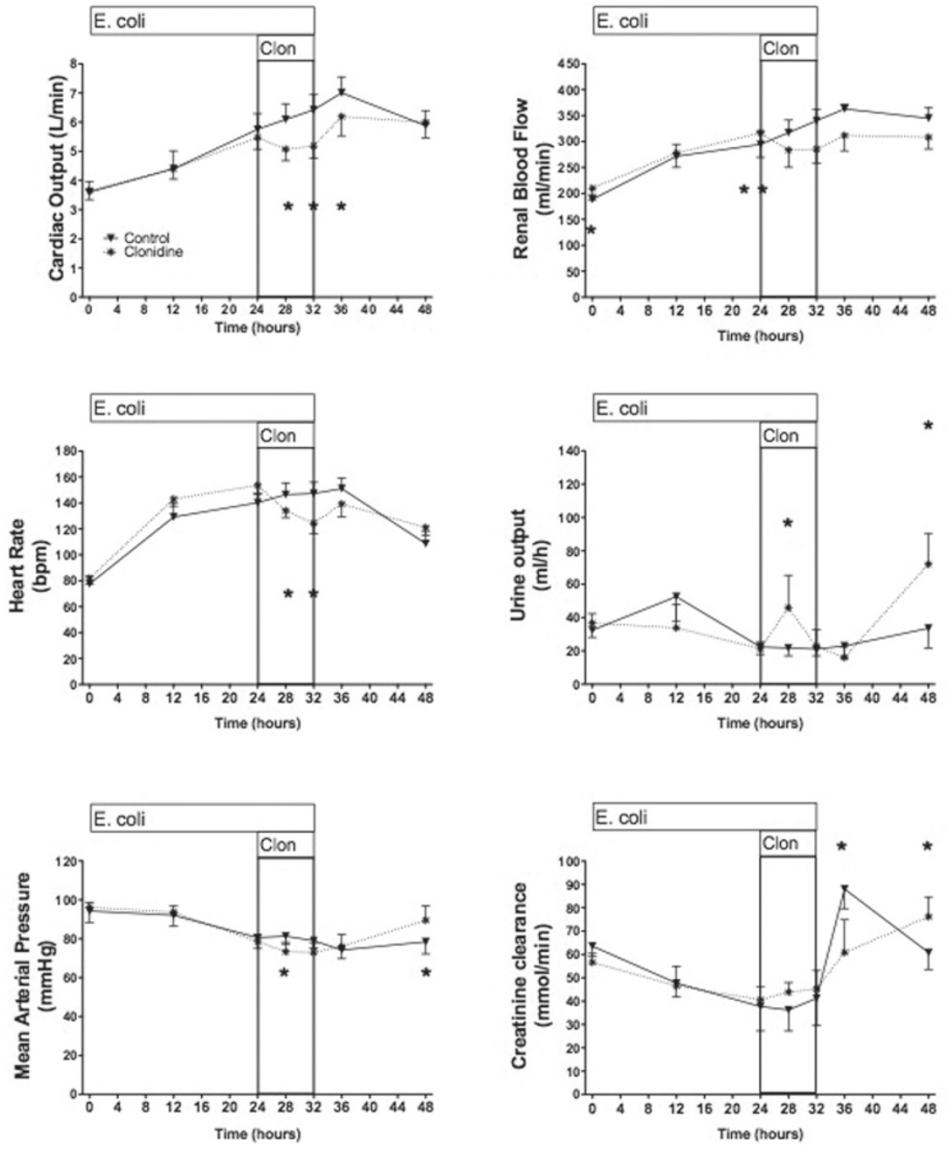

Figure 1 (abstract P414). Haemodynamic and renal effects of clonidine in established sepsis.

be used off-label to augment sedation and delirium treatment. To our knowledge there have been no publications evaluating the efficacy and safety of clonidine in ventilated critically ill adults. A survey in German ICUs showed that clonidine was used for sedation in 62% of units [2]. We undertook an enquiry to investigate the off-label use of clonidine in Dutch ICUs.

Methods An inventory was sent by email to 25 ICUs in the Netherlands, determined by the difficulty to identify a contact person.

Results The response rate was 56%. The results are summarized in Table 1. Clonidine was used in all 14 responding ICUs; in 36% this use was reported as often. Licensed use (for hypertension) was 50%. Indications for off-label use were: substance withdrawal (50%), delirium (71%), and sedation (29%). The route of administration was intravenous in all cases. Nine ICUs reported the use of a loading dose, irrespective of indication, varying from 10 to 150 μg, median 150 μg. Ten ICUs reported the use of continuous infusion, varying from 10 to 100 μg/hour, median 50 μg/hour.

Conclusion Off-label use of clonidine for sedation and treatment of withdrawal symptoms and delirium was common practice in Dutch ICUs. There was a wide range of dosing regimens: infusion schedules varied 10-fold and loading doses 15-fold. Clinical studies are required to establish the safety and efficacy of clonidine in the ICU setting.

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P416

Comparison of dexmedetomidine and propofol for sedation in patients with traumatic brain injury

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Introduction Both propofol and dexmedetomidine decrease systemic blood pressure, heart rate, and cardiac output in a dose-dependent manner. The aim of this study was to compare their safety and efficacy for intravenous sedation during mechanical ventilation.

Methods Eighty-four patients with traumatic brain injury (Glasgow scale 7 to 8) entered the study, mean age 44 ± 13.37 years. All patients

Table 1 (abstract P415). Indication and doses of clonidine used in Dutch ICUs

IC level[a]	Clonidine use	Indication	Loading dose (μg)	Continuous infusion dose (μg/hour)
3	Often	Hypertension sedation	ns	ns
3	Often	Hypertension withdrawal; hypertension delirium; sedation	40 to 120	10 to 80
3	Often	Substance withdrawal; sedation	150	50
3	Often	Substance withdrawal	75 to 150	50
3	Often	Substance withdrawal; hypertension; delirium	10	40 to 100
3	Sometimes	Delirium	ns	30 to 100
3	Sometimes	Hypertension; delirium	150	ns
3	Sometimes	Substance withdrawal; delirium	ns	40
2	Sometimes	Substance withdrawal; delirium	ns	20 to 50
2	Sometimes	Hypertension; sedation	150	40
2	Sometimes	Substance withdrawal; hypertension; delirium	150	12 to 25
1	Sometimes	Hypertension; delirium	150	ns
1	Sometimes	Delirium	50	50 to 100
1	Sometimes	Delirium	ns	ns

ns, not specified. [a]Level of ICU care, with level 3 being the most advanced.

underwent mechanical lung ventilation. Patients were divided into two groups depending on the type of intravenous sedation. In the first group ($n = 42$), sedation was performed by intravenous propofol infusion at a dose of 4 to 12 mg/kg/hour. In patients of the second group ($n = 42$), sedation was carried out by intravenous infusion of dexmedetomidine at a dose of 0.2 to 1.4 mg/kg/hour. The level of sedation was assessed with bispectral index monitoring, targeting index 70. For comparison of methods we evaluated heart rate, blood pressure, SpO_2 30, 90 and 180 minutes after the start of sedation. Both groups were matched for sex, age and comorbidity.

Results Thirty minutes after the start of sedation in patients of the first group, HR was 83 ± 11.31 beats/minute, blood pressure was 127 ± 12.87/64 ± 8.54 mmHg, SpO_2 was 97 ± 3.01%. In patients of the second group 30 minutes after the beginning of sedation, HR was 87 ± 10.01 beats/minute, blood pressure was 131 ± 11.67/68 ± 8.19 mmHg, SpO_2 was 97 ± 2.98%. After 90 minutes in the first group of patients, we observed HR was 81 ± 6.27 beats/minute, blood pressure was 119 ± 11.46/59 ± 4.29 mmHg, SpO_2 was 98 ± 2.35%. In the second group, HR was 82 ± 7.31 beats/minute, blood pressure was 94 ± 13.62/55 ± 7.81 mmHg, SpO_2 was 97 ± 2.76%. In the first group 180 minutes after the start of sedation, HR was 86 ± 6.19 beats/minute, blood pressure was 105 ± 10.34/54 ± 4.28 mmHg, SpO_2 was 98 ± 1.32%. In the second group, HR was 75 ± 6.27 beats/minute, blood pressure was 92 ± 12.54/51 ± 6.91 mmHg, SpO_2 was 96 ± 2.91%.

Conclusion Using dexmedetomidine at a dose of 0.2 to 1.4 mg/kg/hour for intravenous sedation is safe in terms of hemodynamic stability and blood oxygenation for sedation during mechanical lung ventilation in traumatic brain injury patients.

P417

Different effects of propofol and dexmedetomidine on preload dependency in endotoxemic shock with norepinephrine infusion: a randomized case–control study

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Introduction Septic shock is a status characterized by the simultaneous use of vasopressors and sedative drugs in critical care patients. Little is known about the possible interference of these drugs during shock status. We aimed to clarify how propofol could differently affect the preload dependency in an endotoxemic model in comparison with dexmedetomidine, by evaluation of the systemic vascular system and cardiac function.

Methods After animal preparation and under PiCCO monitoring (BL), endotoxemic shock was induced by an intravenous bolus of lipopolysaccharide (LPS, 055:B5) in ketamine-anesthetized rabbits. After fluid resuscitation and norepinephrine infusion (SD0), animals were randomized to propofol (PROP, $n = 8$) or dexmedetomidine (DEX, $n = 8$) sedation, with two incremental doses (SD1 and SD2). The mean arterial pressure (MAP) and central vein pressure (CVP) were monitored. Pulse pressure variation (PPV) and stroke volume variation (SVV) were assessed to evaluate the preload dependency. Global end-diastolic volume, vascular resistances, mean systemic filling pressure, cardiac functional index and vascular resistances were assessed at each time point. Normality was assessed by the Kolmogorov–Smirnov test. Two-way analysis of variance for repeated measures was applied, and the Student–Newmann–Keuls *post-hoc* test when indicated. $P < 0.05$ was considered significant.

Results At the increasing dose of propofol, both PPV and SVV significantly increased in SD1 versus SD0 ($P < 0.01$) and SD2 versus SD0 ($P < 0.001$), but only PPV in SD2 versus SD1 ($P = 0.024$). Dexmedetomidine infusion did not affect PPV and SVV. At SD1 and SD2, PPV and SVV were higher in PROP with respect to DEX ($P < 0.001$). Moreover, propofol infusion increased the heart rate and had no effects on cardiac contractility and vascular resistances. On the contrary, in the DEX group we recorded a significant decrease in heart contractility and increment of vascular resistances at SD2. Nonetheless, both drugs affected the MAP, CVP, mean systemic filling pressure, global end-diastolic volume and venous return.

Conclusion In an endotoxemic shock model, after fluid resuscitation and during norepinephrine infusion, propofol increased more PPV and SVV in comparison with dexmedetomidine. At high dosage the vascular resistances and heart contractility were influenced by dexmedetomidine, but not by propofol.

P418

Propofol: monitoring for complications

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Introduction This re-audit aims to test our strategy for monitoring patients on propofol sedation for prolonged periods. Propofol infusion syndrome (PRIS), once established, is difficult to treat and currently there is limited guidance on how best to monitor for this potentially

life-threatening complication [1]. An audit done in 2011 highlighted that lipid profile and electrocardiograms (ECGs) were rarely monitored. We recommended regular monitoring of these parameters when propofol sedation is used for over 3 days and that propofol-sparing agents are considered in these patients at risk of developing PRIS.

Methods In patients who required propofol sedation for 4 days or more, we prospectively monitored: frequency of performing lipid profile and 12-lead ECG; and frequency of co-administration of a propofol-sparing agent.

Results We collected data from 25 patients. The duration of propofol infusion was 4 to 15 days (mean 8.5 days). Mean propofol dose in the first 4 days was 2.2 mg/kg/hour. Maximum daily propofol dose ranged from 2.1 to 3.8 mg/kg/hour. Lipid profile was checked in 16/25 (64%) patients (20% in 2011) whilst on propofol sedation. However, these were checked following 3 days continuous infusion in only three patients. The triglyceride level was ≥2.2 mmol/l (very high) on first testing in 75% of patients. All patients had a 12-lead ECG done on admission. Seventeen of 25 (68%) had a further ECG performed whilst on continuous propofol infusion (45% in 2011). Additional ECGs were done in 13/17 patients (zero in 2011). ECG changes that we feel were attributable to propofol occurred in two patients, one of whom developed severe PRIS. Fourteen of 25 (56%) patients (55% in 2011) were on concomitant sedative agents. This included the patient who developed PRIS.

Conclusion Awareness of complications from prolonged propofol sedation is increasing amongst our clinicians. This is reflected in the increased frequency of lipid profile and ECG monitoring compared with 2011. However, we feel that more regular and routine monitoring is essential to aid early detection of this potentially fatal complication. We recommend that all patients at risk of developing PRIS should have these parameters monitored on a daily basis as standard.

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P419

Influence of increased intracranial pressure on sevoflurane-fentanyl anesthesia in major abdominal surgery

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Introduction Increased intracranial pressure (ICP) may adversely affect sevoflurane anesthesia and the recovery period due to a disturbed cerebral blood flow. Effect of sevoflurane on cerebral hemodynamics remains controversial and depends on the extent of the initial value of ICP [1]. This study was designed to evaluate the safety of sevoflurane-fentanyl anesthesia during major abdominal surgery in patients with increased ICP.

Methods A total of 124 ASA 3 patients, undergoing major abdominal surgery (duration 5.6 (4.1 to 6.4) hours), were divided into two groups: with normal ICP (≤12 mmHg) (N group, 70 patients) and with ICP >12 mmHg (H group, 54 patients). Initial ICP was evaluated by venous ophthalmodynamometry [2]. ICP, mean arterial pressure (MAP) and cerebral perfusion pressure (CPP) were assessed every hour of anesthesia. Time of recovery of consciousness after anesthesia, complications and length of stay in the ICU and in the hospital were also evaluated.

Results Initial ICP was 8 ± 3 mmHg in the N group and 15 ± 2 mmHg in the H group. During the anesthesia ICP increased in the H group with a total increase of 33% (from 15 ± 2 to 20 ± 3 mmHg (P <0.05)). In the N group ICP was stable without any significant change. Decrease of MAP after induction of anesthesia was similar in the two groups and was stable during anesthesia. CPP was stable in the N group (above 70 mmHg during the anesthesia), but in the H group CPP decreased significantly (from 82 mmHg to 63 mmHg (P <0.05)). Time of recovery of consciousness in the H group was higher (32 ± 6 minutes vs. 20 ± 4 minutes (P <0.05)). The incidence of postoperative delirium was higher in the H group (22.2% vs. 12.8% in the N group (P <0.05)). There were no significant differences between two groups in other complications. Total length of stay in the ICU and in the hospital was higher in the H group (6 ± 2 days vs. 4 ± 2 days (P <0.05) and 15 ± 3 days vs. 11 ± 2 days in N group (P <0.05)).

Conclusion Sevoflurane-fentanyl anesthesia in patients with increased ICP was characterized by a delayed recovery with a higher incidence of postoperative delirium and higher length of stay in the ICU and in the hospital. The main cause of this is a decrease of CPP in patients with high ICP due to low craniocerebral compliance.

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P420

Quantifying sedation satisfaction during bronchoscopy using the Bispectral Index

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Introduction Sedation monitoring with the Bispectral Index (BIS) is uncommon during bronchoscopy but allows for a more objective measure of sedation; we hypothesized that higher BIS scores would correlate with lower patient satisfaction and that lower BIS scores (deep sedation) would result in better patient and physician satisfaction.

Methods Between October 2012 and August 2013, bronchoscopy using conscious (CS) or monitored anesthetic deep sedation (DS) was monitored with BIS. Medication administration and procedures were time-stamped. Sedation was administered blinded to BIS score. DS cases used propofol infusions, CS cases used bolus midazolam and fentanyl. Providers rated sedation satisfaction, cough, and the ability to perform the intended procedure using a 100 mm visual analog scale at the end of the procedure blind to BIS (0 unsatisfied to 100 satisfied). Patients were surveyed at 1 hour and 24 hours regarding overall sedation, symptoms, and procedure recall (unpleasant recall 1, no recall 4). Group differences were considered statistically significant at P <0.05.

Results Twenty-six procedures were monitored, 20 with CS and six endobronchial ultrasound procedures with DS. There was no difference with respect to age or gender. The mean doses of midazolam and fentanyl were 5 mg and 85 μg, respectively. BIS values were lower at all predefined points of the procedure for DS cases versus CS. Physicians were more satisfied with sedation and the lack of cough with DS, but there was no significant difference in patient satisfaction between the two groups with regards to overall sedation, procedure-related symptoms or willingness to have repeat bronchoscopy. Patients with no recall had lower nadir BIS scores (46 vs. 71, P = 0.03) and scores at procedure end (76 vs. 94, P = 0.04) compared with those with any recall. There was no difference in the doses of midazolam or fentanyl in CS cases despite statistically significant differences in patient recall and BIS scores. Junior fellows scored greater satisfaction with sedation, were less bothered by cough and more often felt able to perform the intended procedure compared with senior fellows.

Conclusion Deep sedation resulted in greater physician satisfaction with procedural conditions as well as lower BIS scores but no significant difference in patient satisfaction compared with conscious sedation. Patients with no recall of the procedure had lower BIS scores at the nadir and end of the procedure. BIS may be a novel tool to monitor procedural depth, allowing proceduralists to better monitor the narrow window between adequate sedation and dangerous oversedation.

P421

Risk factor of withdrawal syndrome in the paediatric ICU

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Critical Care 2014, **18(Suppl 1):**P421 (doi: 10.1186/cc13611)

Introduction Critically ill paediatric patients supported on mechanical ventilation frequently receive analgesia and sedation. Iatrogenic withdrawal syndrome occurs with the abrupt discontinuation or too rapid weaning of opioids and benzodiazepines. We induce the

Withdrawal Assessment Tool-1 (WAT-1) [1] to evaluate children during weaning from analgesics and sedatives. The patient is diagnosed with withdrawal syndrome when the score is 3 or >3. We compared the subjects who ever had a score over 3 and those with lower scores and assessed the risk factors and outcome of withdrawal syndrome between two groups.

Methods A total of 932 patients were admitted to our PICU from 1 October 2011 to 31 March 2013. Of these, 127 paediatric patients were supported on mechanical ventilation on the first day in the PICU and received intravenous analgesics and sedatives. A retrospective review of a prospectively collected database. The statistical method was the Mann–Whitney *U* test, and $P < 0.05$ was considered statistically significant.

Results Twenty-eight patients were scored with the WAT-1 during weaning from the drugs. Median age was 14 months (1 to 73 months) and the most common reasons for ventilation were airway trouble and pneumonia. Eight of 28 were diagnosed withdrawal syndrome, 20 were not. There were no significant differences in age, body weight, cumulative morphine and benzodiazepine dose before weaning. In the withdrawal group, the lactate level, catecholamine index, Paediatric Index of Mortality 2 and heart rates were greater when they were admitted to hospital. Further, there are longer length of PICU stay and shorter ventilator-free days for patients with WAT-1 score >3. But all of them are alive at 28 days, so there is no difference in 28-day mortality.

Conclusion Our study suggest that severely ill paediatric patients tended to suffer from withdrawal syndrome and then resulted in short ventilator-free days and longer PICU stay. But there is no difference in mortality.

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P422

Epidural analgesia reduces perioperative myocardial infarction and all-cause mortality after cardiac surgery: but at least 25 epidural hematomas have already happened

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Introduction Epidural analgesia on top of general anesthesia in cardiac surgery might improve relevant clinical outcomes but the incidence of epidural hematoma is under-reported.

Methods An international web-based, online, viral, anonymous survey, a systematic review of the literature, and a meta-analysis of randomized and matched studies were performed.

Results Nine epidural hematomas were identified in 198 published manuscripts. The risk of epidural hematoma (9:13,429) calculated on all published evidence might be therefore estimated to be 1:1,492 (95% confidence interval (CI) = 1:2,857 to 1:833). Through an anonymous, web-based, viral, international survey, we identified at least 16 further nonpublished epidural hematomas together with at least 72,400 epidural analgesia catheters positioned in cardiac surgery in the last 20 years. The risk of epidural hematoma (25:85,829) is therefore 1:3,436 (95% CI = 1:2,325 to 1:5,076) including both published and unpublished data. Out of the 66 randomized and case-matched studies, 57 trials reported the incidence of all-cause mortality at the longest available follow-up with a significant reduction in the epidural group (59/3,137 (1.9%) in the epidural group vs. 108/3,246 (3.3%) in the control arm, RR 0.64 (95% CI 0.48 to 0.85), $P = 0.002$, NNT = 69).

Conclusion Epidural analgesia on top of general anesthesia in cardiac surgery might reduce the incidence of all-cause mortality (NNT 69). The incidence of epidural hematoma in this setting is 1:3,436 (95% CI = 1:2,325 to 1:5,076) including both published and unpublished data. In fact, we identified at least 25 epidural hematomas that occurred so far from the following countries: Belgium ($n = 1$), Brazil ($n = 1$), France ($n = 1$), Germany ($n = 2$), India ($n = 2$), Italy ($n = 1$), Japan ($n = 2$), Korea ($n = 1$), Malaysia ($n = 1$), Norway ($n = 2$), Russia ($n = 3$), Sweden ($n = 1$), the UK ($n = 3$), and the USA ($n = 4$). Even if from the public health point of view the benefits seem to encourage the use of epidural analgesia in cardiac surgery with a possible reduction in perioperative mortality, this topic merits further investigation and the decision to insert the epidural catheter should be discussed with the patient considering both local experience and legal dispute in case of medical complications.

P423

Delirium screening, prevention and treatment in the ICU: a systematic review of implementation strategies

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Introduction The occurrence of delirium heralds a circumstance of higher risk of death, longer stay, higher cost, and greater likelihood of long-term brain dysfunction, and yet the majority of ICU patients worldwide do not get routinely monitored for delirium, thus obstructing timely prevention and management strategies. Determination of effective implementation strategies regarding screening, treatment and prevention of delirium is critical to address needed modifications in the culture of patient care in the ICU. The aim of this study was to summarize the efficacy of and the barriers to implementation of delirium management.

Methods We searched PubMed, Embase, PsychINFO, Cochrane and CINAHL for studies published between January 2000 and October 2012, and included them when implementation strategies and their efficacy and/or potential barriers of implementation were described.

Results In all studies ($n = 34$) multifaceted education strategies were used and combined (median: 5; IQR: 4 to 6). Positive results were reported for both process and clinical outcomes: adherence to delirium screening – improvement after implementation compared with the before measurement, by 15 to 57%; only measured after implementation, between 84 and 92%; delirium knowledge (on a 10-point scale; improved from 6.1 and 6.2 before to 8.2 and 7.4 respectively ($P < 0.001$) after implementation); length of stay in the ICU (4.1 vs. 5.9 days; $P = 0.21$ and 6.3 to 5.35 days; $P < 0.009$) and hospital stay (12 days vs. 18 days; $P = 0.036$ and from 55 to 27 days; $P < 0.0001$); and decreased mortality (29.4% vs. 22.9%; $P = 0.009$; and OR = 0.45; 95% CI = 0.22 to 0.92; $P = 0.03$). The major barriers found impairing implementation concerned clinicians' attitude and healthcare professionals' knowledge.

Conclusion Implementation strategies used suggest a strong potential for multifaceted strategies to be able to affect both process and clinical outcomes. The majority of studies focused only on implementation of delirium screening. There is a knowledge deficit regarding efficacy of well-prepared implementation of integral delirium management considering screening, prevention, and treatment preceded by analysis of barriers. Further research on the extent and contents of implementation interventions aimed at integral delirium management such as those described in the recent ABCDE bundle and PAD guideline are necessary.

P424

Effect of enteral and/or parenteral glutamine supplementation on mortality and morbidity in the critically ill

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Introduction In this study we aimed to compare the effectiveness of enteral, parenteral and combined enteral–parenteral glutamine supplementations in the nutrition of critical care patients.

Methods This is a single-center, randomized controlled clinical trial. During the 5-day study period, all patients received standard enteral nutrition product and were divided into three groups, including parenteral glutamine (Group I), enteral glutamine (Group II) and enteral + parenteral glutamine (Group III) supplementations. Blood

biochemistry, rates of infections, length of stay in the ICU and duration of mechanical ventilation were evaluated.
Results Sixty patients were included in this study. There was no statistically significant difference for biochemical values between the different feeding groups. Frequency of infections ranged as Group II >Group III >Group I and mortality as Group II = Group III >Group I. Length of stay in the ICU and duration of mechanical ventilation were significantly longer in Group II than the others.
Conclusion Although mortality was not significantly different between groups, parenteral glutamine administration causes less stay of ICU and mechanical ventilation. This needs a more powerful randomized controlled study [1].
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P425

Increased threshold for gastric residual volumes and impact on nutrition in the ICU

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Introduction Gastric residual volumes (GRVs) as measured at regular intervals are considered a marker of tolerance of enteral nutrition (EN). There is controversy surrounding this practice, however. The absolute value for the designated cutoff value for GRVs varies widely in the literature. No prospective randomized control trials have suggested that their use improves patient outcomes in the ICU. It has also not been shown, therefore, that GRVs are an accurate predictor of aspiration or pneumonia. However, the use of GRVs as a guide to the continuation of EN can result in a reduction in the percentage of goal calories received by patients. Prior to February 2013, in our ICU the threshold of GRVs prior to withholding of EN was 200 ml. This tolerated volume was increased to 500 ml in February 2013, in compliance with recent guidelines. By increasing the acceptable GRVs to this level, the aim was to increase the percentage of goal calories received by patients via the enteral route.
Methods Following ethical approval, the practice of measuring GRVs and the subsequent management of EN was retrospectively reviewed over a 3-month period, September to December 2012, and prospectively reviewed over a 3-month period, September to December 2013, following the change in practice. Recorded parameters included: length of ICU admission; admitting diagnosis; duration of EN; GRVs; prescribed calories; delivered calories via an enteral route; requirement for PN; duration of PN; and cost of total parenteral nutrition (TPN).
Results The change of practice in terms of GRVs and management of EN led to an increased percentage of prescribed calories that was delivered. There was a reduced requirement for PN and reduced cost of TPN also associated with this change in practice.
Conclusion Increasing the threshold of GRV prior to reducing or stopping EN can result in increased calories delivered to ICU patients and a reduced requirement for and cost of TPN.

P426

Early enteral feeding in the septic critically ill patient: evaluation of our feeding protocol

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Introduction It has been established that early enteral nutrition in critically ill patients improves overall outcome and mortality. In our unit, feeding protocols were established based on the ESPEN recommendations and have been implemented for the last 2 years. The purpose of this study was to evaluate the compliance of our septic patients' nutritional approach with our feeding protocols.
Methods A prospective study was done on a 24-bed mixed ICU over a period of 18 months. Eighty-three patients ≥18 years were included in the study. All patients were dependent on mechanical ventilation and met the CCM criteria for sepsis upon admission to the ICU. APACHE II score, SOFA score, weight, BMI and nutritional status were calculated. Patients were initiated for enteral feeding based on the established feeding protocol within 48 hours of admission. The feeding status of the patient was recorded on the start day (D0), day 3 (D3) and day 7 (D7). Factors affecting the feeding process and its progression were also recorded
Results The patient mean age was 71.4 ± 12.2. LOS in the ICU was 9 to 21 days. Based on BMI, 18% of the patients were malnourished upon admission. APACHE II was 26 ± 7.8 and SOFA was 9.2 ± 4.6. The mortality rate was 42.5%. Enteral nutrition started early in 64 (77.1%) of the patients (D0), on day 3 (D3) 29 (45.31%) patients met their caloric goals and on day 7 (D7) only 18 (28.1%) patients achieved their caloric goals. Discontinuation of enteral feeding was mainly due to procedures, whereas late start and/or decreased hourly intake were due to GI complications, GI intolerance, excessive diarrhoea and hemodynamic instability. There was no association between compliance with the feeding protocol and the LOS, nutritional status, severity or disease progression.
Conclusion Although the initiation of early enteral feeding seems adequate for a good number of septic patients on D0, is still far off for a significant percentage of those patients on D3 and is even worse on D7. The caloric goal achievements were better on D3 but very suboptimal on D7. There was no association, however, between nutritional status and compliance with the feeding protocols. It is therefore mandatory to follow daily the nutritional therapy of the septic patient and not rely only on the feeding protocols.

P427

A nutritional protocol and personalized support reduce the cumulative caloric deficit of cardiac surgery patients

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Introduction Providing adequate feeding in cardiac surgery patients is gaining importance [1]. The aims were to assess the preoperative nutritional status, to compare postoperative energy needs with effectively delivered amounts, and to evaluate the impact of a dietitian on optimizing postoperative energy balances.
Methods A prospective interventional study in adult patients after elective CABG and/or heart valve surgery. The patients' nutritional risk was determined by the NRS 2002 and the Malnutrition Universal Screening Tool (MUST) [2]. A dedicated dietitian managed and assisted the nutritional approach. For each patient, global energy intake (intentional and non-intentional) and balance (difference between energy target and global caloric intake) were calculated daily during and after ICU stay until hospital discharge. The Harris–Benedict equation was used to calculate daily energy requirements. When energy delivery did not reach 60% of calculated needs, a protocol-driven nutritional intervention was initiated.
Results Two hundred patients were enrolled during a 10-month period, representing 2,690 study-days. Mean age was 67 ± 11 years. In total, 42.5% of the patients had a NRS 2002 score >3 and were considered to be nutritionally at risk. MUST identified a high, medium, or low risk in respectively 1%, 4% and 95% of subjects. Mean energy requirement was 2,046 ± 347 kcal and mean daily intake 1,452 ± 335 kcal. Sixty-two percent of the caloric need was met during the entire hospital stay. Nutritional intervention was necessary in 52% of cases: oral feeding supplementation for 546 study-days, enteral feeding: 401 days, parenteral feeding: 367 days. This reduced the mean cumulative caloric deficit to 9,085 kcal.
Conclusion Close monitoring of caloric intake shouldered by interventions based on a predefined algorithm under supervision of a dedicated nutrition team restricts the caloric deficit in cardiac surgery patients.
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P428

Vitamin B and C levels of homeless patients who visit the emergency department with alcohol ingestion

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Introduction Vitamins are essential micronutrients and depletions are reported for chronically ill patients. It is well known that the general nutrition status of the homeless is poor, especially for heavy alcoholics. But there were few data about the actual vitamin status of homeless patients. We want to evaluate the vitamin levels of homeless patients.
Methods This study was conducted at a single urban teaching hospital emergency department. We performed a retrospective chart review of blood vitamin B1, B12, B6 and C levels of homeless patients. These vitamins are a common supplement in our center and sometimes blood levels are drawn if the patient is drunk, needs i.v. hydration and has cachexic features.
Results During study periods, vitamin levels were checked for 156 patients. The number of male patients was 146 (94%) and the mean age was 50 ± 10.2. Vitamin C levels were 15.8 ± 1.3 mg/l. For 84 patients, levels of vitamin C were decreased. For vitamin B1 (152 ± 7.2 nmol/l), vitamin B12 (725.5 ± 35.4 pg/ml), and vitamin B6 (50.3 ± 5.5 ng/ml), there were three, two and 23 patients below the reference ranges respectively. See Table 1.

Table 1 (abstract P428).

(%)	Mean (SD)	Reference range	Lower than reference (%)	Higher than reference
Vitamin B1	158.1 (80.2)	59 to 213	3.1	13.8
Vitamin B12	741.5 (432.2)	200 to 950	2.7	22.6
Vitamin B6	51.9 (53.8)	20 to 202	23.1	1.9
Vitamin C	15.57 (13.4)	26.1 to 84.6	82.7	0

Conclusion The level of vitamin C was markedly decreased. Replacement of vitamin C should be considered for the homeless who visit the emergency department after alcohol ingestion.

P429

Acid–base disorders according to the Stewart approach in septic patients

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Introduction ICU patients often develop acid–base disorders. In clinical practice, there are several methods (for example, Henderson–Hasselbalch) used to interpret acid–base data, but most of them provide little information and fail to identify the cause of the problem. Stewart's approach which is based on physicochemical principles has growing popularity among clinicians in critical care. This method includes three independent variables that determine plasma pH (strong ion difference (SID), PCO_2, and total weak acid concentration – mainly albumins and phosphate).
Methods The prospective analysis of arterial blood gases (ABG) was performed according to the Henderson–Hasselbalch approach and the Stewart method. The results were categorized into three groups according to the Henderson–Hasselbalch concept and the BE values: BE <–2, metabolic acidosis; BE between –2 and 2, normal values; BE >2, metabolic alkalosis. The aim of the study was to compare the efficacy of the traditional Henderson–Hasselbalch approach with acid–base disturbances with the Stewart concept in the population of critically ill septic patients.
Results The analysis included 990 arterial blood gases taken from 43 consecutive septic patients admitted to the ICU. One hundred and ninety-three ABG results met the criteria of metabolic acidosis, 473 were categorized into the metabolic alkalosis group and 324 results were within the range value of BE according to the Henderson–Hasselbalch concept. In the metabolic acidosis group (BE <–2), 34.7% of the results had elevated lactate concentration, 100% revealed hypoalbuminemia, 96.9% had Cl/Na ratio >0.75 revealing SID acidosis, while 42.5% met the criteria of SIG acidosis. In the normal range BE group, 21.3% revealed lactate concentration >2 mmol/l, 100% had hypoalbuminemia, 98.4% had Cl/Na ratio >0.75 revealing SID acidosis and hyperchloremia, while 14.5% showed SIG acidosis. The analysis of the ABG with BE >2 group showed that 18.4% had elevated lactate concentration, 99.1% revealed hypoalbuminemia, 88.8% had Cl/Na ratio >0.75 (SID acidosis) and 4.6% showed SIG acidosis.
Conclusion In critically ill patients with the BE values <–2, with BE in the range of normal value and BE >2 we observed complex acid–base disturbances with coexistence of hyperchloremic acidosis, hyperlactatemia, SIG acidosis and alkalosis caused by hypoalbuminemia. The Stewart approach is more effective in detecting acid–base disturbances and quantifying individual components of acid–base abnormalities and provides a detailed insight into their pathogenesis.

P430

Changes in urinary electrolytes during acute respiratory acid–base modifications

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Introduction The renal system compensates respiratory disorders of acid–base equilibrium by modifying the urinary electrolyte composition [1]. Such a condition mainly involves changes in urinary ammonium excretion as a reaction to prolonged periods of acid–base disequilibrium, leaving the renal response to acute derangements unexplored. We aimed to determine the acute variations of urinary ammonium $[NH4^+]_u$, sodium $[Na^+]_u$, potassium $[K^+]_u$ and chloride $[Cl^-]_u$ concentrations following controlled minimal respiratory acid–base imbalances, and to further investigate whether urinary anion gap ($[AG]_u = [Na^+]_u + [K^+]_u - [Cl^-]_u$) and sodium and chloride difference ($[Na^+]_u - [Cl^-]_u$) might unveil an early activation of the renal response.
Methods Patients admitted to the ICU after major surgery were enrolled, during intubation and sedation. Patients with chronic renal failure were excluded. A urinary catheter was connected to the quasi-continuous urinary analyzer KING®, measuring $[NH4^+]_u$, $[Na^+]_u$, $[K^+]_u$ and $[Cl^-]_u$ over time. Based upon the arterial pH (pHa) at entrance, patients were randomly assigned to controlled hypoventilation (30% reduction of minute ventilation if pHa ≥7.40) or hyperventilation (30% increase of minute ventilation if pHa <7.40) for 2 hours. Samples for blood gas analysis were collected every 30 minutes.
Results Thirty patients were enrolled; 20 were hypoventilated, 10 hyperventilated. At 2 hours from ventilation change, pHa was respectively decreased from 7.44 ± 0.02 to 7.34 ± 0.02 and increased from 7.37 ± 0.03 to 7.44 ± 0.02 (P <0.001) in the two groups. Mean $[NH4^+]_u$ rose by 2.6 ± 3.3 mEq/l in hypoventilated patients and fell by 2.5 ± 2.4 mEq/l in the hyperventilated (P <0.001). No difference in mean $[K^+]_u$ was observed at any time, while $[Na^+]_u$ and $[Cl^-]_u$ progressively decreased in both groups (P <0.05). $[Na^+]_u$ was reduced by 48 ± 43 mEq/l during hypoventilation and by 32 ± 41 mEq/l during hyperventilation (P = 0.14), while $[Cl^-]_u$ decreased by 29 ± 69 and by 46 ± 66 mEq/l respectively (P = 0.93). Whereas $[AG]_u$ did not differ between groups, $[Na^+]_u - [Cl^-]_u$ variation of hyperventilated patients was greater than that of hypoventilated (17 ± 34 vs. –18 ± 54 mEq/l, P <0.05).
Conclusion During acute respiratory modifications, changes in urinary ammonium can be observed within the first 2 hours even while maintaining arterial pH within a physiologic range. This response seems to be better associated with changes in the difference between urinary sodium and chloride rather than anion gap.
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P431

Admission hypomagnesemia as a mortality predictor in medical critically ill patients

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Introduction Magnesium is the second most abundant intracellular cation and serves as a cofactor in more than 300 enzymatic reactions. Hypomagnesemia is a common electrolyte imbalance in critically ill patients; yet it is frequently overlooked. Previous studies highlighted the relationship between hypomagnesemia and mortality in these patients [1,2]. This study was carried out on patients admitted to the critical care unit and seeks to find admission hypomagnesemia's role as a 28-day mortality predictor in medical critically ill patients.
Methods This is a cohort prospective study with prognostic research recruiting 150 critically ill patients in a major tertiary hospital. Blood samples were collected for estimation of serum total magnesium on admission, and then the patients were followed over 28 days.
Results This study was conducted consecutively from April to July 2013. Most subjects were male (62%) with mean age 52.6 ± 15.93 years. The occurrence of sepsis (33.3%) and cardiac disturbances (24.7%) were the most common problems among patients. The mean MSOFA score for the hypomagnesemics was higher than the normal group (4.91 ± 4.19 vs. 3.77 ± 3.52). Subgroup analysis in the MSOFA 0 to 7 group had significant $P = 0.015$ (chi-square) and crude RR = 2.2 (95% CI = 1.19 to 4.06). From survival analysis, the survival mean of hypomagnesemia patients was lower than the normal group (19.4 vs. 22.8 days), and so was the survival percentage (52.7% vs. 74.7%).
Conclusion There was a high prevalence of hypomagnesemia in medical critically ill patients and it was associated with a high mortality rate.
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P432

Impact of reduced frequency of phosphate testing on detected phosphate levels and phosphate prescription in critical care

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Introduction Phosphate is essential for cell and bone function [1]. In critical illness, hypophosphatemia is common and practice is often to correct even mild derangement [2]. Its supplementation has significant cost and risk including hypotension and hypocalcaemia. We investigated whether changing frequency of routine serum phosphate testing had effects on the detected incidence of abnormal plasma levels and prescription of phosphate.
Methods This was a service improvement project using observational, anonymous data. We collected data on serum phosphate levels in a 33-bed ITU over two 6-month periods before and after introduction of a new testing regime (phases 1 and 2). In phase 1, phosphate levels were tested daily. In phase 2, phosphate levels were tested three times per week. Replacement was at clinical discretion. Pharmacy data on phosphate prescription were compared for both phases.
Results A total of 4,253 tests were performed in phase 1, and 3,641 in phase 2 – a reduction of 612 (14.4%). The ICU workload was similar in both phases. There was no significant difference in mean phosphate levels or detected incidence of abnormal phosphate levels in phase 1 versus phase 2. Mean level was 1.13 ± 0.40 mmol/l versus 1.14 ± 0.43 mmol/l ($P = 0.42$). Severe hypophosphatemia (<0.4 mmol/l) was relatively uncommon: $n = 18$ in phase 1 (0.42% of tests) versus 19 (0.52%), $P = 0.42$, in phase 2. Mild hypophosphatemia (0.4 to 0.7 mmol/l) was frequent, with 1,203 episodes (28.2% of tests) versus 1,088 (29.8%), $P = 0.42$. Hyperphosphatemia (>1.5 mmol/l) was also common in both phases with 608 detected episodes (14.3% of tests) versus 572 (15.7%), $P = 0.49$. Pharmacy data show phosphate replacement fell significantly, from 687 prescriptions in phase 1 to 395 in phase 2, with drug cost-savings estimated at £1,430.
Conclusion Reducing testing from daily to three times weekly was not associated with a significant change in mean phosphate levels nor with detection of abnormally high/low phosphate levels. Daily testing, however, is associated with higher rates of phosphate prescription. It is known that there is significant diurnal variation in serum phosphate [2] and we speculate that mild hypophosphataemia self-corrects without intervention. Treating mild hypophosphatemia may therefore not be indicated.
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P433

Effect of albumin and total protein concentration on plasma sodium measurements in the ICU

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Introduction Direct ion-selective electrode without dilution is the most effective method for determination of the concentration of the ionized fraction of sodium [1]. We tested the hypothesis that the difference between indirect and direct sodium assays would be related to the plasma albumin concentration or the total protein concentration.
Methods A retrospective observational study was conducted in which plasma sodium concentrations, from 101 paired venous and arterial samples from patients admitted to the ICU, were respectively analyzed on the arterial blood gas (ABG) analyzers (direct ion-selective electrode) and the central laboratory auto-analyzers (indirect ion-selective electrode). A paired *t* test was performed comparing the central laboratory and ABG measurements. Correlation and regression analysis were performed between total protein concentration, albumin and the differences between the central laboratory and ABG assays for sodium.
Results The central laboratory sodium measurement was, on average, 1.46 mmol/l more than the ICU assay, limits of agreement 1.18 to 1.74 mmol/l greater, $P < 0.001$. Bland–Altman analysis of the central laboratory result minus the ICU sodium measurement had limits of agreement of 1.3 to –4.2 mmol/l. The correlation between the assay differences and total protein concentration and albumin were respectively $r = 0.24$ ($P = 0.01$) and $r = 0.20$ ($P = 0.04$). The difference in plasma sodium concentration between the assays increased as the plasma concentration albumin or total protein concentration decreased (respectively: $r^2 = 0.04$ and $r^2 = 0.06$).
Conclusion The difference between indirect and direct sodium assays was found to be statistically related to the plasma albumin concentration and the total protein concentration. Although the relationship was found to be weak, the total protein concentration should be monitored when measuring sodium by indirect ion-selective electrode.
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P434

Main causes of water–electrolyte disturbances in patients with acute brain injury: central diabetes insipidus and cerebral salt wasting syndrome

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Introduction Water–electrolyte disturbances are one of the most common complications of acute brain injury of various origins, threatening the life of the patient and requiring timely correction. In this work we studied the structure of water–electrolyte complications in patients in the neurological intensive care with acute brain injury.
Methods We analyzed 259 cases of water–electrolyte disturbances that developed in patients treated in the Department of Intensive Care of

Russian Polenov's Neurosurgical Institute from 2001 to 2012. Patients were between 16 and 55 years old. A total of 142 patients were operated for brain tumor, 72 of them of basal–supratentorial localization; eight severe brain trauma; 62 of the hemorrhagic type of stroke, one herpes encephalitis. We excluded from this study the patients with heart and renal failure receiving diuretics. We measured BP, HR, CVP, hourly and daily urine output, level of K and Na in plasma, brain natriuretic peptide (BNP) one to four times a day, and levels of K and Na in urine in single and daily servings. All patients were receiving dexamethasone at a dose between 8 and 32 mg/day as an anti-edema therapy, and thus levels of ACTH and cortisol were not investigated.

Results Central diabetes insipidus (CDI) developed in 106 patients. Against the background of substitution therapy, we did not observe the development of complications, hypovolemia, hypernatremia, or hyperosmolality. Out of 48 cases of CSWS, in 12 cases the symptoms interleaved with the symptoms of CDI. For 24 patients, CSWS was complicated by depressed consciousness, for three patients by convulsions against the background of hypovolemia, hyponatremia, or hypo-osmolality. No correlation between BPN level and absence of CSWS symptoms was found.

Conclusion In patients with acute brain trauma we observed two syndromes causing water–electrolyte disturbance – CDI and CSWS. CSWS generally is more severe than CDI. We could not determine a correlation between BPN level and the absence of presence of the CSWS symptoms.

P435

Cardiac surgery alters the sensitivity of the dynamic interaction between the pituitary and adrenal glands

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Introduction Both ACTH and cortisol are secreted in a diurnal rhythm. Underlying this is an ultradian rhythm of discrete pulses [1] as a result of the feedforward:feedback interactions between cortisol and ACTH [2]. These pulses are critical for normal function; pulsatile and constant infusions yield different transcriptional responses [3] and patients on optimal (nonpulsatile) glucocorticoid replacement have twice the age-related mortality of the general population [4]. We have now characterised the ultradian rhythm and pituitary–adrenal interaction of patients undergoing coronary artery bypass grafting (CABG).

Methods Twenty male patients presenting for elective CABG (on-pump and off-pump) were recruited. Blood samples were taken for 24 hours from placement of the first venous access. Cortisol was sampled every 10 minutes, ACTH was sampled every hour and cortisol binding globulin (CBG) was sampled at baseline, at the end of operation and at the end of the 24-hour period.

Results Cortisol and ACTH were pulsatile throughout the perioperative period and the cortisol–ACTH interaction persists (Figure 1). The sensitivity of this interaction (calculated by the ratio of cortisol to ACTH pulse amplitude) changed at about 8 hours post surgery such that the adrenal sensitivity to ACTH increased.

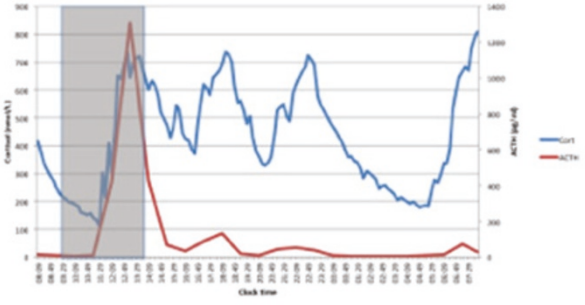

Figure 1 (abstract P435).

Conclusion Both cortisol and ACTH remain pulsatile during and after cardiac surgery and the pituitary–adrenal interaction persists, although the sensitivity of the adrenal glands changes throughout the perioperative period. Our study shows that endogenous glucocorticoid levels reach very high oscillating levels following cardiac surgery, which not only invalidate the interpretation of point measures of adrenal function to diagnose adrenal insufficiency but also demonstrate that constant infusions of hydrocortisone are unphysiological.

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P436

Melatonin blood values and total antioxidant capacity in critically ill patients

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Introduction Endogenous melatonin is decreased in critically ill patients; oral supplementation could help them to cope with sleep disruption and sepsis. Among patients who took part in a trial on melatonin and need for sedation [1], some were studied with blood sampling to describe their melatonin blood values and the relationship with total antioxidant capacity (TAC) in plasma.

Methods Inclusion criteria: mechanical ventilation previewed at ICU admission >8 days and mortality predicted at ICU admission over 13% (SAPS II >32 points). After the clinical run-in period of 48 hours, samplings were taken to measure baseline blood melatonin and TAC, beginning from the third ICU night and day (midnight and 02:00 p.m.). At 8:00 p.m. of the third ICU day, treatment with 3 mg + 3 mg melatonin (Group M) or placebo (Group P) began: each patient received two tablets per day, at 8:00 p.m. and midnight, until ICU discharge. Further samplings were taken during the early (fourth night and day) and the late (eighth night and day) treatment phases. Melatonin was measured through an ELISA essay; TAC was measured with a specific kit.

Results Sixty-four critically ill patients were enrolled. Endogenous melatonin was shown decreased in the run-in period and in the placebo group compared with healthy subjects. All patients reached satisfying pharmacological values with enteral administration: peak of blood melatonin value (pg/ml) was 2,514 (982 to 7,148) for the M group versus 20 (15 to 62) for the P group (P <0.001) during the first treatment night, while maintaining significant differences also during the daytime: 51 (23 to 180) M group versus 14 (11 to 24) P group (P = 0.001). The same trend was observed in the late treatment samples (eighth ICU day). Regarding TAC values (nmol Trolox equivalent/µl plasma), a significant difference was highlighted during the night (107 (97 to 123) M group vs. 61 (42 to 89) P group, P <0.001), but not during the daytime (37 (30 to 69) M group vs. 28 (25 to 50) P group, P = 0.092). Correlation between melatonin and TAC: Spearman's rho = 0.33 (P <0.001).

Conclusion Enteral administration of melatonin was adequate in the early phase of critically illness, with pharmacokinetics similar to published data [2]. The administration of melatonin seems to increase the TAC, with a possible meaningful role in critically ill patients.

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P437

Continuous prediction of glucose-level changes using an electronic nose in critically ill patients

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Introduction Many if not most critically ill patients are treated with insulin during their stay in the ICU [1]. Intensive monitoring of the blood glucose level is a prerequisite for efficient and safe insulin titrations

in these patients [2]. Current continuous glucose measurement techniques rely on subcutaneous glucose measurements [3] or measurements in blood [4]. We hypothesized that changes in volatile organic compound (VOC) concentrations in exhaled breath reflect changes in the blood glucose level. Changes in VOC concentrations can be analyzed continuously using a so-called electronic nose (eNose) [5]. Our aim was to investigate exhaled breath analysis to predict changes in glucose levels in intubated ICU patients.

Methods Exhaled breath was analyzed in 15 intubated ICU patients who were monitored with a subcutaneous CGM device. eNose results were compared with subcutaneous glucose measurements and linear regression models were built, including subject-specific models, and whole-sample models. The models were validated using temporal validation by training the model on the first 75% of measurements and prospectively testing on the last 25% of measurements. Performance of the models was measured using an R^2 value, Clarke error grids (CEG) and rate-error grid analysis (R–EGA).

Results Changes in VOC concentrations were associated with changes in subcutaneous glucose levels. R^2 performance had a mean value of 0.67 (0.34 to 0.98) for subject-specific models, and a mean value of 0.70 (0.52 to 0.96) for the model for the whole sample. However, when externally validating the model, the predictive performance dropped to a mean R^2 of 0.19 (0.00 to 0.70) for subject-specific models, and 0.04 for the model for the whole sample. Point accuracy in CEG was mostly good with >99% in zones A and B; trend accuracy, as visualized with R–EGA, was low.

Conclusion Exhaled breath prediction of glucose levels seems promising. However, performance of the current models is too low to be used in daily practice.

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P438

Evaluation of blood glucose control in ICU patients with Space GlucoseControl: a European study

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Introduction Regardless of the ongoing debate on optimum target ranges, glycaemia control (GC) remains an important therapeutic goal in critically ill patients. Dozens of different insulin protocols for ICUs have been developed with different complexity, effectiveness, blood glucose (BG) variability and safety. Although comparison of existing protocols is difficult due to significant differences in processes and outcome measures, computerized clinical decision support systems generally achieved better GC with consistently lower hypoglycaemia rates than that achieved with paper-based protocols [1]. The enhanced Model Predictive Control (eMPC) algorithm, developed by the CLINICIP group, is the effective clinically proven protocol, which has been successfully tested at multiple institutions on medical and surgical patients with different nutritional protocols [2,3]. The eMPC models the behaviour of glucose and insulin in ICU patients with a variable sample interval based on the accuracy of the BG prediction. It has been integrated in the B.Braun Space GlucoseControl (SGC) system, which allows direct data communication between pumps and Space Control with the incorporated eMPC algorithm. Although SGC is already clinically used in dozens of ICUs worldwide, there are few only published experiences with its use [4].

Methods The primary objective of this multicentre European non-interventional study was to evaluate the performance (efficiency) of SGC under routine conditions in adult ICU patients requiring BG control. The primary endpoint was the percentage of time within the target range, and secondary outcome measures were the frequency of hypoglycaemic episodes and BG measurement intervals. Patients in this trial were assigned to the target range 4.4 to 8.3 mmol/l. Nutritional management (enteral, parenteral or both) was carried out at the discretion of the each centre.

Results Seventeen centres from nine European countries included a total of 508 patients. During the study a total of 29,575 BG values were entered into the SGCs and the same number of recommendations were rendered. The mean time-in-target was 77.5 ± 20.9%. The mean proposed next measurement time was 2.0 ± 0.5 hours. Only four episodes of hypoglycaemia <2.2 mmol/l occurred (0.01% of measurements).

Conclusion SGC is a safe and very efficient system to control BG in ICU patients.

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P439

Evaluation of Symphony CGM, a non-invasive, transdermal continuous glucose monitoring system for use in critically ill patients

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Introduction Glycemic control in the ICU has been shown to reduce morbidity, mortality and length of stay. However, current methods of blood glucose (BG) monitoring are invasive, intermittent and labor-intensive. Continuous glucose monitoring (CGM) has potential to improve safety/efficacy of BG control. The performance of a non-invasive, transdermal CGM system (Symphony CGM; Echo Therapeutics, Philadelphia, PA, USA) was evaluated in post-surgical ICU patients.

Methods Adult surgical patients with planned ICU admission of ≥24 hours at four medical centers were consented. Following admission to the ICU, the skin of an upper arm was cleaned and a 6 mm diameter site was prepared with controlled micro-abrasion using the Symphony CGM system. A transdermal CGM sensor containing glucose oxidase was applied. Following a 1-hour warm-up period, a calibration was performed. Blood samples were obtained from a radial artery catheter approximately every hour, centrifuged to plasma, and glucose was measured using a YSI 2300 STAT Plus Glucose Analyzer (reference BG). A maximum of 30 reference BG samples were collected for each patient. Samples were collected as frequently as every 15 minutes for trend analysis. CGM was prospectively calibrated every 4 hours. All treatment decisions were based on BG alone. Safety was assessed by visual inspection of the site using a dermatological scale following sensor removal. A study was defined as evaluable for CGM sessions >16 hours.

Results Thirty-two subjects completed the study. Additional subjects were not considered evaluable due to early discharge from the ICU, failure or early removal of the radial artery catheter, or administration of intravenous acetaminophen. The study cohort was 19% female, 28% diabetes, 56% cardiac surgery, with a mean age of 65 ± 13 years. Overall mean absolute relative difference between CGM and reference BG was 12.5%. Continuous glucose error-grid analysis, which assesses point and trend accuracy, showed 98.2% of readings in the A zone (clinically accurate) and 1.2% in the B zone (benign errors). Glucose values ranged from 49 to 324 mg/dl. No device or study-related adverse events were reported.

Conclusion The Symphony CGM system demonstrated clinically relevant accuracy and excellent safety in a variety of patients and ICU environments. Future studies are needed to determine whether Symphony CGM can be used to direct therapy and improve BG control in this patient population.

P440

Time-course evaluation of blood glucose changes in response to insulin delivery in critically ill patients

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Introduction Intravenous insulin by infusion is commonly used for blood glucose control in the ICU and blood glucose is almost exclusively monitored by intermittent sampling. The rate of change in blood glucose concentration [BG] when the insulin infusion rate is changed is not known, and as a result the optimum time to measure [BG] after changing the infusion rate is unclear.
Methods Following institutional ethics approval and patient consent, using a GluCath Continuous Glucose Monitoring system sensor deployed via a radial artery catheter we studied the change in [BG] in response to a 1 unit/hour increase in the insulin infusion rate during the first 48 hours after cardiac surgery. [BG] was recorded every 10 seconds. Insulin was infused at a concentration of 1 unit/5 ml/hour via a volumetric pump. We recorded [BG] for 2 hours after changing the insulin infusion rate. Data affected by artifacts produced by blood draws and subsequent flushing of the arterial catheter were excluded and linear interpolation was used to estimate missing [BG] data.
Results There were five episodes where the insulin infusion increased by 1 unit/hour. [BG] decreased modestly for 50 minutes, after which there was marked interpatient variability in subsequent [BG] trend (Figure 1). The median (range) change in BG (mmol/l) at 30 minutes: –0.5 (–0.7/+0.1), 60 minutes: –0.1 (–0.7/+1.0), 90 minutes: –0.3 (–0.7/+0.6) and 120 minutes: –0.5(–1.2/+2.9).
Conclusion Within the first hour the change in [BG] was consistent but beyond this time it was highly variable. Further studies are needed to understand the dynamics of [BG] in response to changes in insulin infusion rates, but these data suggest [BG] should be checked hourly until stable.

P441

Glycaemia and critical care outcomes

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Introduction The aim of this study was to determine the impact of preadmission or first 24-hour blood glucose (BG) measurements in UK ICUs on mortality.
Methods The Intensive Care National Audit & Research Centre case-mix programme database on adult admissions to general, neuroscience and cardiothoracic critical care units was used for analysis. Within the database, the highest and lowest blood glucose (BG) values measured during the first 24 hours from admission were recorded. BG control value was defined as BG (≥4.0 ≤9.9 mmol/l). Other BG levels were defined as: very low, ≤2.2 mmol/l (≤40 mg/dl); low, >2.2 ≤3.9 mmol/l (40 to 70 mg/dl); high, ≥10.0 <11.1 mmol/l (180 to 200 mg/dl); and very high, ≥11.1 mmol/l (200 mg/dl).

Table 1 (abstract P441). Critical care outcomes

Variable	Very low	Low	Control	High	Very high
Number of patients	11,471	70,106	521,839	77,423	187,553
ICU mortality* (%)	55	31	13	18	26
ICU LOS*	7	6	4	5	6

*P <0.001.

Results There was an increased incidence of mortality in those patients with at least one BG measure below 3.9 mmol/l (70 mg/dl) compared with those without (Table 1). There was a link between BG levels and LoS for surviving patients with the longest hospital stays (critical care and total hospital) experienced by those with BG levels below 2.2 mmol/l (40 mg/dl).
Conclusion There is a strong association between BG levels during admission and mortality and LoS outcomes. Although it is not possible to make the link with causation from our dataset, we present results from the largest single dataset of critical care unit patients [1,2].
Acknowledgement Funding from Edwards Lifesciences.
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P442

Continuous monitoring of blood glucose using a fiberoptic-based intravascular sensor during postoperative care in the ICU

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Introduction While there is ongoing discussion of the optimal range for glycemic control in hospital intensive care, recent publications from Mackenzie and colleagues [1] and Krinsley [2-4] suggest not only that mean BG should be considered, but also that glucose variability and complexity may be equally important. This has increased the need for continuous systems which can provide early warnings of hypoglycemia and effectively measure variability. GlySure Ltd has developed an intravascular glucose monitoring system to simplify the application of hospital protocols for tight glycemic control (TGC) at the point of care. Experience with the original research-based instrumentation [5] has now been incorporated into a combined pre-production monitor and

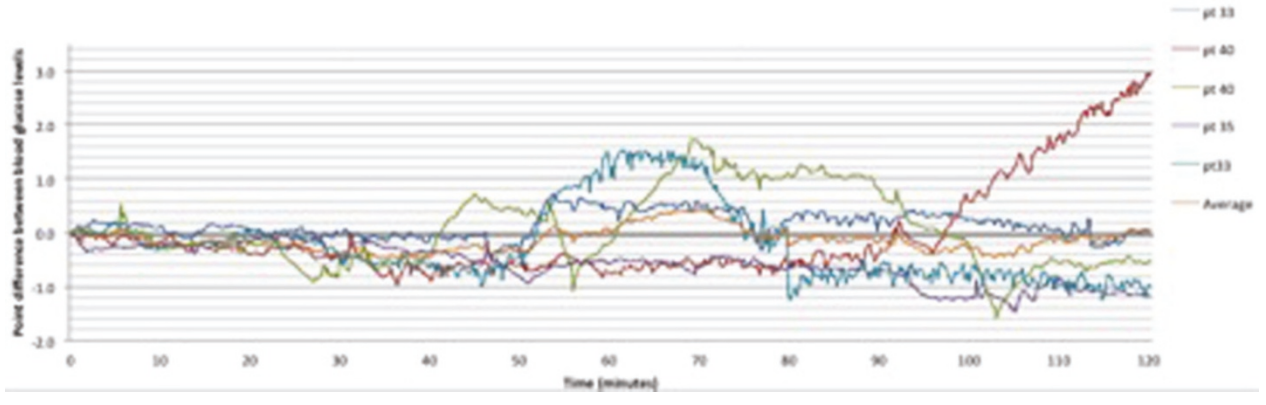

Figure 1 (abstract P440). Blood glucose change after infusion change and after calibration.

autocalibration unit. We have now completed a 34-patient trial using this device and present the data collected from this study.

Methods The study used GlySure sterile, single-use sensors and a 5-lumen 9.5-Fr CVC device, allowing the fluorescence optical-based sensor to be placed into the patient's right internal jugular vein. The screen data were blinded to the bedside staff. Data from the monitor were later compared with sample measurement from the Yellow Springs (YSI) glucose analyzer. The data accuracy was measured using the mean absolute relative difference (MARD), an error calculation tool.

Results The device met the primary safety and effectiveness endpoints of the trial. The 456 sample values recorded by the monitor based on 8-hour calibrations were correlated with samples taken from the YSI and the MARD for the study was 9.40%. The analysis showed that 89.23% of the data fell within the A zone of the Clark error grid, with the rest falling within the B zone.

Conclusion The results demonstrate a good correlation with the accepted standard of blood glucose determination in ICU practice. Early detection of glycemic excursions can provide carers with the opportunity for an early intervention and thus achieve the elusive target of TGC around the chosen target range.

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P443

First clinical study data from therapeutic use of a novel continuous glucose monitoring system in the ICU

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Introduction The aim of this study was to determine the safety and efficacy of treating patients using a novel intravenous continuous glucose monitoring (CGM) system (GlucoClear™; Edwards Lifesciences). The practical benefit of controlling blood glucose in the critically ill remains contentious, largely because of the lack of tools to adequately measure and therefore manage levels in real time. A system that is able to provide instant, constantly calibrated, accurate values is a major bonus to ICU care and we report here the first clinical use of a novel CGM system directly used to manage postoperative glycaemia.

Methods All consecutive consenting adult patients undergoing cardiac surgery involving cardiopulmonary bypass and requiring postoperative insulin (>98% of patients) were enrolled in the study with a target enrolment of 100. Blood glucose was measured via a dedicated peripheral intravenous catheter with values reported every 5 minutes. The primary outcome was the number of data points in the target glycaemic control range (4.4 to 8.0 mmol/l), using a dynamic insulin protocol. Secondary endpoints include mean glucose levels, time in range and number of hypoglycaemic and hyperglycaemic episodes.

Results For the first 45 patients, mean age was 67.7 years (male 52.8%), 54% had undergone valve surgery with or without CABG and the majority (67%) had no history of diabetes. The CGM sensor was typically sighted in the forearm or hand (90.5%) and was resited on 7.5% occasions. Median monitoring time in the ICU was 28.4 hours. Mean glycaemic value was 6.8 mmol/l. From the possible 18,609 glucose values (one per 5 minutes), 16,808 values were recorded (90.3%). Overall, 13,389/16,808 values (79.6%) were within the target range. No hypoglycaemic episodes (≤2.2 mmol/l) were recorded at any point. There were 219/16,808 values (1.3%) in the hyperglycaemic range (≥10.0 mmol/l).

Conclusion This new CGM system enabled significantly improved glycaemic control despite the challenges of working with an entirely new system of glucose control in a unit with over 200 nurses. Performance notably improved with experience and also highlighted that even previously validated dynamic algorithms will need to be refined to maximise the benefit of GGM. Overall, the evidence from the first applied clinical use of this novel CGM showed that proper safe, tight glycaemic control can be achieved. Further investigations are required to demonstrate the reduction in morbidity and mortality using CGM, and we plan to embark on further studies to address this.

P445

Impact of corticosteroid administration in septic shock on glycemic variability

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Introduction The purpose of this study was to assess the relation between glycemic control and the severity of sepsis in a cohort of patients with vasopressor-dependent septic shock treated with corticosteroids [1,2].

Methods In a prospective, controlled study, 134 patients with septic shock were randomized into three study groups: group A (n = 43), 200 mg/day hydrocortisone hemisuccinate in four daily doses; group B (n = 47), same dose of hydrocortisone hemisuccinate in continuous administration; group C (n = 44), no hydrocortisone hemisuccinate. Patients with diabetes mellitus were excluded. The duration of hydrocortisone treatment was a maximum 7 days. The target blood glucose (BG) level was below 180 mg/dl. BG values were analyzed by calculating mean daily values, standard deviation (SD) of BG values as an index of glycemic variability, and insulin doses. The local ethics committee approved the study.
Results There were no differences between the three groups at the beginning of the study regarding demographic data and the clinical characteristics, including BG value. BG levels were strongly correlated with severity of septic shock estimated by APACHE II score (r = +0.241; P = 0.005) or Simplified Acute Physiology Score II (r = 0.280; P = 0.001) – Pearson correlation. The risk of death is significantly increased if SD of BG is more than 20 mg/dl (67.7% vs. 20.8%, P = 0.000). A total 94.4% of deceased patients in group A registered a SD of BG more than 20 mg/dl versus 89.5% in group B or 40% in group C (P = 0.006). In total, 53.5% of patients in group A needed insulin therapy versus 25.5% in group B or 27.3% in group C. The dose was between 30.28 ± 6.65 UI/day in group A, 37.85 ± 11.95 UI/day in group B, and 14.28 ± 5.76 UI/day in group C (P >0.05).
Conclusion BG variability is highly associated with mortality compared with BG mean daily value or insulin dose. SD levels above 20 mg/dl were associated with a significantly higher mortality rate relative to those with SD levels below 20 mg/dl.
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P446

Blood glucose target in acute phase suggested by the analysis of the relationship between blood glucose profile and the severity of the diseases

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Introduction Blood glucose (BG) control in acute illness improves outcome. However, how to manage BG levels, or BG target, is not clearly elucidated. In this study, the BG target was suggested by the analysis of the relationship between BG profile and the severity of the diseases.
Methods Ninety-six patients were studied. The following parameters were calculated during the first week after ICU admission. (1) Maximum value of SOFA score (SOFAmax). (2) Mean, standard deviation, maximum, minimum, and difference of BG levels (BGm, BGsd, BGmax, BGmin, BGd (BGmax – BGmin), respectively). BG levels were measured basically every 6 hours. (3) Correlation between SOFAmax and BG parameters using two-dimensional (correlation coefficient r_t) and linear regression analysis (r_l).
Results (1) Mortality of the patients with SOFAmax 0 to 3, 4 to 5, 6 to 7, 8 to 9, and 10 or more were 0%, 14%, 23%, 40%, and 89%, respectively. (2) r_t and r_l (r_t/r_l) between SOFAmax and BG parameters: BGsd (0.49/0.36), BGmax (0.47/0.32), BGm (0.45/0.23), BGd (0.44/0.32), and BGmin (0.25/0.06). (3) BG ranges that indicate SOFAmax less than 5 calculated from the two-dimensional correlation curves between SOFAmax and BGsd, BGmax, BGm, and BGd were 35 ± 25, 250 ± 112, 150 ± 33, and 156 ± 115 mg/dl, respectively.
Conclusion BG parameters except BGmin were two-dimensionally related to the severity. Therefore, a part of the severe patients seemed to have lower BG levels and lower BG variability. Targeting those BG parameters in early phase within the abovementioned levels was considered to link to better outcome.

P447

Anti-inflammatory and antioxidant effects of ranolazine on primary cultured astrocytes

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Introduction Because of its ability to block late INa [1], ranolazine is used as an antianginal agent for the treatment of chronic angina pectoris when angina is not adequately controlled by other agents [2]. Besides its cardiovascular effects, ranolazine improves different neuronal functions, and thus its use has been proposed for the treatment of pain and epileptic disorders [3,4]. Since astrocytes are involved in neuronal inflammatory processes, and autoimmune and neurodegenerative diseases [5], we have investigated the anti-inflammatory and antioxidant effects of ranolazine in primary cultured astrocytes.
Methods We incubated differentiated rat astrocytes in primary culture (10 days of culture) [5] for 24 hours with ranolazine (10^{-5}, 10^{-6}, 10^{-7} M). We measured the protein expression levels of PPARγ and Cu/Zn-SOD by western blot technique. Protective effect of ranolazine on cell viability was assayed using MTT conversion assay. Finally, to evaluate the effect of ranolazine on the IL-1β cytokine and TNFα mediators, we used the enzyme-linked immunosorbent assay technique.
Results Compared with control cells, treatment with ranolazine induced an increment of anti-inflammatory PPARγ and reduced the proinflammatory mediators IL-1β and TNFα in primary cultured astrocytes. Ranolazine (10^{-6} M) also increased the expression of antioxidant protein Cu/Zn-SOD and caused a significant increase in cell viability.
Conclusion Ranolazine decreases inflammatory mediators IL-1β and TNFα, and increases anti-inflammatory PPARγ as well as the antioxidant Cu/Zn-SOD in astrocytes in culture. These results suggest that ranolazine could be useful as a neuroprotective drug in pathologies inducing inflammatory damage and oxidant processes.
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P448

Tuberculous meningitis: a 10-year case analysis of critical care admissions

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Introduction Tuberculous meningitis (TBM) is the least common extrapulmonary manifestation of tuberculosis. Although the UK incidence of TBM is relatively low, it carries a high mortality and morbidity [1]. Neurological deterioration continues to be an important reason for ICU admission [2]. Little is known about the outcomes for TBM patients requiring ICU admission. Our aim is to evaluate patient demographics, TBM clinical data, and the necessity for organ support, and whether this can be associated with outcome.
Methods A retrospective study at a tertiary centre of patients with TBM admitted to our ICU between 2000 and 2012. Data were retrieved on demographics, microbiology, radiology and pharmacological findings and type and level of organ support. APACHE II and SOFA scores were calculated. Patients were stratified into two groups: CSF PCR+ve and CSF PCR–ve.
Results Eight patients (six males:two females) were evaluated. Total mean age was 43.9 ± 8.09 years. A reduction in GCS was the main reason for ICU admission. All patients received ≥3 anti-TBM drugs and steroids. Two CSF PCR+ve patients had primary drug resistance to isoniazid. There was also a longer mean delay in the time of onset of anti-TBM treatment in CSF PCR+ve patients (4 ± 2.88 days). Higher APACHE II and SOFA scores on admission (mean = 23, 8.5) were

associated with a positive CSF PCR result. Increased requirements for mechanical ventilation (100%), tracheostomy (50%), inotropes (75%), neurosurgical intervention (predominantly CSF drainage) (100%) and enteral feeding (50%) were all significant for this group. Mortality and long-term neurological morbidity were substantially higher for PCR+ve patients (75% and 25%). In contrast, the majority of culture-negative patients survived (75%), and experienced good recoveries at follow-up. Overall mortality was 50%.

Conclusion This is the second documented case analysis of TBM and ICU admission in adult patients [1,2]. Findings show that poor outcomes are associated with positive CSF PCR results. Factors linked to poor outcomes include delays in initiating anti-TBM treatment, neurosurgical interventions, and an increased requirement for multiorgan support. Earlier drug susceptibility testing would be preferable particularly for patients with positive CSF PCR cultures. Given the potential severity of TBM, a high index of clinical suspicion remains critical towards optimizing outcomes.

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P449

Intrathecal lactate to predict spinal cord ischemia in major abdominal surgery

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Introduction The aim was to evaluate the role of intrathecal lactate as an early predictor of spinal cord injury during thoracoabdominal aortic aneurysmectomy. Forty-four consecutive patients were scheduled to undergo thoracoabdominal aortic aneurysmectomy. Two patients had a type B dissecting aneurysm; all other 42 patients suffered from degenerative aneurysm.

Methods During surgery, samples of cerebrospinal fluid and arterial blood were simultaneously withdrawn to evaluate lactate concentration. Samples were collected at five fixed times during and after surgery: T1 (beginning of the intervention), T2 (15 minutes after aortic cross-clamping), T3 (just before unclamping), T4 (end of surgery), and T5 (4 hours after the end of surgery).

Results Mean lactate levels in cerebrospinal fluid rose consistently from the beginning of the intervention steadily until after surgery (T1 = 1.83 mmol/l, T2 = 2.10 mmol/l, T3 = 2.72 mmol/l, T4 = 3.70 mmol/l, T5 = 4.31 mmol/l). Seven patients developed spinal cord injury; two of them had delayed injury occurring 24 hours after the end of surgery; the remaining five had early onset. In this group of five patients, preoperative cerebrospinal fluid lactate levels were significantly (P = 0.04) higher than those of the other 40 patients preoperatively (2.12 ± 0.35 vs. 1.79 ± 0.29 mmol/l).

Conclusion The preoperative cerebrospinal lactate concentration is elevated in patients who will develop early-onset spinal cord injury after thoracoabdominal aortic aneurysmectomy. This may allow a better stratification of these patients, suggesting a more aggressive strategy of spinal cord function preservation and possibly guaranteeing them a better outcome.

P450

Predictors of ventilatory outcome in cervical spinal injuries

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Introduction Spinal cord injuries affect 50 persons per million every year in North America [1], with over 50% occurring at the cervical level [2]. Cervical spinal cord injuries (CSI) are at particular risk for mechanical ventilation (MV), pulmonary complications and increased length of hospital stay. A few small cohort studies looked at predictors of MV [3-6], and to our knowledge there are no studies addressing factors associated with prolonged MV. The purpose of this study was to compare known clinical predictors of MV and determine predictors of prolonged MV.

Methods We conducted a retrospective chart review of consecutive CSI admitted between 1 January 2005 and 1 March 2009. We recorded data related to the injury, the duration of MV, respiratory complications, ICU and hospital length of stay and patients' outcomes. A review of the literature identified known predictors (ASIA level, ISS, level of injury, and so forth). Univariate and multivariate logistic regression were used to identify predictors of MV and prolonged MV.

Results Of the 208 patients, 82% were male and the mean age was 51 years. Hospital mortality was 8.7%. Main causes of injury were motor vehicle accidents (39.7%) and falls (43.2%). Injuries below C4 level represented 51.5% of the population. A complete loss of motor function (ASIA level A and B) was found in 34.9% of patients. The mean and median ISS score was 20.7. In total, 78 patients required MV (37.5%) and 30 patients required prolonged MV (14.4%). After multivariate analysis, four predictors of MV were identified: pneumonia (OR = 52.83); ISS score >22 (OR = 4.09); age (OR = 1.02); level C1 to C4 (2.34); and two predictors of prolonged MV: ASIA score A and B (OR = 5.57) and pneumonia (OR = 8.76).

Conclusion In our study ISS, cervical level and age were associated with MV but not with the need for prolonged MV, whereas pneumonia was an independent risk factor for both. This is a potentially preventable risk factor where specific strategies can be applied to improve patients' outcome.

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P452

Evaluation of the ocular microcirculation in brain-dead patients: first step towards a new method of multimodal neuromonitoring?

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Critical Care 2014, **18(Suppl 1):**P452 (doi: 10.1186/cc13642)

Introduction Multimodal neuromonitoring is a part of goal-directed therapy in severe neurosurgical pathology that leads to better understanding and therefore accurate and timely correction of disturbances of cerebral perfusion. The aim of our study was to evaluate and compare microcirculation in the conjunctiva of the eye and sublingual mucosa in brain-dead patients and healthy volunteers. No studies to our knowledge with this purpose were performed previously. We hypothesized that direct videomicroscopic evaluation of conjunctival microcirculation is linked to cerebral blood flow.

Methods We evaluated microcirculation of the eye conjunctiva and sublingual mucosa of 10 brain-dead diagnosed patients and 10 healthy volunteers. Brain-death diagnoses were certified by cerebral angiography. Direct *in vivo* observation of the microcirculation was obtained with sidestream dark-field imaging. Assessment of microcirculatory parameters of convective oxygen transport (microvascular flow index (MFI), proportion of perfused vessels (PPV)), and diffusion distance (perfused vessel density (PVD) and total vessel density (TVD)) was performed according to international criteria.

Results All brain-dead patients required vasopressor support to sustain perfusion of donor organs. The MFI of small vessels was significantly lower in brain-dead patients in comparison with healthy controls in ocular conjunctiva (2.6 (2.4 to 2.8) vs. 3.0 (3.0 to 3.0), P = 0.03) and in sublingual mucosa (2.8 (2.6 to 2.9) vs. 3.0 (3.0 to 3.0), P = 0.04). TVD and PVD of small vessels were significantly lower in brain-dead patients in comparison with healthy controls in ocular conjunctiva (10.2 (5.2 to 14.8) vs. 17.0 (15.4 to 27.2) mm/mm^2, P = 0.023 and 5.2 (2.9 to 7.2) vs. 10.1 (8.5 to 16.7) l/mm, P = 0.023), but there was no difference in sublingual mucosa.

Conclusion We were able to identify a significant reduction of capillary density in the eye conjunctiva but not in sublingual mucosa when

comparing microcirculation of brain-dead diagnosed patients and healthy volunteers. However, the presence of conjunctival flow in case of general cerebral flow is completely absent, making it difficult to use conjunctival flow as a substitute for brain flow.

P453

External validation of an early warning alert for elevated intracranial pressure in the Avert-IT database

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Introduction After severe traumatic brain injury (TBI), episodes of elevated intracranial pressure (ICP) are associated with poor outcome. Previously we developed a model to predict increased ICP, 30 minutes in advance, using the dynamic characteristics of routinely monitored minute-by-minute ICP and mean arterial blood pressure (MAP) signals [1]. The model was developed using data from the Brain-IT database [2]. Here we present external validation results of this model, on a more recent cohort of adult TBI patients from the AVERT-IT project [3].
Methods A retrospective analysis of physiological data collected at the minute resolution, from 43 adult patients from the AVERT-IT project. A total of 67 episodes of ICP above 30 mmHg lasting at least 10 minutes were identified in this cohort. Four-hour time series of ICP and MAP anteceding each episode by 30 minutes were analyzed. Additional time series not preceding elevated ICP episodes were used for validation.
Results Table 1 summarizes the main findings. Performance of the model in the original study [1] is reproduced in the first column. The model retains identical performance for all criteria in the cohort of more recent TBI patients of the AVERT-IT database.

Table 1 (abstract P453).

Database	Brain-IT	Avert-IT
AUROC	0.85	0.83
aBrier SS (%)	34	30
Cal large	0.00	0.01
Cal slope	0.99	1.03
Accuracy (%)	77	77

Conclusion The obtained external validation results, on a previously unseen cohort of adult TBI patients, confirm the robustness of the model to accurately predict future increased ICP events 30 minutes in advance. The general applicability of the model is probably due to its sparseness, as it only uses two routinely monitored signals as input, namely ICP and MAP. These results are a large step forward in our work toward an early warning system for elevated ICP that can be used worldwide.
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P454

New support system using a mobile device for diagnostic image display and treatment of acute stroke in Japanese depopulated areas

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Introduction Stroke is the main cause of deterioration of activity of daily living in Japan. The social problem in Japan is the difference in medical quality between the urban and depopulated areas. To improve the problem, telemedicine using a mobile device between general physicians and stroke specialists became important with the increasing demand for rapid and correct diagnosis for treatment of acute stroke. We developed a system for rapidly exchanging diagnostic images and clinical information in depopulated areas to develop the standard thrombolytic therapy using alteplase for acute ischemic stroke [1,2].
Methods A system was consisted of communicating patient data and imaging between the hospital system and participating staff members in and out of the hospital using mobile devices. The system can transfer clinical data and large volumes of CT and MRI, and expert opinion in real time. We developed the system (k-support) in the Kaifu area, which is a typical depopulated area in Tokushima Prefecture, Japan, between the general physicians in Tokushima Prefectural Kaifu Hospital and specialists in stroke and cardiovascular disease at Tokushima University Hospital from February 2013.
Results The k-support system was managed in 102 emergency patients, 65 patients (64%) were classified as neurological disease, 41 (40%) as stroke, 11 (11%) as head injury, two (2%) as epilepsy. The detail of stroke was ischemia in 35 (34%), hemorrhage in four (4%) and SAH in two (2%). Two ischemic stroke patients were treated with intravenous thrombolysis of alteplase using the k-support system and a 'drip-and-ship' paradigm. One patient using alteplase showed complete recanalization of the middle cerebral artery. The consultations resulted in hospitalization in 42%, transfer in 37% and return home in 20%.
Conclusion Before introduction of the k-support system, the standard thrombolytic therapy using alteplase for acute ischemic stroke could not operate in the Kaifu area due to the absence of stroke specialists and the long distance to a neighboring stroke center. The telemedicine system using a mobile device as the k-support system can be used anytime, anywhere and by anyone. This system can communicate with the doctors, between general physicians in depopulated areas and specialists in urban areas, and may become a useful tool for acute patient management in not only stroke but also other emergency diseases.
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P455

Effects of cardiac output-guided hemodynamic management on fluid administration after aneurysmal subarachnoid hemorrhage

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Introduction In patients with aneurysmal subarachnoid hemorrhage (SAH), hypervolemic therapy may result in fluid overload that may be associated with adverse clinical outcomes [1,2]. We hypothesized that a goal-directed transpulmonary thermodilution (TPT) monitoring protocol aiming for normovolemia may result in decreased fluid intake while sustaining adequate volume status in poor-grade SAH patients.
Methods Following the introduction of the hemodynamic protocol in 2011, 26 consecutive patients with SAH were included until 2013. Using TPT (PiCCO; Pulsion), cardiac output (CO), global end-diastolic volume index (GEDVI) and extravascular lung water index (EVLWI) were determined. Fluid administration was targeted at fluid unresponsiveness. Indications for start of the protocol were: hypotension (in spite of fluids), pulmonary edema or cardiac stunning, daily fluid balance ≤–1 l, cerebral ischemia (DCI) with progressive symptoms. Data were collected on fluid intake and output up to 3 days before and 3 days after the start of TPT. We assessed the course of fluid input and output and hemodynamic parameters before and after the start of the protocol with the generalized estimating equation.
Results Mean age was 55 ± 16, and median Glasgow Coma Scale on admission was 8 (IQR 6 to 13). TPT was started at a median of 1 day after ICU admission (IQR 0 to 4). DCI developed in 70% and the in-hospital death rate was 45%. Compared with days preceding the protocol (day –3 to –1), TPT (day 0 to 3) was associated with decreased fluid intake (compared with day 3 as reference; day –1: +1.14 ± 0.31 l, P <0.001; day 0: +0.68 ± 0.29 l, P = 0.019; day 1: +0.73 ± 0.31 l, P = 0.02), increased

fluid output (day –2: –0.91 ± 0.46 l, P <0.05 compared with day 3), and consequently a strong decrease in fluid balance (day –3: +2.10 ± 0.56 l, P <0.001; day –2: +2.66 ± 1.14 l, P = 0.02; day –1: +1.41 ± 0.37 l, P <0.001). The decreased fluid intake and fluid balances did not result in decreased CO, GEDVI or EVLWI on days 1 to 3 compared with day 0 (mean PCCI 3.5 l/minute/m², mean GEDVI 761 ml/m², mean EVLWI 10.8 ml/kg).

Conclusion Our data suggest that in poor-grade SAH patients goal-directed fluid management with TPT is feasible to decrease intake and increase diuresis without adverse effects on cardiac output or preload parameters. Future research should assess the effect of such a protocol on clinical outcomes.

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P456

Effect of transient cerebral ischemia on the expression of receptor for advanced glycation end products in the gerbil hippocampus proper

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Introduction The receptor for advanced glycation end products (RAGE) is a multiligand receptor of the immunoglobulin superfamily that has been implicated in multiple neuronal and inflammatory stress processes. In the present study, we investigated changes in RAGE immunoreactivity and its protein levels in the gerbil hippocampus (CA1 to 3 regions) after 5 minutes of transient global cerebral ischemia.

Methods The ischemic hippocampus was stained with cresyl violet (CV), NeuN (a neuron-specific soluble nuclear antigen) antibody and Fluro-Jade B (a marker for neuronal degeneration).

Results Five days after ischemia–reperfusion, delayed neuronal death occurred in the stratum pyramidale (SP) of the CA1 region. RAGE immunoreactivity was not detected in any regions of the CA1 to 3 regions of the sham group. RAGE immunoreactivity was detected only in the CA1 region from 3 days post ischemia, and the RAGE immunoreactivity was newly expressed in astrocytes, not in neurons. In addition, the level of RAGE protein was highest at 5 days post ischemia. In brief, both the RAGE immunoreactivity and protein level were distinctively increased in astrocytes in the ischemic CA1 region from 3 days after transient cerebral ischemia.

Conclusion These results indicate that the increase of RAGE expression in astrocytes at post ischemia may be related to the ischemia-induced activation of astrocytes in the ischemic CA1 region.

P457

Correlation of thermal Doppler flowmetry and microdialysis values in patients with severe subarachnoid hemorrhage and traumatic brain injury

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Introduction The purpose of this study is to investigate the relationship between continuously monitored regional cerebral blood flow (CBF) and microdialysis values in severe subarachnoid hemorrhage and traumatic brain injury patients.

Methods Advanced multimodal neuromonitoring including measurements of CBF (QFlow, Hemedex) and brain lactate, pyruvate, lactate/pyruvate ratio, glycerol and glucose values using microdialysis (CMA600, microdialysis) were performed in 21 patients with severe subarachnoid hemorrhage (n = 17) and traumatic brain injury (n = 4). Thirteen of the patients were successfully discharged from the ICU while eight did not survive. Additional recorded parameters include $PbrO_2$ (Licox, GMS) ICP, CPP, MABP, CVP, local brain temperature, body core temperature, PCO_2, and blood glucose among others. The cerebral monitoring probes were inserted via a Bolt (ICP, $PbrO_2$, microdialysis) and an additional burr hole (CBF). All probes were positioned in the penumbra and location was verified by brain CT. The $PbrO_2$ arm of this study and its significance is still underway and will be announced later. Thirteen of the patients were successfully discharged from the ICU while eight did not survive.

Results The final data are currently under statistical evaluation, which will be completed at the time of presentation. However, there is indication of a link between brain glucose levels and CBF values, but it is not clear as to the CBF–$PbrO_2$ correlation that is the second part of this study under evaluation. This may be due to the fluctuation of brain glucose because of brain ischemia, hyperemia, hypermetabolism or hypometabolism. So far we are able to establish a correlation of CBF and lactate/pyruvate ratio only in persistently low CBF values.

Conclusion This will be a final report of a study in human patients with severe subarachnoid hemorrhage and traumatic brain injury. The results indicate correlations of varying significance between the pooled data still under statistical analysis. We hope that the outcome of our study will be able to answer questions regarding the pathophysiology of severe brain injury and guide us in the titration of therapy, as it is needed by each individual patient [1-4].

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P458

New look at the 20 mmHg ICP threshold

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Introduction We present a method based on minute-by-minute ICP monitoring and outcome (GOS) to visualize in a clinically useful way the dynamic aspects of secondary injury.

Methods A retrospective analysis of data from 165 adult patients from the Brain-IT database [1]. A color-coded contour plot was made for the association between good outcome and the number of secondary insults of ICP during the ICU stay, as defined by continuous values of insult duration and thresholds.

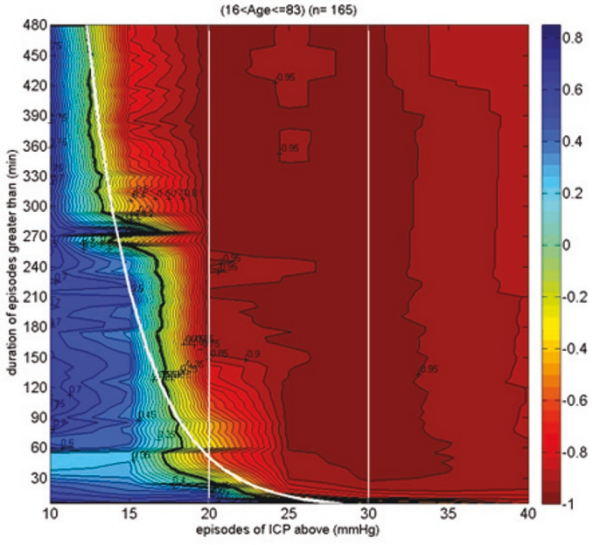

Figure 1 (abstract P458).

Results Figure 1 visualizes in blue the region associated with good outcome for continuous values of thresholds and durations of secondary insults. The thick black line indicates the transition towards the negative association region in red. A best-fit exponential curve is superimposed. This clearly shows that insults below 20 mmHg of ICP can be detrimental if sustained for long periods. Alternatively, they can be tolerated for higher thresholds but only for shorter periods.
Conclusion Secondary injury is dynamic such that not only thresholds but also insult duration are relevant. The proposed visualization goes beyond the static 20 mmHg ICP threshold introduced in [2] and provides a more accurate representation that could help the clinician in identifying when the patient's outcome could be making a turn for the worse.
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P459

Model of intracranial hypertension of tumor etiology in laboratory rats

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Introduction The objective of this research is the creation of an experimental model of intracranial hypertension (ICH) of the tumor etiology in white nonlinear rats.
Methods Work was executed in the neurophysiology laboratory on 12 white nonlinear rats, weight 280 to 320 g, preselected according to criteria of bioethical rules. For modeling ICH in animals, standard anesthesia was carried out. A longitudinal section was spent in the projections of saggital suture from the frontal to occipital bone. The offensive surgical stage anesthesia showed loss of palpebral and lingual reflexes. Further, according to the stereotactic atlas coordinates, a burr hole was performed, through which sterile two-component anti-allergen and depyrogenized gel in the amount of 0.025 ml was applied into the fourth ventricle with an intracerebroventricular microinjector. The injector was at an angle of 12° in order to avoid injuring vessels, its distal end entering a depth 4.5 mm in the fourth ventricle, and was installed and documented in the burr hole for measuring intracranial pressure. Monitoring during operations included: respiration, heart rate, ECG, thermometry, and control of diuresis.
Results In all animals the heart rate decreased to an average of 180 beats/minute during 90 minutes after the introduction of the intracerebroventricular two-component gel. Also there was a decrease in respiration rate by an average of <70 breaths/minute. Behavioral responses of animals were evaluated. The average intensity and the duration of such actions as shaking, friction, licking and carding decreased. Decline in grooming was possibly associated with breached central regulation in the brain of studied rats. Macroscopically in the preparation we observed a pronounced hyperemia of obtained materials, which may indirectly indicate the syndrome of ICH. Survival of the animals was: 3 days – 100%, 7 days – 100%, 14 days – 92%, 21 days – 83%.
Conclusion The main result of this work can be considered creation of a successful and workable model of ICH. The developed model is the testing ground to assess especially anesthesia protection in patients with the syndrome of ICH including tumor etiology and has no analogs.

P460

Arterial–jugular bulb differences in pCO_2, lactate, serum sodium and C-reactive protein in neurocritical patients

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Introduction Several reports indicate the potential usefulness of monitoring brain metabolic parameters and their correlation with the system [1-4]. We want to establish differences and correlation in pCO_2, lactate, serum sodium and C-reactive protein (CRP) between arterial and jugular venous bulb blood.
Methods An observational study. Between 1 January and 31 October 2013 we included neurocritical patients (NCP) with multimodal neuromonitoring (MMN). Daily samples of arterial blood and venous jugular bulb blood were obtained for measuring pCO_2, lactate, serum sodium and CRP.
Results There were 45 NCP, six (13%) with MMN (five men). Mean age was 37 ± 11 years (35 to 61). Diagnostics: two TBI, two SAH, one stroke, one lupus encephalitis. APACHE II was 27 ± 6.5 (25 to 39). Glasgow Coma Scale at admission was 14 ± 4 (4 to 14). pCO_2 (mmHg): arterial 41 ± 6.3 versus jugular 45 ± 7.4 (r = 0.7, P = 0.007). Lactate (mg/dl): arterial 11 ± 5.6 versus jugular 13.5 ± 3.9 (r = 0.7, P = 0.9). Sodium (mEq/dl):

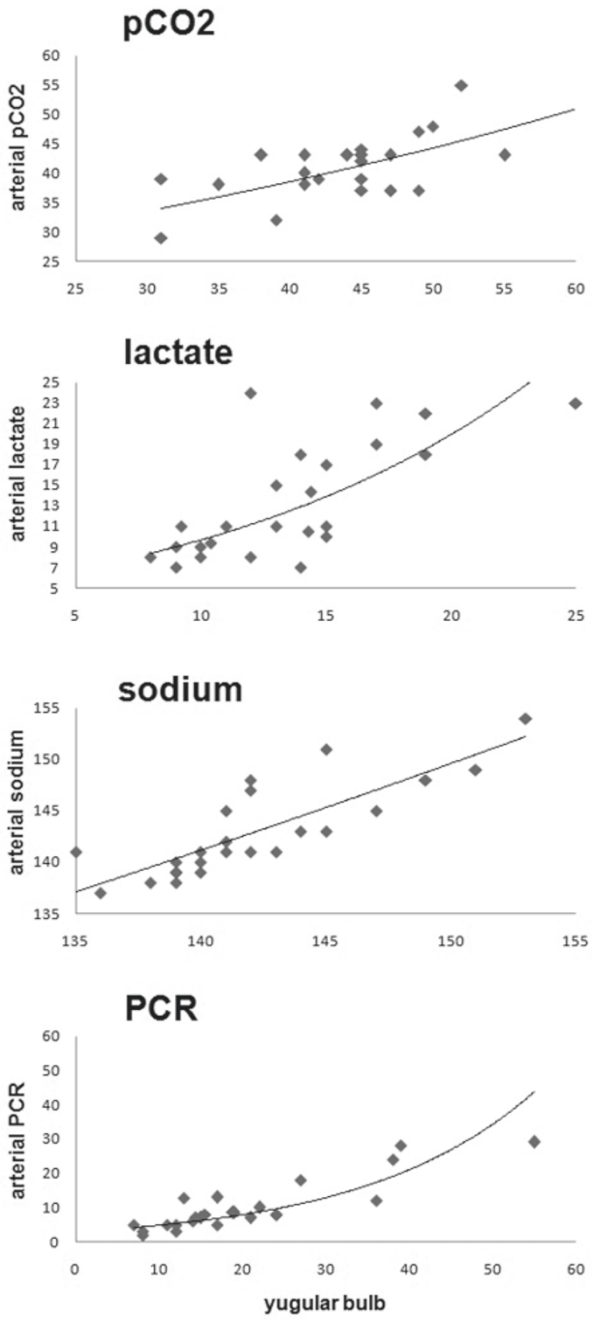

Figure 1 (abstract P460).

arterial 141 ± 4.5 versus 141 ± 4.4 (r = 0.8, P = 0.15). CRP (mg/dl): arterial 8 ± 7.4 versus 17 ± 11.6 (r = 0.9, P <0.001). The correlation and trend curves are shown in Figure 1.

Conclusion A suitable correlation is observed for the arterial–jugular bulb in different variables. There is a significant difference in CRP and pCO_2 values being persistently higher in the jugular, particularly for CRP. Studies are required to define its interpretation and potential usefulness.

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P461

Efficacy of terutroban in preventing delayed cerebral ischemia after subarachnoid hemorrhage: a functional isotope imaging study on a rat model

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Introduction After a subarachnoid hemorrhage (SAH), delayed cerebral ischemia (DCI) remains the principal cause of morbid mortality. F2-isoprotanes are recognized as biomarkers of DCI. These lipid metabolites, by fixing the thromboxane and prostaglandin (TP) receptor, induce vasoconstriction and platelet aggregation. Our objective was to evaluate the efficacy of terutroban (TER), a TP receptor-specific antagonist, in preventing DCI after SAH.

Methods Twenty rats were assigned to one of three groups: a double 250 µl intracisternal injection (ICI) was realized with saline in the CONTROLS group (n = 6) or with autologous arterial blood in the SAH (n = 8) and SAH+TER (n = 6) groups. Treated animals received an oral administration of 30 mg/kg/day TER during 5 days following blood injection. Rats were evaluated using a functional isotope imaging technique (high-resolution microSPECT). Brain capture of three 99m technetium radiolabeled tracers was evaluated: HMPAO at day (D) 0, 2 and 5 for cerebral perfusion quantification, DTPA at D3 for blood–brain barrier (BBB) integrity study and annexin V-128 at D4 for apoptotic activity study. Radioactivity was measured in a predefined region of interest: cerebrum, cerebellum and brainstem. Statistical analysis: one-way ANOVA followed by Student's t test.

Results Brain HMPAO perfusion microSPECT (Figure 1) reveals a transient hypoperfusion after ICI (D2) and a lasting hypoperfusion in the SAH group. TER curtailed the SAH-induced decrease of the HMPAO uptake. TER also significantly counteracted the SAH-induced increase of DTPA in the brainstem (SAH 2.6 ± 0.7 vs. SAH+TER 1.3 ± 0.1 ppm/mm³; P <0.05) and increase of annexin V-128 in the cerebrum (SAH 1.2 ± 0.1 vs. SAH+TER 1 ± 0.06 ppm/mm³; P <0.05).

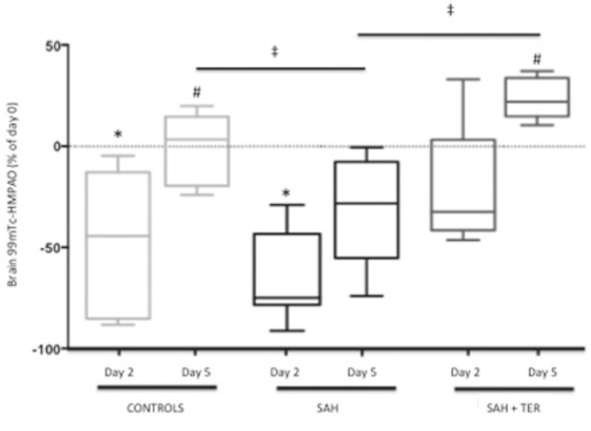

Figure 1 (abstract P461). HMPAO uptake at day 2 and day 5. *P <0.01 versus day 0; #P <0.01 versus day 2; ‡P <0.01.

Conclusion We made the first microSPECT scan description of a DCI rat model. After induction of SAH, TER improves cerebral perfusion, prevents BBB disruption in the brainstem and decreases apoptotic phenomenon in the cerebrum.

P462

Accuracy of transcranial color-coded duplex sonography in predicting clinical vasospasm and delayed cerebral ischemia in patients with subarachnoid hemorrhage

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Critical Care 2014, **18(Suppl 1):**P462 (doi: 10.1186/cc13652)

Introduction Cerebral vasospasm (VSP) and delayed cerebral ischemia (DCI) play a central role in worsening the neurological outcome in patients with aneurismal subarachnoid hemorrhage (aSAH) [1]. Transcranial color-coded duplex sonography (TCCS) is a non-invasive tool to detect VSP and predict DCI, but its clinical utility is limited by low accuracy. Our aim was to perform a sensitivity/specificity analysis of TCCS in predicting clinical VSP and DCI.

Methods Consecutive patients admitted to our ICU for aSAH were enrolled in the study. CBF-Vm and the pulsatility index (PI) were obtained by TCCS in both mean cerebral arteries (MCAs) at two scheduled time points, <3 days (T1) and 7 to 10 days (T10), and at least once every other day after bleeding. The highest Vm between left and right and the corresponding PI were chosen for analysis. All patients underwent brain MRI plus TOF-MRI angiography at T1 and T10 to assess radiologic VSP. Symptomatic VSP was defined as a new neurologic deficit associated with radiological VSP. The occurrence of DCI was evaluated on DWI sequences. The C statistic (ROC curves) and nonparametric t test were used for analysis.

Results Forty-three consecutive patients were recruited. Thirty-seven patients had simultaneous TCCS measures and MRI (mean age 58 years, 28% WFNS 4 to 5). Eleven patients (30%) developed symptomatic VSP and 26 (70%) did not (NVSP). Vm increased significantly from T1 to T10 in both groups (VS: P = 0.03, NVSP P = 0.01). The accuracy of TCCS at T10 (Vm) for predicting vasospasm was described by an AUC of 0.86 (CI = 0.74 to 0.98) and a cutoff value >115 cm/seconds (90% sensitivity, 73% specificity). Interestingly, a cutoff value >168 cm/second corresponded to the best specificity (92% specificity), but low sensitivity (45%). The accuracy of PI for predicting VSP was lower (AUC 0.75). The accuracy of TCCS for predicting DCI was also poor (AUC 0.57). Considering larger DCI only (volume >2 ml), the accuracy was slightly increased (AUC 0.75).

Conclusion TCCS is useful to predict clinical VSP with good accuracy. The Vm cutoff value >115 cm/second might be considered as a warning threshold, while higher values (>168 cm/second) identify high-risk patients. The accuracy of TCCS in predicting DCI is low, which indicates that mechanisms other than VSP are likely to play a role.

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P463

Functional MRI examination results in patients with vegetative state: revealing of the Wernicke's area

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Introduction The aim was to evaluate the prognostic importance of the MRI examination using Block Design fMRI in patients in a vegetative state (VS).

Methods Twenty-two patients corresponding to the international standards of VS underwent high-resolution MRI (T2 and T1, isomatrix with slice thickness 1.00 mm, T2 FLAIR FS, DWI, SWI) examination and Block Design fMRI (paradigm of passive speech). The patients were aged from 4 to 42 years. Causes of VS: TBI in 19 patients, hypoxia in three patients. By the time of the examination the patients were in VS from 1 to 4 months.

Results Wernicke's area activation was observed in nine patients (eight patients with TBI, one with hypoxia). During the subsequent examination, which lasted from 3 to 12 months, seven patients with activated Wernicke's area showed further consciousness expansion up to the minimal consciousness state (further consciousness expansion was seen in two patients). Two other patients with activated Wernicke's area did not show any signs of consciousness. Two patients revealed significant activity in the Broca's area.
Conclusion According to the first results of the study one can conclude that behind the outwardly similar clinical symptoms in patients in VS lies a diverse (due to the organization of brain functions) group of patients. fMRI enables one to reveal the first signs of cognitive activity; that is, reveals the linguistic value of speech addressed to the patient which cannot be detected during routine neurological examination.

P464

Brain death determination in Europe: one condition with too many nuances

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Introduction A patient is declared brain dead (BD) when physicians determine permanent loss of brain functions. Unfortunately, criteria for defining BD vary across different countries [1]. We therefore decide to survey BD diagnostic modalities in Europe in order to describe differences.
Methods A multiple-choice questionnaire was developed on an online platform [2]. Direct link was sent to national representatives of the European Society of Intensive Care Medicine and NeuroIntensive Care section's members. Thirty-three countries were contacted. Answers were reviewed. In cases of discrepancies or missing data, participants were contacted for further clarification. Descriptive statistics have been applied.
Results Twenty-eight participants returned the questionnaire (85%). Every country has either specific law (93%) or guidelines issued by the scientific society (89%). Clinical examination, essential to the diagnosis, is the only requirement in 50% of countries. Coma, apnea, absence of corneal and cough reflexes are always necessary. Blood pressure and electrolytes are checked in 64% as mandatory prerequisites. The apnea test is legally defined in 86% of countries. Eighty-two percent of countries require achievement of a target $paCO_2$ level while the Netherlands' law states target apnea duration. Number of physicians (median 2, range 1 to 4), number of clinical examinations (median 2, 1 to 3), and minimum observation time (median 3 hours, 0 to 12) are variable requisites in different countries. In 50% of nations, additional tests are required. Hypothermia (4%), anoxic injury (7%), inability to complete clinical examination (61%), toxic drug levels (57%), and inconclusive apnea test (54%) are legal indications to perform additional tests. Cerebral blood flow investigation is mandatory in 18% of countries, while it is either optional or used only in selected cases in 82%. Conventional angiography is still the preferred method (50%), followed by transcranial Doppler (43%), angioCT (39%), CT perfusion and angioMR (11%). EEG is always (21%) or optionally (14%) recorded. Russia and Croatia evaluate both EEG and cerebral blood flow (7%).
Conclusion There are still areas of uncertainty and disparities in brain death diagnosis in European countries. This predisposes to misdiagnosis and confusion both for clinicians and families. Measures to promote uniformity of brain death procedures and clinical practice are therefore desirable.

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P465

What do brain-dead patients ultimately die of?

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Introduction After a patient is declared brain dead, the cessation or withdrawal of therapy in Japan is quite a difficult operation because of the legal issues involved. Therapy is continued except in the case of donation of organs for transplantation from brain-dead patients until their cardiac arrest. Consequently, we may determine what the final cause of death is in brain-dead patients. Our hypothesis is that brain-dead patients ultimately die of cardiac failure.
Methods From January 2011 to December 2012, brain-dead adult patients in our ICU were investigated. The declaration of brain death is determined by clinical neurological examinations, electroencephalography, and the auditory brain-stem response test. Age, sex, primary diagnosis, Glasgow Coma Scale (GCS) on admission, the number of days from the diagnosis of brain death until cardiac arrest (days), the final cause of cardiac arrest, urine volume for the last 24 hours (ml), serum potassium levels (mEq/l), PaO_2 (mmHg) and $PaCO_2$ (mmHg) on the last day were evaluated. Values are expressed as mean ± SD. Data were analyzed by Kruskal–Wallis test and Mann–Whitney *U* test. $P < 0.05$ was considered statistically significant.
Results Of a total 1,221 patients admitted to our ICU, 37 patients (18 men, 19 women, age 65 ± 20) were clinically diagnosed with brain death. Primary diagnoses were 18 post-cardiac arrest syndromes, 14 cerebrovascular diseases, and four traumatic subarachnoid hemorrhages. GCS on admission was 4.5 ± 2.7 and days to cardiac arrest after diagnosed brain death was 8.6 ± 13.2. Urine volume for the last 24 hours was 997 ± 1,712 and serum potassium level was 4.8 ± 1.7. PaO_2 and $PaCO_2$ were 131.9 ± 80.6 and 48.9 ± 13.8, respectively. The final causes of cardiac arrest were 20 cardiac failures, 11 renal failures and six respiratory failures, although with mechanical ventilator support. The final cause of cardiac arrest due to respiratory failure had significantly longer stay in the ICU and days after diagnosis of brain death than cardiac failure or renal failure (27.2 ± 22.6 days vs. 9.2 ± 10.0 and 8.1 ± 4.6, $P < 0.05$; 23.2 ± 24.0 vs. 6.0 ± 9.0 and 5.4 ± 5.2, $P < 0.05$, respectively).
Conclusion There were significantly longer days until final cardiac arrest that was caused by respiratory failure than by cardiac failure or renal failure. Many different observations in each case were shown, such as urine volume or potassium level on the last day. Not only cardiac failure but also other failures might lead to final cardiac arrest.

P466

Acute and long-term outcomes of ICU-acquired weakness: a cohort study and propensity matched analysis

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Introduction ICU-acquired weakness is a frequent complication of critical illness. It is unclear whether it is a marker or mediator of poor outcomes. We aimed to determine acute and long-term outcomes and costs of ICU-acquired weakness among long-stay (≥8 days) ICU patients and to assess the impact of recovery of weakness at ICU discharge.
Methods Data were prospectively collected during an RCT (Clinical trials.gov: NCT00512122) [1,2]. Impact of weakness (MRC sum <48) on outcomes and costs was analyzed with 1:1 propensity score-matching for baseline characteristics, illness severity and risk factor exposure prior to assessment. Among weak patients, impact of persisting weakness at ICU discharge on risk of death after 1 year was examined with multivariable Cox proportional-hazard analysis.
Results A total 227 of the 405 (56%) long-stay assessable ICU patients were weak; 122 weak patients were matched to 122 not-weak patients. As compared with matched not-weak patients, weak patients had a lower likelihood at any time for live weaning from mechanical ventilation (HR: 0.709 (0.548 to 0.918), $P = 0.009$), live ICU (HR: 0.738 (0.570 to 0.955), $P = 0.021$) and hospital discharge (HR: 0.682 (0.521 to 0.893), $P = 0.005$). In-hospital costs/patient (+30.5%, €+5,443/patient, $P = 0.04$) and 1-year mortality (30.6% vs. 17.2%, $P = 0.015$) were also higher. The 105/227 (46%) weak patients not matchable to not-weak patients had even worse prognosis and higher costs. At any time within the first year following ICU admission, compared with patients who recovered from weakness and adjusted for potential confounders, those with persistent weakness and MRC sum between 36 and 47 at

ICU discharge had a higher likelihood of death (HR: 1.937, 95% CI: 1.048 to 3.581, $P = 0.035$). This likelihood of late death was even higher for those patients with a more severe degree of persistent weakness (MRC sum <36) (HR: 1.815, 95% CI: 3.693 to 7.514, $P < 0.001$).

Conclusion Patients with ICU-acquired weakness had worse acute morbidity outcomes, consumed more resources and revealed higher mortality after 1 year than patients without weakness. Persistence of weakness at ICU discharge further increased late mortality.

Acknowledgement GH and HVM contributed equally to this study.

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P467

Early electrophysiological diagnosis of ICU-acquired weakness

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Introduction An early diagnosis of ICU-acquired weakness (ICU-AW) is difficult because disorders of consciousness preclude strength assessment [1]. Electrophysiological (EMG) studies may be an alternative approach [2]. In this study we investigated feasibility and diagnostic accuracy of EMG studies to diagnose ICU-AW in unconscious patients.

Methods Newly admitted unconscious ICU patients (RASS <–3), ventilated for ≥2 days, were included in this single-center prospective cohort study. EMG testing included ulnar (motor/sensory), peroneal (motor) and sural (sensory) studies. Myography was performed when coagulation was normal (dorsal interossei I/II, deltoid and tibial muscles). Reliability of results was checked by an experienced neurophysiologist, blinded for strength. Motor/sensory studies were abnormal if amplitudes were below the 2.5th percentile reference values [3]. Myography was abnormal if spontaneous abnormal activity was found in ≥1 muscles. Upon awakening, strength was assessed (ICU-AW: average MRC <4 [1]), blinded for EMG. Feasibility was determined as the percentage of measurements that could be performed and were reliable. Diagnostic accuracy was analyzed using sensitivity and specificity.

Results We included 35 patients (ICU-AW: 17). EMG testing was done on day 4 (IQR: 3 to 6). Feasibility was 94%, 89%, 77%, 34% and 31% for ulnar motor, peroneal motor, ulnar sensory, sural sensory and myography studies, respectively. Figure 1 displays amplitude values. Sensitivity/specificity was 100%/0%, 100%/31%, 31%/100%, 50%/25% and 67%/38%, respectively.

Conclusion Feasibility of ulnar and peroneal studies was acceptable; feasibility of sural and myography studies was low. Diagnostic accuracy was low for all studies. This may be improved with new reference values.

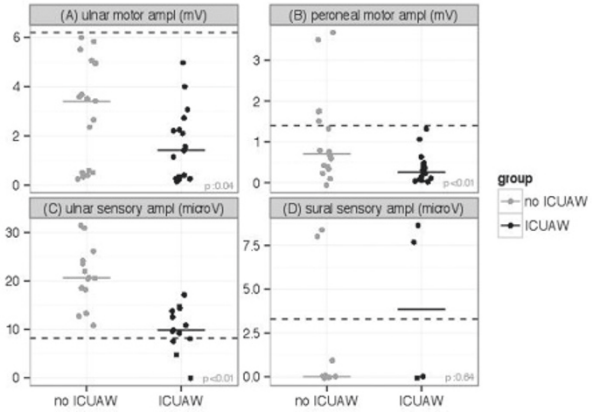

Figure 1 (abstract P467). Dotted lines represent 2.5th percentile reference values [3].

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P468

Choosing a cerebral near-infrared spectroscopy system for use in traumatic brain injury: deriving the ideal source detector layout

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Introduction Cerebral near-infrared spectroscopy (NIRS) represents an exciting prospect for the non-invasive monitoring of cerebral tissue oxygenation in traumatic brain injury (TBI). Earlier attempts at clinical application of cerebral NIRS demonstrated that further work was needed [1]. The basic layout of the probe portion of these devices consists of a light source and a light detector, arranged at calculated distances and configurations in order to observe target tissue. We aim to determine which commercially available NIRS probe represents the most sensitive layout of sources/detectors for the greatest sensitivity in observing tissue oxygenation at the optimal depth for TBI.

Methods The optimal depth for grey matter target tissue (grey–white matter junction) was ascertained by reviewing a series of brain CT scans of patients who had sustained a TBI. Set (average) measurements were derived from these identifying the target depth of the grey matter strip from the point of probe placement. Currently there are five commercially available cerebral NIRS systems. Table 1 presents the variety of configurations offered by each device. Source detector layouts were modelled and simulated using the NIRFAST® computational light modelling software (developed at the University of Birmingham) [2]. The novel approach of this modelling system makes no extrapolated assumptions based on subtraction.

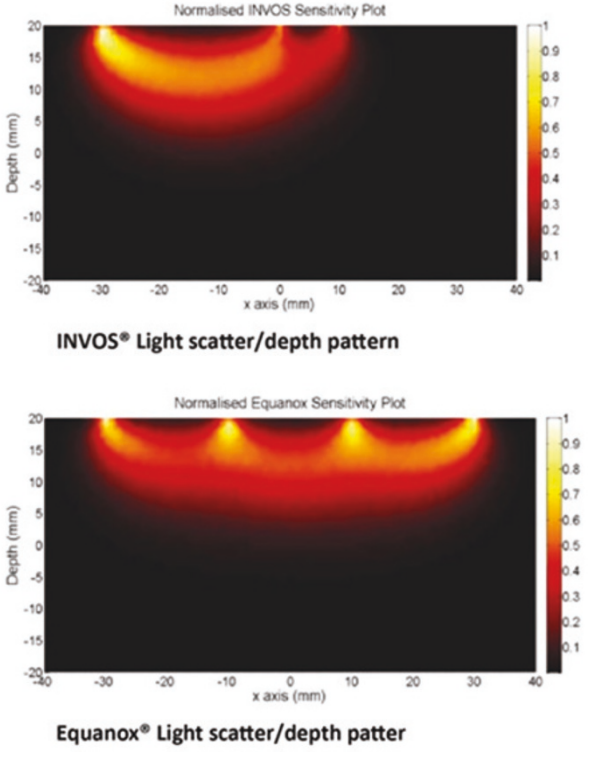

Figure 1 (abstract P468). Light scatter predictions of available systems/probes illustrated.

Table 1 (abstract P468). Available source detector layouts

Probe	Wavelengths (nm)	Sources	Detectors	Spacing (mm)	Peak depth sensitivity
Optiplex TX (ISS, IL, USA)	690, 830	4	1	30, 35, 40, 45	8
INVOS (Covidien, MA, USA)	730, 810	1	2	30, 40	8
EQUANOX (Nonin, MN, USA)	730, 810, 880	2	2	20, 40	7
FORE-SIGHT (CAS Medical, CT, USA)	690, 780, 805, 850	1	2	20, 50	10
NIRO-200NX (Hamamatasu, Japan)	735, 810, 850	1	2	19.2, 20	9

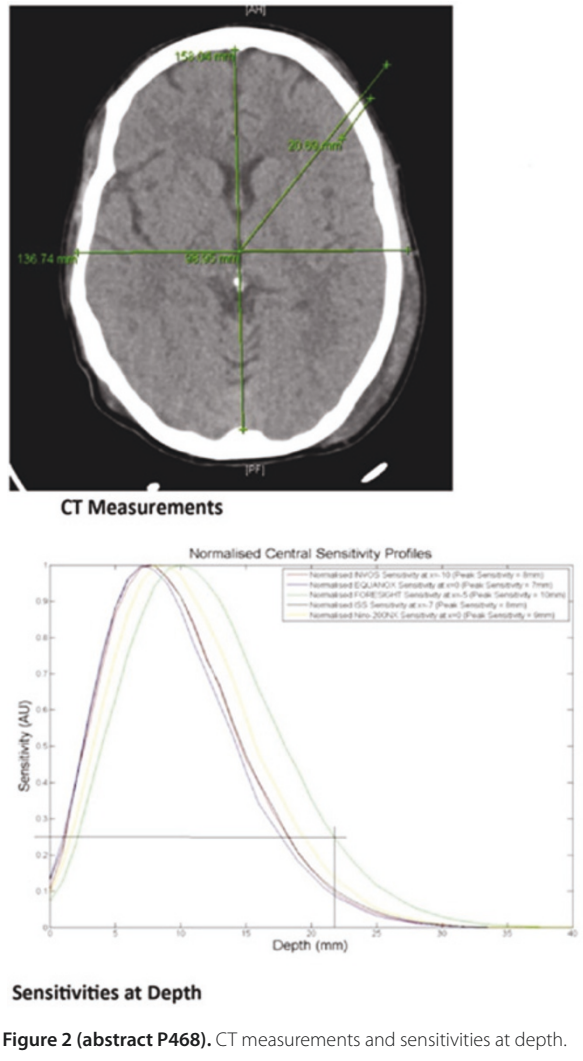

Figure 2 (abstract P468). CT measurements and sensitivities at depth.

Results We reviewed 32 trauma series CT brain images and the average depth to grey matter was derived as 21.37 mm (range 16.59 to 31.03 mm, SD 2.33) from the surface (Figure 1). The spectrum of sensitivity of the five probes was modelled (Figure 2). As is apparent here, the FORE-SIGHT (CAS Medical, CT, USA) probe currently offers the greatest sensitivity at our derived target depth.

Conclusion Based on the computational modelling of our work, the FORE-SIGHT NIRS device by CAS Medical source detector layout provides the greatest sensitivity at depth for the purposes of cortical monitoring in trauma. Variations in the layout have a significant impact on the quality of signal detected.

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P469

Single-subject assessment of the distribution of white matter abnormalities measured by diffusion tensor imaging in patients with severe traumatic brain injury

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Introduction Traumatic axonal injury (TAI) is a major contributor to adverse outcomes following traumatic brain injury (TBI). Diffusion tensor imaging (DTI) is a magnetic resonance imaging technique, which provides a robust measure of white matter integrity in patients with TBI. Certain brain regions have been identified as particularly susceptible to TAI by means of DTI. Few studies, however, have focused on describing the distribution of DTI abnormalities in individual TBI patients. The aim of this project was to conduct an exploratory analysis of the extent and distribution of axonal injury in TBI patients at a single-subject level.

Methods Patients admitted to the ICU for severe TBI underwent brain MRI and DTI (32 directions, $b = 1{,}000$, voxel size $2 \times 2 \times 2$ mm^3) between 2 weeks and 3 years after injury. For each individual patient, we enrolled five age-and-sex-matched healthy volunteers who underwent the same DTI protocol and were used as controls (31 total). We used a region of interest (ROI) automated analysis [1] to quantify white matter integrity. The fractional anisotropy (FA) maps were segmented using a white matter parcellation map covering the entire brain. Our primary outcome was the normalized difference in FA between each patient and the controls. Abnormalities were defined as values that were more than 2 SD below the mean of the values for the matched controls for each ROI.

Results Twelve TBI patients with a median age of 30 years (range 20 to 38) and a median GCS of 5 (range 5 to 7) were included. The majority of them had diffuse axonal injury according to CT and conventional MRI. Analysis of individual ROIs revealed that all subjects had numerous abnormal ROIs, varying from 14 to 64 (median 21) out of 78 regions assessed. The most frequently altered regions were the frontal lobe, orbital–frontal regions, corpus callosum, internal capsules, superior and inferior longitudinal fasciculi, cingulum, cerebellar structures and corona radiata. Thalamus, hippocampus and occipital lobes were less frequently affected.

Conclusion The extent and distribution of TAI varies on a patient basis. These findings highlight the need for standardized methods to precisely assess TAI in single subjects. Such single-subject methods will probably improve prognostic accuracy and may be useful in clinical trials.

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P470

Long-term outcome after severe traumatic brain injury

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Introduction Traumatic brain injury is a major public health issue, which results in significant mortality and long-term disability [1,2]. The

profound impact of TBI is not only felt by the individuals who suffer the injury but also their caregivers and society as a whole. In this study we observed the long-term outcome of patients with severe traumatic brain injury admitted to our intensive care.

Methods This study includes all patients (n = 160) with severe head trauma (GCS <9) admitted to the ICU of the emergency department of a tertiary referral center (Careggi Teaching Hospital, Florence, Italy) from 2009 to 2012. All patients will undergo a clinical assessment after 1 year, which is routine post-intensive follow-up. As an objective index of ability to function after injury, the Glasgow Outcome Scale (GOS) will be used. The neurological evaluation to determine the outcome of patients by GOS is performed in two different modes. All eligible patients 1 year after discharge from the ICU are contacted by telephone by a nurse of the intensive care staff and invited to make a visit to the surgery follow-up, where a intensivist evaluates the patient and determines the GOS. For the patients who were still hospitalized at 6 months in rehabilitation departments, GOS assessment is performed by a doctor of the structure and notified by telephone.

Results The ICU and hospital mortality was respectively 33.7% (n = 54) and 36.9% (n = 59). The mortality at 1 year was 44.4% (n = 71). The results of the neurological follow-up at 1 year were: GOS 2: 5.6% (n = 9), GOS 3: 10% (n = 16), GOS 4: 13.1% (n = 21), GOS 5: 26.9% (n = 43).

Conclusion According to the other studies, our data confirm that the severe traumatic brain injury is associated with a high mortality at 1 year. One-half of the survivors have a different level of disability.

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P471

Vitamin D level could affect the recovery rate in traumatic brain injury: a retrospective study

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Critical Care 2014, **18(Suppl 1):**P471 (doi: 10.1186/cc13661)

Introduction Recent studies have shown that 1,25-dihydroxyvitamin D3 (vitamin D) deficiency may affect negatively the clinical course of traumatic brain injury (TBI) [1]. This problem becomes important with respect to the older patient considering a 50% prevalence of vitamin D deficiency [2]. Data from the Third National Health and Nutrition Examination Survey [3] document more than 60% of Caucasians affected by D deficiency [4] so that all patients with TBI of any age are theoretically at risk of unfavorable outcome [2]. The objective of this preliminary study was to determine whether low levels of vitamin D at admission to the ICU (<24 hours) could negatively affect neurological recovery of patients with TBI.

Methods We retrospectively analyzed the data of 46 patients affected by TBI (65% severe, 9.5% moderate, 28.5% moderate) both isolated or associated with other extracranial lesions. The sampling of vitamin D was carried out within 24 hours from ICU admission. We had registered GCS at the moment of presentation (GCS in) and at discharge (GCS out) and their difference (GCS diff) compared with levels of vitamin D. Patients that died in the ICU were assigned a GCS out = 0. See Table 1.

Results Our data, according to other studies [5], confirm the presence of a deficiency of vitamin D (Table 1); however, they do not demonstrate a statistical significance correlation at the univariate regression (R = 0.04; P = 0.786) between vitamin D level and outcome from the ICU. There was no correlation stratifying patients for age, for TBI class, for Injury Severity Score and for BMI.

Conclusion Vitamin D deficiency is really prevalent in our TBI cases but does not seem to affect neurological recovery at ICU discharge; however, these preliminary results should be exposed to several criticisms and need to be confirmed with prospective studies.

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Table 1 (P471)

Descriptive statistics			TBI Isolated	TBI Associated	*P* value
Dead	8.70%	Percentage	22	78	
Male	87%	GCS in	4 ± 3	8 ± 5	0.043
Age	50 ± 21	GCS out	10 ± 4	10 ± 5	0.933
BMI	26.36 ± 4.14	GCS diff	6 ± 4	3 ± 6	0.151
ISS	29 ± 15	Vitamin D (ng/ml)	17 ± 8.5	17 ± 9.8	0.597
Vitamin D deficiency (<30 ng/ml)	73.90%	Length of stay ICU (days)	12 ± 7	8 ± 9	0.261

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P472

Could selected probiotics have beneficial effects on clinical outcome of severe traumatic brain injury patients?

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Critical Care 2014, **18(Suppl 1):**P472 (doi: 10.1186/cc13662)

Introduction Severe traumatic brain injury (TBI) is a major cause of death in people between 19 and 45 years old. Gastrointestinal dysfunction is the most common complication due to mucosal ischemia, motility disorders, and disruption of the gut barrier, with severe consequences: malnutrition, weight loss, and high risk of infections [1]. Therefore, maintaining the intestinal barrier function is a systematic engineering project. Selected new probiotics due to the capacity to bind and neutralize toxins, and to interfere with pathogen adherence, by immunomodulatory properties, mopping up the infection, could improve recovery of critically ill patients [2]. Our aim was to assess the effects of a new probiotic in an early enteral regimen on clinical outcome of severe TBI patients, in terms of VAP incidence, tolerance to enteral nutrition, duration of mechanical ventilation, and mortality rate.

Methods A prospective randomized 1-year study of 64 patients 19 to 78 years old allocated to receive for 10 days either an early enteral diet plus a new probiotic (Bioent; *Lactobacillus bulgaricus* 10 trillion CFU/cp + activated charcoal) every 6 hours (Group A) or the same formula without probiotics (Group B). The diets were isocaloric and isonitrogenous, and there were no differences between groups in gender, age, and nutritional status. We assessed the VAP incidence, duration of mechanical ventilation, tolerance to enteral nutrition, length of ICU stay, duration of diarrhea episodes, and mortality rate. The ANOVA test and t test were carried out; P <0.05 was considered significant.

Results The infection rate was higher in group B, the duration of mechanical ventilation was shorter in group A, and the patients in group A received 91.7% of total caloric needs by an enteral route versus 74.68% in group B. There is a significant difference in the number of diarrhea episodes, and the ICU length of stay was significantly lower in group A; there was no significant difference in the mortality rate between groups. See Figure 1.

Conclusion Early administration of new probiotics to severe TBI patients could have beneficial effects in terms of reduction of GI dysfunction, VAP incidence and length of ICU stay.

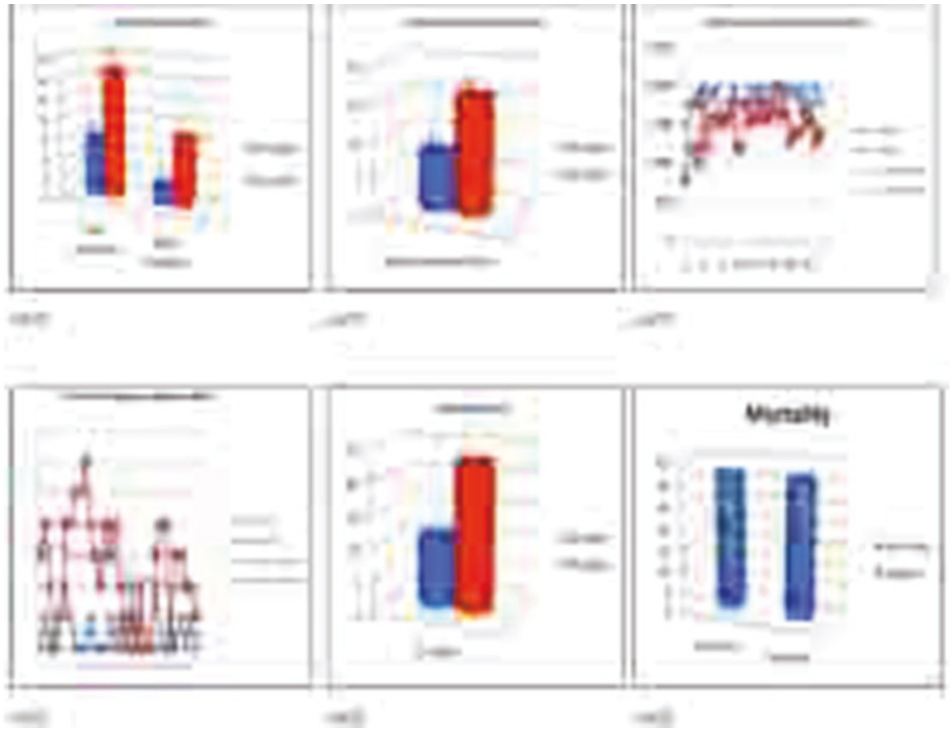

Figure 1 (abstract P472).

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P473

Effect of blood alcohol level on outcome of patients with traumatic brain injury

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Critical Care 2014, **18(Suppl 1):**P473 (doi: 10.1186/cc13663)

Introduction We investigated whether blood alcohol levels (BAL) had any impact on presentation and outcome in patients with traumatic brain injury (TBI).
Methods Forty-six patients with TBI requiring intubation between January 2000 and December 2012 were included. Patients were grouped into BAL-positive (>0.5‰; $n = 24$) and BAL-negative (<0.5‰; $n = 22$). Physiological parameters and outcome (survival to hospital discharge (STHD)) and neurological outcomes (Glasgow Outcome Scale (GOS), Cerebral Performance Category (CPC) and Glasgow Coma Scale (GCS)) were analyzed. Differences between groups were analyzed using Student's *t* test and results presented as mean ± SD.
Results There were no significant differences in gender and age distributions between the BAL-negative and BAL-positive groups (73% vs. 88% male; $P = 0.218$; 53 ± 21 vs. 43 ± 17 years; $P = 0.098$). There were also no differences in initial systolic blood pressure (BP; 144 ± 30 vs. 132 ± 37 mmHg; $P = 0.241$) and respiratory rate (RR; 13 ± 6 vs. 12 ± 7/minute; $P = 0.891$) but BAL did affect the initial GCS score (7 ± 3 vs. 5 ± 2; $P = 0.022$). There was no effect on CPC (3.5 ± 1.9 vs. 2.8 ± 1.8; $P = 0.185$), GOS (2.4 ± 1.8 vs. 3.0 ± 1.7; $P = 0.270$), and GCS at discharge from the hospital (14 ± 2 vs. 14 ± 2; $P = 0.801$). There were also no differences in length of hospital stay (LOHS; 15 ± 23 vs. 23 ± 34; $P = 0.372$) and STHD (1.6 ± 0.5 vs. 1.3 ± 0.5; $P = 0.083$).
Conclusion BAL did not have a significant effect on presenting physiological parameters such as systolic BP and RR. It did, however, affect the presenting GCS score, which was significantly lower in the BAL-positive group. BAL did not seem to have an effect on functional outcome or mortality measured by STHD. No favorable neuroprotective or deleterious effect was observed, demonstrated by no significant differences in CPC, GOS or GCS scores at discharge.

P474

Long-term outcome prediction using IMPACT and APACHE II in patients with traumatic brain injury treated in the ICU

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Introduction The International Mission for Prognosis and Analysis of Clinical Trials (IMPACT) is currently the most robust prognostic model in patients with traumatic brain injury (TBI). No studies have compared this TBI-specific prediction model with general ICU models, such as the Acute Physiology and Chronic Health Evaluation II (APACHE II) [1,2]. This study investigates the performance and the correlation of the IMPACT and APACHE II models for long-term outcome prediction in patients with TBI.
Methods The study population consisted of TBI patients admitted to a designated ICU in southern Finland during a 4-year period (2009 to 2012). The IMPACT and APACHE II performances were assessed by calculating discrimination (by area under the curve), calibration (by GiViTI calibration test and Hosmer–Lemeshow *C* statistic) and precision (by Brier score). Correlation between the IMPACT and APACHE II was tested by Spearman's rho. Primary outcome was 6-month mortality.
Results Of the total 897 included patients, overall 6-month mortality was 22%. The IMPACT and APACHE II showed similar AUCs (0.81, 95% CI = 0.77 to 0.84; 0.80, 95% = CI 0.76 to 0.83) and Brier scores (0.134, 0.135). Calibration tests revealed significant ($P < 0.05$) deviations between observed and predicted risk for both models. A moderately strong, positive correlation between the IMPACT and the APACHE II

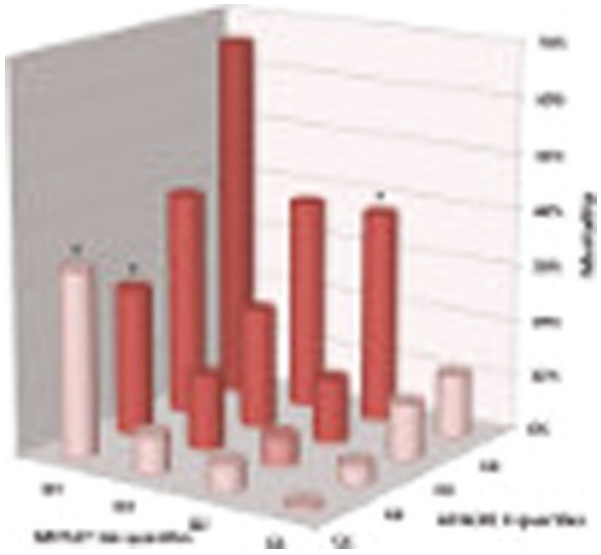

Figure 1 (abstract P474). Area under the curve for the new models.

was noted (Spearman's rho = 0.566, P <0.001). The IMPACT and the APACHE II were found to identify slightly different groups of patients that eventually do not survive (Figure 1).

Conclusion The IMPACT and the APACHE II models showed equal performance for 6-month mortality prediction. A moderately strong, positive correlation, with some major discrepancies between the models, was found. Thus, features of both the IMPACT and APACHE II models are valuable for optimal outcome prediction in patients with TBI treated in the ICU.

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P475

Validating and comparing the CAM-ICU and the ICDSC in mild and moderate traumatic brain injury patients: a multicenter prospective study

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Introduction The Confusion Assessment Method for the ICU (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC) are recommended for routine delirium screening. However, literature about delirium assessment in traumatic brain injury (TBI) remains scarce. The aim of our study was to evaluate the validity and reliability of the CAM-ICU and the ICDSC for delirium assessment in patients with mild to moderate TBI.

Methods A prospective observational study of mild to moderate TBI adult patients in two critical care trauma centers. Patients underwent delirium assessment on days 3, 5 and 7 with the CAM-ICU and the ICDSC. Psychiatrists or neurointensivists evaluated delirium using the DSM-IV criteria for delirium. Assessments results were blinded and performed independently. Criterion validity of the CAM-ICU and the ICDSC were calculated from 2 × 2 frequency tables using standard definitions of sensitivity, specificity, positive and negative predictive value, and overall accuracy. Because delirium was assessed repeatedly, estimates of 95% CIs for binary repeated data using generalized estimating equation in conjunction with the Huber–White estimator were performed. Inter-rater reliability for the CAM-ICU and ICDSC was assessed with the kappa coefficient.

Results During an 8-month period, 61 patients (mean age 56.4 ± 18.5 years, mean APACHE II score 11.4 ± 6.5, mean GCS 13 ± 2) were enrolled. The overall sensitivity and specificity for CAM-ICU (62% and 74%, respectively) and ICDSC (64% and 79%, respectively) were similar. The overall kappa for inter-rater reliability for the CAM-ICU and ICDSC was 0.64 and 0.68, respectively. In subgroup analyses, the CAM-ICU and ICDSC showed increased sensitivity and decreased specificity in moderate TBI as well as deeper levels of sedation (RASS –2 to –3).

Conclusion Criterion validity and inter-rater reliability of the CAM-ICU and ICDSC were good. Severity of TBI and depth of sedation influence delirium assessments. Clinicians should be aware of those limitations before using these clinical tools in this population.

P476

Functional status after 3 years in ICU patients with traumatic brain injury

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Introduction The aim was to study the functional status at 1 year and after 3 years in ICU patients with traumatic brain injury (TBI).

Methods A prospective cohort study of patients with TBI admitted to Carlos Haya Hospital, Malaga, between 2004 and 2008.

Results We studied 531 patients, age 40.35 ± 19.75 years, APACHE II 17.94 ± 6.97, GCS admission 7.53 ± 3.83 points. Cranial tomography at admission was: diffuse injury type I (10.4%), diffuse injury type II (28.1%), diffuse injury type III (24.5%), diffuse injury type IV (8.3%), evacuated mass lesion (22.6%), non-evacuated mass lesion (6.2%). Hospital mortality was 28.6%. One-year mortality was 171 (32.2%) (missing: 6.6%). After 3 years, mortality was 181(34.1%) (16.2% missing). We followed 496 patients for 1 year after admission (35 were missing) and assessed their functional status using the GOS. Thus, 22.7% were normal and 20% presented some limitations but were self-sufficient, representing 55.6% of those who survived hospital admission. A total of 57.3% presented bad evolution (died: 34.5%, vegetative: 3%, disabled not self-sufficient: 19.8%). After 3 years we followed 445 patients and 86 (16.2%) were missing. Thus, 132 patients (29.7% of 445 patients) were normal and 15.3% presented some limitations but were self-sufficient, representing 75.76% of those who survived hospital admission. Fifty-six percent of 445 patients presented bad evolution (died: 40.7%, vegetative: 2.2%, disabled not self-sufficient: 12.1%). Of 445 patients studied after 3 years of admission 171 died, and of the 274 who survived 198 (72.2%) were in a similar functional situation after 1 year, 11 (4.01%) had worsened functional situation, of which 10 had died, and 65 (27.72%) had improved situation (P <0.001).

Conclusion This study shows that approximately 75% of the patients who survived after 3 years from admission to the ICU with traumatic brain injury presented good recovery with functional situation normal or with some limitations but self-sufficient. Between 1 and 3 years after admission, approximately 25% of patients improved their functional situation.

P477

Demographic profiles and extent of critical care resources utilisation in patients with severe traumatic brain injury: a Tan Tock Seng Hospital National Neuroscience Institute study

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Introduction Trauma is the fifth principal cause of death in Singapore, with traumatic brain injury (TBI) being the leading specific subordinate cause [1].

Methods This 8-year retrospective review of patients with severe TBI admitted to the neuroICU (NICU) of the National Neuroscience Institute, Tan Tock Seng Hospital between 2004 and 2011 reports the

demographic profiles of severe TBI in the local context, with implications in the management of severe TBI, particularly the utilisation of critical care resources.
Results A total of 780 patients were admitted with TBI during the study period, of which 365 patients (46.8%) sustained severe TBI. The majority (75.3%) of the severe TBI patients were male. There was a bimodal preponderance of severe TBI cases in young adults (age 21 to 40) and older people (age >61). Motor vehicle accidents (48.8%) and falls from <2 m (35.1%) were the main mechanisms of injury. Invasive monitoring was frequently employed in these patients with severe TBI: arterial blood pressure monitoring in 298 patients (81.6%), central venous pressure monitoring in 219 patients (60.0%), and intracranial pressure monitoring in 173 patients (47.4%). The incidence of use of tiered therapy such as sedation, mild hyperventilation, osmotherapy with mannitol, cerebrospinal fluid drainage, barbiturate coma and decompressive craniectomy to control ICP converged with international practices.
Conclusion Young adults and older people involved mainly in motor vehicle accidents and falls respectively were among the high-risk groups for severe TBI. Management of these patients goes beyond the ICU and involves, but is not limited to, social support, emotional motivation and community reintegration of these patients [2]. TBI among the high-risk groups is largely preventable. Public awareness and prevention programmes will go some way in reducing the incidence of TBI amongst the high-risk groups.
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P478

Outcome measures in randomized controlled trials of patients with severe traumatic brain injury: a systematic review

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Introduction Traumatic brain injury (TBI) is a major cause of death and long-term disability worldwide, and understanding its effect on health is critical. Although mortality has been a gold standard for years, functional scales and quality of life have been used as main outcome measures over the last decades due to their usefulness and aid in decision-making for medical teams, patients, and families. Despite this preference, no consensus exists for the most optimal outcome measure. We systematically reviewed outcome measures used in randomized controlled trials (RCTs) in patients with severe TBI admitted to an acute care hospital.
Methods We searched MEDLINE, EMBASE, Cochrane Central, BIOSIS and references of eligible trials. RCTs published over the last 7 years (2006 to October 2013) in 18 selected journals (based on impact factor) were considered for inclusion. RCTs performed in adults with severe TBI (GCS ≤8) were eligible. The primary endpoint was the outcome measures used in RCTs. The secondary outcomes were the timing of assessment and the methodological quality of trials using the Cochrane risk of bias assessment tool. Two independent reviewers selected trials and collected data using a standardized form.
Results From 5,602 citations retrieved after removal of duplicates, 36 RCTs met eligibility criteria. The outcome measures most frequently used were neurophysiologic indices (n = 18, 50%), the Glasgow Outcome Scale (n = 17, 47%), mainly at 6 months, nonspecific complications (n = 15, 42%), mortality (n = 12, 33%), and biomarkers (n = 10, 28%). Nine trials reported only physiologic indices and did not present any clinical or functional outcome measures. The methodological quality of included RCTs was heterogeneous. We observed a low risk of bias for sequence generation (n = 29, 80%), allocation concealment (n = 20, 55%), complete data reporting (n = 30, 83%), selective reporting (n = 36, 100%), and sample size (n = 21, 58%) but a high risk of bias for blinding (n = 20, 55%).
Conclusion Outcome measures used to evaluate the effect of intervention in RCTs performed in patients with severe TBI in acute care are heterogeneous. A significant proportion of trials did not consider evaluating the functional status or other clinically meaningful outcomes, and very few trials assessed outcomes beyond 6 months. Thus, a significant proportion of RCTs in patients with severe TBI are based on outcome measures not clinically useful to guide or change practice in this population.

P479

Predicting 6-month mortality of patients with traumatic brain injury: usefulness of common severity scores

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Introduction Severity of illness scoring systems is paramount for the evaluation of quality of care of critically ill and trauma patients [1-3]. The purpose of the present study was to evaluate the usefulness of the Acute Physiology and Chronic Health Evaluation II (APACHE II), Simplified Acute Physiology Score II (SAPS II) and Sequential Organ Failure Assessment (SOFA) scores in predicting long-term outcome of patients with moderate-to-severe traumatic brain injury (TBI).
Methods A Finnish multicenter ICU database was screened for TBI patients admitted in 2003 to 2012. Logistic regression was used for customization of the APACHE II, SAPS II and SOFA for 6-month mortality prediction. An adjusted SOFA model, including age, and a reference model, including only age and Glasgow Coma Scale, were built for comparison. A randomized split-sample technique was used for internal validation and prognostic performance was determined by assessing discrimination, calibration and precision.
Results A total of 1,625 patients were included. Overall 6-month mortality was 33%. The APACHE II and SAPS II-based models showed good discrimination (area under the curve (AUC) 0.79, 95% confidence interval (CI) = 0.75 to 0.82; and 0.80, 95% CI = 0.77 to 0.83), calibration (P >0.05) and precision. The SOFA-based model showed poor discrimination (AUC 0.68, 95% CI = 0.64 to 0.72) and precision but good calibration (P >0.05). The adjusted SOFA model displayed better discrimination (AUC 0.79, 95% CI = 0.76 to 0.82). The reference model showed comparable performance with all scoring system-based models regarding discrimination (AUC 0.77, 95% CI = 0.74 to 0.80), precision and calibration. See Figures 1 and 2.
Conclusion A simple prognostic model, based only on age and GCS, displayed a fairly good prognostic performance in predicting 6-month mortality of ICU-treated patients with moderate-to-severe TBI. The use of more complex scoring systems added little to the prognostic performance.
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P480

Work activities after 3-year follow-up in ICU patients with traumatic brain injury

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Introduction The aim was to study work activities after 3 years in patients admitted to the ICU with traumatic brain injury (TBI).
Methods A prospective cohort study in an ICU of a reference hospital. We studied ICU-admitted patients consecutively with TBI between 2004 and 2008. We used validated scales including the Glasgow Outcome Scale (GOS) and the Project for the Epidemiological Analysis of Critical Care Patients Quality of Life questionnaire.

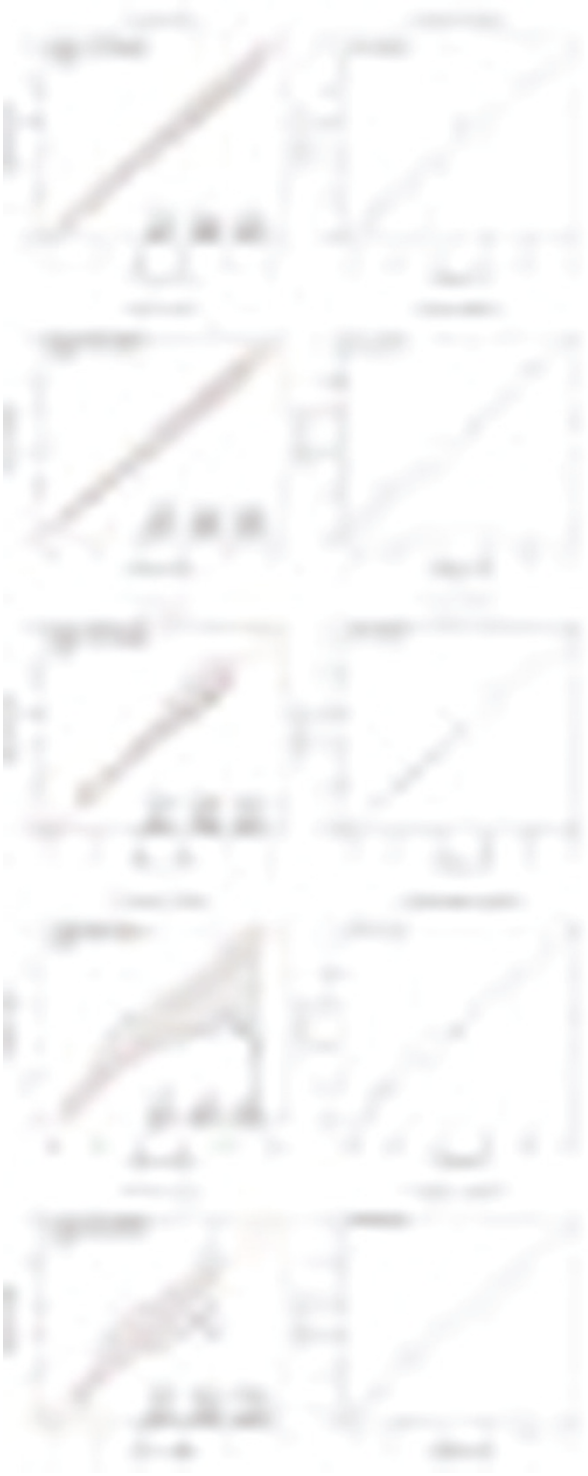

Figure 1 (abstract P479). Calibration.

Results We studied 531 patients, age 40.35 ± 19.75 years, APACHE II 17.94 ± 6.97 points, Glasgow Coma Scale at admission 7.53 ± 3.83 points. Cranial tomography at admission was: diffuse injury type I (10.4%), diffuse injury type II (28.1%), diffuse injury type III (24.5%), diffuse injury type IV (8.3%), evacuated mass lesion (22.6%), non-evacuated mass lesion (6.2%). Hospital mortality was 28.6%, 171 (32.2%) patients died after 1 year (6.6% missing) and 181 (34.1%) died after 3 years

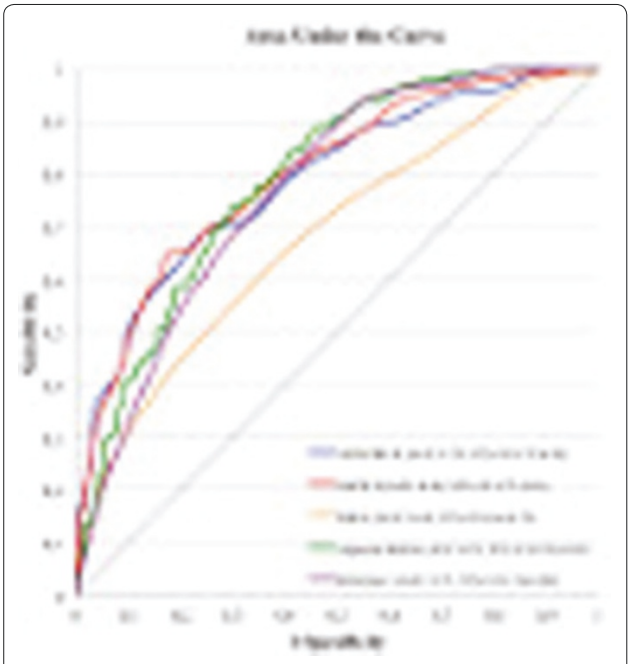

Figure 2 (abstract P479). Discrimination.

(16.2% missing). Regarding work activities, after 1 year, 28.5% of 326 patients evaluated have no difficulties with work, 4.6% have difficulties but work as before, 10.1% work only part-time or have changed to a job requiring minimum effort and 56.7% of patients do not work. After 3 years, 41.2% of 238 patients evaluated have no difficulties with work, 4.6% have difficulties but work as before, 12.6% work only part-time or have changed to a job requiring minimum effort and 41.6% of patients do not work. Evolution between 1 and 3 years by the McNemar test was statistically significant (P <0.001). A total of 173 patients were in similar situation, only one had deteriorated and in 62 (26.05%) patients the evaluation of work activity had improved.

Conclusion After 1 year of admission from the ICU with TBI, more than 50% of patients have difficulties with work. After 3 years the number of patients who work has increased although approximately 40% of the surviving patients do not work.

P481

Enteral administration of antiepileptic agents could have efficacy for prevention of post-traumatic seizures in severe traumatic brain injury

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Critical Care 2014, **18(Suppl 1):**P481 (doi: 10.1186/cc13671)

Introduction Antiseizure prophylaxis is recommended for preventing only early post-traumatic seizures (PTS) in the guidelines for the management of severe traumatic brain injury (TBI) by the Brain Trauma Foundation. Phenytoin is recommended to reduce the incidence of early PTS prophylaxis. Early enteral nutrition has recently shown theoretical advantages for prevention of bacterial translocation to maintain normal turnover of gut mucosa and is commonly used for TBI patients. Our hypothesis is that the enteral administration of antiepileptic agents is also useful for early PTS.

Methods This retrospective observational study included all adult patients admitted to our tertiary academic medico-surgical ICU due to TBI from September 2011 to August 2012. Patients who have epilepsy as a past history were excluded. Clinical data were collected from electrical medical archives. The baseline characteristics collected were age, gender, diagnosis, antiepileptic agents, timing of start and adverse effects of those agents, and methods of administration.

Results Of 65 patients with TBI, 25 patients (18 men, seven women; mean age 56.7 ± 20.1) who were administered antiepileptic agents for PTS prophylaxis were studied. Fifteen cerebral contusions, 10 acute subdural hematomas, nine traumatic subarachnoid hemorrhages, two cerebral infarctions, two pneumocephalus and one traumatic intracerebral hemorrhage were shown in 25 patients. All patients were alive 28 days after the injury. Fourteen patients (56%) were intravenously administered (13 phenytoin and one phenobarbital), while 11 patients (44%) were administered with enteral feeding (four valproates, four carbamazepine and three zonisamides) as PTS prophylaxis. The average start day of PTS prophylaxis was 2.6 days after the injury by intravenous administration, and 2.2 days by enteral administration, respectively. Two patients with phenytoin showed hepatic dysfunction as an adverse effect and no patient showed early PTS both by intravenous and by enteral administrations.
Conclusion The present study has some limitations because it is a single-center retrospective analysis. However, enteral administration of antiepileptic agents could be useful for PTS prophylaxis. Considering cost, adverse effects and serum monitoring, there is a possibility of enteral administration of antiepileptic agents as an alternative to intravenous phenytoin.

P482

Simulation-based education for cardiopulmonary resuscitation and airway management protocols: a brief report of a systematic review and meta-analysis

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Critical Care 2014, **18(Suppl 1):**P482 (doi: 10.1186/cc13672)

Introduction We aimed to summarize the efficacy of simulation-based education in cardiopulmonary resuscitation and airway management [1].
Methods We searched the MEDLINE, Scopus and EMBASE databases for all peer-reviewed articles enrolling physicians/medical students in a simulation of either cardiopulmonary resuscitation or airway management protocols compared with no intervention or traditional teaching methods. We categorized the outcomes of the studies into four groups: task success, process skill, time skill, knowledge. Task success was defined as evaluation of successful completion of the task, process skill as evaluation of the procedure, time skill as the time required to complete the task, and knowledge as the objective assessment of conceptual understanding. When studies investigated more than one outcome, we considered the primary outcome, the overall measure or the most clinically relevant outcome.
Results From 8,528 articles, we selected 24 studies (13 randomized controlled studies, eight pre–post studies, three case–control studies) involving 1,149 participants. Compared with no intervention or traditional teaching methods, simulation was associated with a significant improvement from mild to moderate of all outcomes (Figure 1). Log of odds ratio for task success was 2.03 (0.46 to 3.59) in favor of simulation. Pooled effect size for process skill was 0.48 (0.11 to 0.84), for time skill was 0.29 (0.13 to 0.73) and for knowledge was 0.41 (0 to 0.84).
Conclusion Simulation is an effective educational method to improve performance of physicians/medical students in the application of protocols for cardiopulmonary resuscitation and airway management.
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P483

Video analysis of cardiopulmonary resuscitation performance of ambulance crews during transportation

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Introduction High quality of chest compressions during cardiopulmonary resuscitation (CPR) is a critical determinant of outcome from out-of-hospital cardiac arrest (OHCA). Unfortunately, however, victims often do not receive adequate chest compression for various reasons, particularly during transportation. Recent studies have demonstrated the interruption time of chest compression using transthoracic impedance analysis, but more information is needed to evaluate the performance of CPR provided by ambulance crews and reveal reasons for hands off chest during CPR.
Methods All ambulances of the Hiroshima City Fire Department are equipped with a specially designed transmission device (RVT-SD200; Sony) that transmits high-resolution visual images and patient vital data using video cameras and a bio-monitor. We analyzed video data of OHCA patients transported by ambulance from November 2012 through December 2012, and evaluated the performance of CPR during transportation in accordance with the 2010 guidelines. The hands-off time was calculated as the time without chest compressions divided by the total CPR time.
Results Thirty-two resuscitation episodes during transportation by ambulance were analyzed. Median CPR time per episode was 846 seconds (range 126 to 1,833 seconds). In total, the fraction of time without chest compression was 19.5 ± 7.6% (mean ± SD). Reasons for interruption and its fraction of time in total hands-off time were as follows: 36% accounted for rhythm analysis/pulse check, 31% for ventilation, 11% for setting up automated chest compression devices, 8% for tracheal intubation/placement of supraglottic airway devices, 4% for intravenous line placement/administration of adrenaline, 3% for rescuer change, and 7% for adjustment of patient position/correction of rescuer posture and others.
Conclusion The fraction of time without chest compression observed in this study was comparative with those found in other studies in spite of the difficult situations, such as during transportation. Most frequent reasons for hands-off time were rhythm analysis and ventilation even though the ambulance crews strictly adhered to the guidelines.

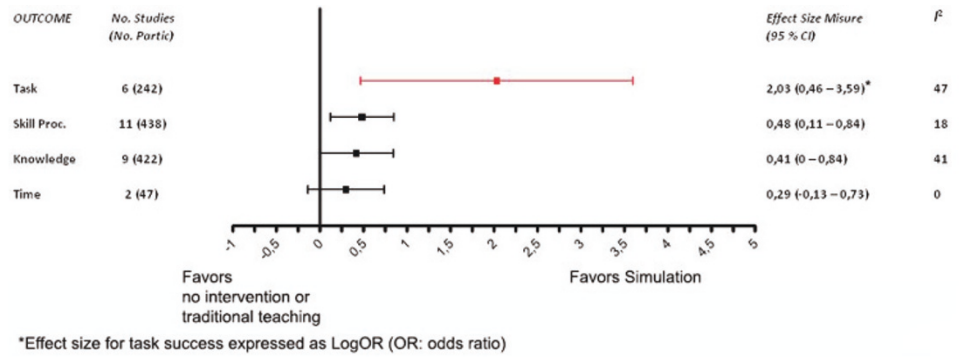

Figure 1 (abstract P482).

P484

Implementation of the PulsePoint smartphone application for crowd-sourcing bystander resuscitation

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Critical Care 2014, **18(Suppl 1):**P484 (doi: 10.1186/cc13674)

Introduction Only a minority of patients suffering out-of-hospital cardiac arrest receive any bystander cardiopulmonary resuscitation (CPR). Bystander CPR is associated with improved odds for survival. The PulsePoint smartphone application alerts users in the vicinity of a cardiac arrest to facilitate immediate citizen bystander resuscitation. Addressing implementation barriers may provide an opportunity to increase effectiveness of the application. PulsePoint is currently active in over 400 communities in the United States. Our objective was to identify modifiable barriers to optimal implementation of the PulsePoint smartphone application.
Methods We conducted a structured survey delivered via Survey Monkey optimized for mobile devices. All alerted PulsePoint users between 28 June 2012 and 1 November 2013 were sent an invitation to participate in the survey. Survey responses associated with test activations and emergency medical services (EMS) professionals on active duty were excluded from the analysis.
Results Of 4,827 survey requests sent, 995 responded and completed our survey (response rate 21%). Respondents identified themselves as firefighters (30%), paramedics (19%), EMTs (16%), nurses (4.4%), MDs (0.83%) and other professions (50%). Of those who received a PulsePoint alert, 23% (157/690) responded by making their way towards the location of the emergency. Of those who responded, 70% (110/157) arrived on scene. Most of those who did not arrive said they saw professional rescuers already on scene and turned back (52%, 24/47). Of those who arrived on scene, only 34% (37/110) found a person unconscious and not breathing normally. The majority found a person on scene who was not suffering cardiac arrest. Of those who arrived on scene prior to EMS and also found a cardiac arrest victim on scene who required resuscitation, 80% (8/10) performed bystander CPR.
Conclusion We observed a very high proportion of bystander CPR (80%) for victims of out-of-hospital cardiac arrest when PulsePoint users arrived before EMS. This suggests that optimized PulsePoint implementation may increase community bystander CPR rates. Alert specificity for cardiac arrest may be too low (the cry wolf scenario) with current default activation criteria. Also, the current activation radius (0.5 mile) may be too large because EMS frequently arrive before the PulsePoint responder.

P485

Emergency room advanced life support after cardiac arrest: outcomes and survival, nursing care and team response

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Critical Care 2014, **18(Suppl 1):**P485 (doi: 10.1186/cc13675)

Introduction An organized team response and trained nursing staff in the emergency room critical patient area (ER-CPA) are the main factors to determine cardiopulmonary resuscitation (CPR) success rates. The objective was to evaluate outcomes in the emergency room after advanced life support (ALS) by reanimation teams, to improve nursing care, quality of resuscitation and survival.
Methods We included all adult patients receiving ALS in the ER-CPA during 1 year. Cases not allowed CPR are excluded. A retrospective design, multivariate with ALS performed, gender, age, cause of arrest, precedence, outcome and hospital derivation, and 100% of cases studied.
Results A total of 149 patients were attended in the ER-CPA with ALS maneuvers during the studied period (9.23% of a total 1,613). Thirty-four of them were nonheart-beating donors. The protocol was performed with 23 effective donors and 31 organs were obtained for transplant. Respiratory arrest (n = 31) was the best outcome group, with 100% survival and in-hospital ICU transfer. The cardiac arrest (CA) group depended on cause of CA: cardiac arrhythmia (n = 12), survival 50%; surgical etiology (nontraumatic), survival 50%, mean age 70; myocardial infarction (n = 12), survival 83%, mean age 61; sepsis (n = 6), survival 67%, mean age 48; drugs overdose (n = 2), survival 100%; traumatic cardiac arrest (n = 15), 89% mortality, mean age 41; and CA with unknown etiology, survival 38%, mean age 68.
Conclusion Emergency room cardiac arrest arrivals are not correlated with ER-CPA total activity. Good survival rates are probably related to a special quick response protocol and trained teams. Outcomes research to detect potential improvement in nurse care is needed, and should be evidence guided. Worst results in survival rates must be detected as the main topics for nursing care development.

P486

What is the role of head computed tomography in post-resuscitation care?

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Introduction Guidelines recommend to perform head computed tomography (CT) in nontraumatic cardiac arrest only if the patient remains unconscious after return of spontaneous circulation [1]. Nevertheless, in cardiac arrest due to neurological causes, head CT would dramatically change the therapeutic strategy in these patients [2]. The aim of this study is to present the experience of our ICU in nontraumatic out-of-hospital cardiac arrest (OHCA) patients and to demonstrate that neurological abnormalities can be the primary cause of cardiac arrest.
Methods We collected data for all patients with nontraumatic OHCA admitted to the ICU from 1 January 2012 to 31 December 2012. We recorded mean age, male-to-female ratio, cause of cardiac arrest and mortality in the ICU.
Results Thirty-four survive cardiac arrest patients were admitted to the ICU. Mean age was 66 years. The male-to-female ratio was 2:1. Sixteen patients died in the ICU. Head CT scans obtained in the immediate post-arrest period found significant abnormalities in four patients (three subarachnoid hemorrhage and one ischemic ictus) with immediate modification of treatment.
Conclusion Head CT abnormalities can be found in cardiac arrest patients. Further investigations are necessary to evaluate the impact of cardiac arrest from neurological causes and to establish the role of neuroimaging in these patients.
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P487

To see or not to see: does video CPR perform better than telephone CPR?

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Introduction The ALERT algorithm, a simple and effective compression-only telephone CPR (t-CPR) protocol, has been previously demonstrated to help bystanders initiate CPR. According to their worldwide availability, mobile phone communications may play an increasing role in emergency calls. Preliminary studies suggest that they might improve dispatcher's understanding of the rescuer's situation. However, there is currently no validated protocol for videoconference-assisted CPR (v-CPR). We initiated the present study to validate an original protocol of v-CPR based on the ALERT algorithm and to evaluate the potential benefit of this assistance in comparison with classical t-CPR.
Methods We developed a strictly worded algorithm for v-CPR, adapted from the ALERT t-CPR protocol, with additional re-evaluation loops,

every 2 minutes. A total of 120 students without prior CPR training were recruited from upper secondary school, during regular class hours, and randomly assigned to the t-CPR group (n = 60) versus the v-CPR group (n = 60). The Resusci®Anne SkillReporter™ manikin was used to evaluate CPR performance. Data were transferred from the manikin into a computerized database using the Laerdal SkillReporting System V.2.2.1 software. Further analysis was based on audio-recordings and video-recordings. Primary outcome measures were the results of the Cardiff evaluation test; the secondary measures were global scoring of a complete 7-minute period of CPR.

Results The mean chest compression rate increased significantly in the v-CPR group as compared with t-CPR (110 ± 16 vs. 86 ± 28; P <0.0001), while depth remained constant (48 ± 13 mm vs. 47 ± 16 mm, P = NS). Hand positioning was correct in 91.7% of cases with v-CPR, but only in 68% with t-CPR (P = 0.001). The hands-off period was almost nonexistent in the v-CPR group (0 vs. 7 seconds; P = 0.0016), but the median no-flow time was significantly greater in the v-CPR group (146 vs. 122 seconds, P < 0.0001). As a consequence, global evaluation of CPR performance revealed a significant improvement in v-CPR group score as compared with the t-CPR group (6 vs. 5, P < 0.001).

Conclusion Video-assisted CPR using this original algorithm allows bystanders to reach compression rates and depths close to international guidelines and to reduce hands-off events during CPR.

P488

Initial anticoagulation strategy for extracorporeal cardiopulmonary resuscitation patients

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Introduction Extracorporeal cardiopulmonary resuscitation (ECPR) is increasingly being used in emergency and critical care medicine in Japan. Although a major complication of this procedure is bleeding, the optimal heparin dose and activated coagulation time (ACT) remain unknown.

Methods We retrospectively evaluated the initial heparin doses, ACT values, and complications of patients who received ECPR between February 2011 and November 2013 at the Emergency and Critical Care Center, Mie University Hospital, Japan.

Results ECPR was performed in 45 patients, and the ACT was evaluated in 32 patients. All patients were administered 3,000 U unfractionated heparin at the time of priming the circuit. Patients for whom cannulation took a longer time received an additional 2,000 to 3,000 U unfractionated heparin. The average heparin dose administered was 53.6 U/kg body weight. The average ACT was 231.3 seconds. In 17 of the 32 patients, the ACT exceeded 200 seconds. Three patients experienced fatal bleeding in the chest wall, which could not be stabilized by conservative treatment. One patient developed a cerebral infarction. There were no significant differences between the patients with fatal bleeding and those without fatal bleeding with regard to the heparin dose, ACT, and duration of CPR.

Conclusion According to the Extracorporeal Life Support Organization guidelines, the target ACT should be around 1.5 times the normal ACT. However, it is difficult to obtain the normal ACT in emergency situations. Many of our patients' ACTs exceeded 200 seconds, and three patients experienced fatal bleeding that was possibly due to chest compression. Post-cardiac arrest patients often experience coagulopathy due to either cardiac arrest or hypothermia therapy. Therefore, an anticoagulation protocol other than the pulmonary extracorporeal membrane oxygenation protocol is required for ECPR patients. We evaluated our anticoagulation protocol for ECPR and observed that our patients' ACTs frequently exceeded the target value and some experienced fatal bleeding. The anticoagulation protocol for post-CPR patients may need to be reconsidered.

P489

Predictors of poor outcome in out-of-hospital cardiac arrest

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Introduction Out-of-hospital cardiac arrest (OOHCA) causes 60,000 UK and 300,000 US deaths each year. Survival to hospital discharge in the developed world has historically been 7 to 10% with obvious cognitive impairment in 10% of survivors. Primary percutaneous coronary intervention (PPCI) and targeted temperature management (TTM) (or at least hyperthermia avoidance) have been shown to improve survival in comatose patients post OOHCA. There is no reliable method to predict poor outcome on presentation. We aimed to identify factors associated with poor outcome in our single-centre regional referral OOHCA population.

Methods We performed a pragmatic single-centre retrospective review over 18 months commencing 1 January 2011 of all patients admitted to our regional OOHCA centre ICU following successful resuscitation from OOHCA. In keeping with guidelines, all patients were assessed for suitability for PPCI and TTM. A good outcome was defined by a Pittsburgh Cognitive Performance Category (CPC) score of 1 to 2 (independence, mild impairment) on hospital discharge. A poor outcome was defined as death or CPC 3 to 4 (moderate to severe impairment, coma) on hospital discharge. CPC scoring was determined

Table 1 (abstract P489). Presenting features and outcome at hospital discharge of ICU OOHCA patients

	Good outcome (CPC 1 to 2)	Poor outcome (dead or CPC 3 to 4)	Total	*P* value
Age	63.3 ± 16.8	63.6 ± 14.4	63.5 ± 14.7	NS
Male sex	21/26 (81%)	29/43 (67%)	50/69 (72%)	NS
Arrest occurring 08:00 to 20:00	14/19 (74%)	16/36 (44%)	30/55 (55%)	<0.05
VF/VT as initial rhythm	25/26 (96%)	25/43 (58%)	50/69 (72%)	<0.001
Bystander CPR	12/26 (46%)	24/43 (56%)	36/69 (52%)	NS
Time from collapse to ROSC (minutes)	18.3 ± 11	32.3 ± 26	27.1 ± 23	<0.05
Advanced airway management	14/24 (58%)	38/42 (90%)	52/66 (79%)	<0.005
Cardiac cause	24/26 (92%)	30/43 (70%)	54/69 (78%)	<0.05
Angiography	19/26 (73%)	23/43 (53%)	42/69 (61%)	NS
Therapeutic hypothermia	24/26 (92%)	41/43 (95%)	64/69 (93%)	NS
Presenting pH	7.21 ± 0.11	7.08 ± 0.18	7.13 ± 0.17	<0.01
Presenting base deficit (mmol/l)	−7.9 ± 6.2	−13.8 ± 5.9	−11.5 ± 6.7	<0.001
Presenting lactate (mmol/l)	4.3 ± 3.0	8.3 ± 4.5	6.8 ± 4.4	<0.0005

from physiotherapy and occupational therapy assessments in the clinical notes. Continuous data were analysed using a two-tailed *t* test or Mann–Whitney *U* test, categorical data with a chi-squared test.
Results Sixty-nine patients were admitted to our ICU following successful resuscitation from OOHCA in the 18-month period. Presenting features and outcomes are shown in Table 1.
Conclusion Good outcome was associated with a shockable rhythm on presentation, cardiac cause, arrest occurring in daylight hours (08:00 to 20:00) and shorter time between collapse and ROSC. Poor outcome was associated with placement of an advanced airway device, lower pH, higher base deficit and higher lactate.

P490

Mean initial cerebral saturation and time to start advanced life support in out-of-hospital cardiac arrest: are they correlated?

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Introduction During advanced life support (ALS) it is still impossible to predict return of spontaneous circulation (ROSC) or outcome. Cerebral saturation (rSO_2) measurements with near-infrared spectroscopy can be used in cardiac arrest circumstances and could play a role in predicting ROSC or neurologic outcome [1]. It is known that an initial rhythm of asystole and a long no/low-flow time has a worse outcome. We measured rSO_2 during ALS in out-of hospital cardiac arrest (OHCA) patients and compared the mean rSO_2 during the first minute with the time between the emergency call (EC) and start of ALS.
Methods With IRB approval, rSO_2 was prospectively measured between December 2011 and November 2013 in 51 OHCA cases with presumed cardiac cause during ALS. One sensor of the EQUANOX Advance was applied to the right side of the patient's forehead when the medical emergency team arrived. The measurement was continued until death of the patient or arrival at the ICU. Survivors (S) are defined as sustained ROSC longer than 20 minutes. CPR data were collected using the Utstein CPR data registration. The Mann–Whitney test and Pearson chi-square were utilized for comparison of S and nonsurvivors (NS) data. The Pearson test was used to examine correlation.
Results Of the 51 patients, 21 were S. Mean age was 70 years (± 15) in the S, of which 10 (48%) were male, and in the nonsurvivors (NS) mean age was 70 years (± 17) ($P = 0.916$) with 23 (77%) male patients ($P = 0.042$). The initial rhythm was asystole in 11 S and in 20 NS ($P = 0.386$), pulseless electrical activity in two S and NS ($P = 1$), and ventricular fibrillation in eight S and six NS ($P = 0.207$). The arrest was witnessed in 15 NS and 16 S ($P = 0.083$). Lay rescuer BLS was performed in 17 NS and nine S ($P = 0.4$). A significant difference in time of EC and start of ALS was observed between S (12 minutes; 8 to 15) and NS (14 minutes; 12 to 17) ($P = 0.03$). Mean initial rSO_2 was 34% (± 23) and 24% (± 12.5) in S and NS ($P = 0.077$). We observed a negative correlation between mean initial rSO_2 and time between EC and ALS (correlation coefficient –0.243; $P = 0.041$).
Conclusion A tendency towards higher mean initial rSO_2 in S compared with NS was observed together with a negative correlation between mean initial rSO_2 and time between the EC and start of ALS. Also a significant difference in time between the EC and start of ALS between S and NS is observed. Larger studies are needed to confirm the possible function of rSO_2 as a surrogate for time between the EC and start of ALS.
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P491

Predicting survival in patients admitted to intensive care following out-of-hospital cardiac arrest using the Prognosis After Resuscitation score

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Introduction Out-of-hospital cardiac arrest (OHCA) has a poor prognosis even after successful resuscitation [1]. No scoring system has been fully validated for predicting survival following OHCA. The Prognosis After Resuscitation (PAR) score was developed from meta-analysis in 1992. A score >5 (from seven variables) predicts nonsurvival following in-hospital cardiac arrest (IHCA) [2,3]. Porter and colleagues demonstrated that PAR >5 is a useful predictor of nonsurvival for combined IHCA/OHCA ICU admissions [4]. We aim to evaluate PAR application to adult ICU admissions at University Hospitals Bristol (UHB), UK following OHCA.
Methods The Innovian (Dräger) electronic clinical information database was searched retrospectively for all OHCA ICU admissions from 2010 to 2012. Data were extracted using an electronic *pro forma* in Microsoft Excel. Missing/incomplete data were excluded. Survival was defined as survival to discharge from the acute hospital (UHB).
Results There were 247 admissions to the ICU following OHCA from 2010 to 2012. Seven patients were excluded for missing/incomplete data. In total, 102 patients (42.5%) survived to discharge. PAR ranged from –2 to 18. Zero was the most frequent score. Only one of 15 admissions with PAR >5 (PAR 13) survived. A total of 101 patients with PAR ≤5 survived (45%). Acute myocardial infarction was identified as the precipitating event in 111 patients (46%).
Conclusion Only one of 240 OHCA patients admitted to the ICU over a 3-year period with PAR >5 survived until discharge. PAR scoring has been shown to be useful in helping decide the appropriateness of ICU admission for combined IHCA/OHCA. Our data support its use in isolated OHCA. PAR ≤5 appears to be poorly predictive of survival. However, PAR >5, combined with clinical evaluation, could help identify OHCA nonsurvivors and avoid ICU admissions that do not benefit the patient.
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P492

Post Arrest Consult Team: a knowledge translation strategy for post-cardiac arrest care

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Introduction Lack of standardized care contributes to low survival in admitted out-of-hospital cardiac arrest (OHCA) patients. The objective of our study was to implement a Post Arrest Consult Team (PACT) and improve the quality of care for admitted OHCA patients.
Methods We conducted a prospective cohort study with concurrent controls from February 2011 to February 2013 in a network of 29 Toronto-area hospitals. The PACT was implemented in two hospitals and functioned as a consult service with a nurse and physician on-call 24/7. Patients from other network hospitals acted as concurrent controls. The PACT focused on four key processes of care: targeted temperature management (TTM); coronary angiography; avoidance of premature withdrawal of life-sustaining therapy (WLST <72 hours) on the basis of neuroprognostication; and electrophysiology assessment. We included nontraumatic OHCA patients who were >18 years old, survived at least 6 hours, and were comatose. We excluded patients with do-not-resuscitate orders, intracranial or other severe bleeding. We used generalized linear mixed models to assess whether PACT implementation was associated with higher odds of achieving each of the four targeted processes of care while adjusting for secular trends unrelated to the intervention.
Results The primary analysis included 162 patients from two intervention hospitals and 892 from 27 control hospitals. Thirty-two percent of the patients were female and the mean age was 65.3 ± 16.5 years. Almost one-half (46%) of patients had a shockable initial cardiac arrest rhythm, 41% had bystander CPR, and 5% had an AED applied. PACT did not improve use of TTM (ratio of ORs = 1.03, 95% CI = 0.89 to 1.20), angiography for patients without ST-elevation

myocardial infarction (ratio of ORs = 1.10, 95% CI = 0.87 to 1.40), or electrophysiology assessment (ratio of ORs = 1.06, 95% CI = 0.81 to 1.38) as compared with concurrent control hospitals. Patients in the intervention group were less likely to have life support withdrawn within 72 hours on the basis of neuroprognosis compared with patients in the concurrent control group (ratio of ORs = 0.62, 95% CI = 0.39 to 0.98).
Conclusion PACT was associated with reduced WLST <72 on the basis of neuroprognostication but did not improve other important post-cardiac arrest processes of care. Further work is underway to identify factors that influenced implementation. This will guide future consideration of the PACT model in other settings.

P493

One-year assessment of in-hospital cardiac arrest

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Introduction This retrospective audit evaluated adult patients who suffered in-hospital cardiac arrest (IHCA) against the recent National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report [1]. It looked specifically at the recognition of the acutely unwell, the interventions made, the decisions taken from admission through to the post-arrest period and the outcomes following cardiopulmonary resuscitation (CPR). The audit aims to guide future improvements in preventing cardiac arrest and enhancing end-of-life care decision-making.
Methods Medical notes of adult patients suffering IHCA, over a 1-year period, were identified and data were collected using a validated NCEPOD audit tool. These data included patient demographics, initial clerking and consultant review, patient care during the 48 hours prior to cardiac arrest, the resuscitation status of the patient, the resuscitation attempt, the post-cardiac arrest care and survival to discharge rates.
Results Medical notes were available for assessment for 69 out of the 82 patients that were identified as having IHCA between 1 October 2011 and 30 September 2012. The frequency of IHCA showed no correlation to day of the week or month. Initial clerking was incomplete in history-taking (16% vs. 14% in NCEPOD) and in examination (46% vs. 24% in NCEPOD). The majority of patients were appropriately escalated in a timely fashion (94% vs. 82% in NCEPOD), but first consultant review was delayed beyond 12 hours in 49% of cases (48% in NCEPOD). A total 81% of patients suffered cardiac arrest 24 hours after admission (68% in NCEPOD). Warning signs for cardiac arrest were considered present in 59% of cases (75% in NCEPOD), with a significant proportion going unrecognised (27%) despite multiple medical reviews. Out-of-hours CPR attempts (68% vs. 59% in NCEPOD) seemed be associated with poorer survival. The survival to discharge rate after in-hospital cardiac arrest was 10.1%. This compares with 14.6% in the NCEPOD data and 20% in larger studies [2]. Ninety per cent of patients had no documentation of resuscitation status (78% in NCEPOD).
Conclusion The results from this audit highlight persistent deficiencies in the care pathway for the acutely unwell patient. Improvement will be focused on earlier consultant review and better recognition of warning signs with appropriate action taken. Furthermore, earlier routine and senior clinician-led discussions on appropriate end-of-life care are vital.
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P494

Endovascular hypothermia after cardiac arrest in a Chilean ICU

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Introduction For more than a decade, mild hypothermia has been a standard for enhancing the neurological prognosis in comatose survivors of cardiac arrest (CA). Despite this, in our country there are still few centers that apply hypothermia post CA regularly. We describe a Chilean experience with endovascular hypothermia post CA, in three ICUs of the same university clinical center [1-3].
Methods A descriptive cohort study. All surviving comatose patients after CA were included, and underwent endovascular hypothermia management according to protocol. CoolGard™ internal cooling equipment was used. Variables: delay between CA and hypothermia (34°C), time in hypothermia, complications, ventilatory and hemodynamic management. Main outcome measures: mortality and neurological follow-up to 6 months with Glasgow Outcome Score Extended (GOSE).
Results Twenty-seven patients were managed in the ICU post CA (18 outpatients). Twenty-four were men (89%), mean age 33.5 ± 19 years (16 to 76). Delay was considered (time between CA and achieving target temperature of 34°C): median 10.5 ± 3.3 hours (3 to 18 hours). Hypothermic maintenance (from when it reaches 34°C until it returns to 36°C): 24 ± 18 hours (24 to 48 hours). Complications of hypothermia: five hypokalemia (18.5%), three ventricular arrhythmias (11%), one vein thrombosis (3.7%). There were no deaths during hypothermia. Hospital mortality was two cases (7.4%). At 6 months it was three (11%). Neurological outcome at discharge and 6 months are shown in Figure 1. Good outcome (GOSE 5 to 8) occurred in 11 patients (40%) at discharge. Good outcome at 6 months occurred in 20 patients (74%).
Conclusion Our series shows a low mortality and a very good neurological outcome. There was no mortality or severe complications associated with endovascular hypothermia. It is a safe and feasible technique implemented in Latin American critical care units. Even the delay in achieving the objective of hypothermia is very long.
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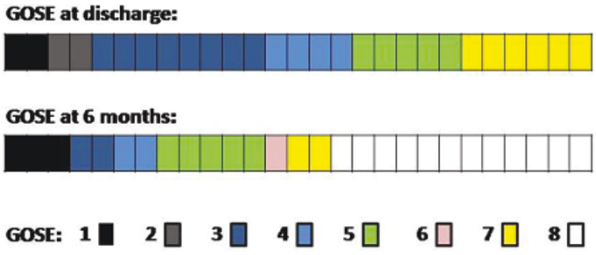

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P495

Knowledge and use of therapeutic hypothermia in cardiac arrest victims among healthcare staff in Greece

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Introduction Therapeutic hypothermia (TH) improves the neurologic outcome of patients who survive after cardiac arrest but suffer from severe secondary neurological damage [1]. In 2010, the use of TH after cardiac arrest was included in the ERC guidelines. The purpose of this study was to investigate the knowledge of the medical and nursing staff on the implementation of TH in patients after cardiac arrest [2].
Methods Data were collected by an anonymous questionnaire designed for the purpose of research, addressed to medical and nursing staff of Greek hospitals. The questionnaire consisted of questions about knowledge and behavior related to TH induction, target temperature and duration of cooling. Information about the potential barriers to implementation of TH was also collected.
Results We obtained 344 questionnaires from 16 hospitals. The population of the study was registered nurses (RN) (63.8%) and doctors

(36.2%). The majority of health staff (81.5%) had never implemented TH. A total 45.8% of respondents stated that the main reasons for not using TH were the lack of information and training about the method, the lack of nursing staff, the lack of available cooling methods and the required time. The most common methods of application were cold packs and intravenous fluids. Only 30.2% of the doctors and 5.5% of the nurses (P <0.001) actually had the knowledge to implement TH, and this was demonstrated by correct answers. Of the respondents who answered that they did know the method, only 23.9% answered correctly; about the target temperature, the maintenance and rewarming phase. A total 59.1% of doctors, despite having attended the Advanced Cardiac Life Support seminar, were not able to answer correctly the knowledge questions. Continuous education of health professionals and the existence of a protocol were proposed by 65% of participants as the best way of increasing knowledge and adherence with ERC guidelines about TH.

Conclusion Therapeutic hypothermia is rarely used in Greek hospitals. The level of knowledge is mainly related to the lack of education and the lack of information about new techniques. Programs for continuing education are necessary for the use of new therapeutic techniques in the field of health.

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P496

Induced hypothermia of 33°C does not affect host response compared with maintaining 36°C

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Introduction Induced hypothermia is applied in the ICU and in the operating theater to reduce ischemia–reperfusion injury. It is thought that induced hypothermia may hamper the immune response and therefore carry the risk of acquiring or aggravating an infection. We investigated the effect of hypothermia on host response by comparing survivors of cardiac arrest in which body temperature was kept at either 33°C or 36°C.

Methods As a substudy to the Target Temperature Management trial [1] in which cardiac arrest patients admitted to the ICU were randomized to maintaining either 33°C (n = 11) or 36°C (n = 9) for 24 hours, blood was drawn at the start and end of the target temperature phase as well as after reaching normotemperature. Host response was measured via monocyte human leukocyte antigen-DR (HLA-DR) expression and via whole blood stimulation with TLR ligands lipopolysaccharide (LPS) and lipoteicoic acid (LTA) for 24 hours. Plasma levels of interleukin (IL)-1β, IL-1RA, IL-6, IL-8, IL-10, tumor necrosis factor alpha (TNFα), macrophage inflammatory proteins (MIP)-1, monocyte chemotactic protein (MCP)-1 and soluble CD40 ligand levels were determined with ELISA or Luminex. Statistics were by unpaired Mann–Whitney U tests.

Results HLA-DR expression was decreased compared with healthy controls, without differences between 33°C and 36°C. Following whole blood stimulation with LPS, TNFα and IL-6 production was lower after cardiac arrest compared with healthy controls. The 33°C and 36°C groups differed at baseline in TNFα levels after LPS whole blood stimulation. After 24 hours of temperature management, there was no difference in both TNFα and IL-6 production between the groups following TLR ligand stimulation. After cessation of temperature management only TNFα levels increased after LTA stimulation. Plasma levels of IL-1RA, IL-8 and IL-10 were decreased after cardiac arrest compared with healthy controls. In plasma levels of IL-1β, MIP-1 and soluble CD40 ligand there were no differences between the 33°C and 36°C groups at all time points. Apart from baseline differences, there were no differences between 33°C and 36°C in plasma levels of IL-1RA, IL-8, IL-10 and MCP-1.

Conclusion Cardiac arrest induces a decrease in proinflammatory response. There were no differences in immune host response after 24 hours of targeting body temperature at 33°C or 36°C. These results suggest that hypothermia does not alter host immune response.

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P497

Derived electromyography is an accurate measure of shivering burden during targeted temperature management

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Introduction Shivering complicates targeted temperature management (TTM) by increasing metabolism, oxygen consumption, resting energy expenditure, and carbon dioxide production and is associated with lower brain tissue oxygen levels; all of these may limit the effectiveness of TTM. However, the recognition and measurement of shivering are subjective and ill-defined. The Bedside Shivering Assessment Scale (BSAS) is the only validated tool to describe the intensity of shivering. We hypothesized that the derived electromyography (dEMG) value measured by the bispectral index monitor (BIS) would agree with energy expenditure due to shivering, compared with the BSAS.

Methods We measured continuous indirect calorimetry during a 2 to 5 hour time span during targeted temperature management in 12 patients being treated for hypoxic ischemic encephalopathy after cardiac arrest. Patients were excluded if seizing, requiring >FiO_2 0.5, exhibiting early spasticity, or not shivering. The BSAS was measured every 15 minutes by a blinded observer and shivering was treated for a BSAS ≥1, as per institutional protocol. The association of dEMG and BSAS as a predictor of resting energy exposure (REE) was measured using linear regression and Pearson's correlation.

Results The study population included 12 patients. Average age was 54 years, nine patients were male, eight patients had a CPC of 1 to 3 on hospital discharge. There were a total of 182 measurements of BSAS, dEMG, and REE. There is improved correlation between REE and dEMG compared with REE and BSAS (0.24 (CI = 0.10 to 0.37) vs. 0.10 (CI = –0.04 to 0.24); P <0.001 vs. 0.14). Each increase in dEMG resulted in an increase of 14 kcal of energy expenditure (P = 0.003).

Conclusion Continuous dEMG power measured by Covidien BIS monitors is a more accurate and less subjective measure of shivering burden compared with the intermittent BSAS. Introducing dEMG into clinical practice may improve recognition of shivering, allow quantification of the metabolic cost of shivering, and serve as a more reliable research tool for diagnostic and treatment strategies of shivering.

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Shivering during targeted temperature management after cardiac arrest: a physiologic description

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Introduction Targeted temperature management (TTM) is used to treat hypoxic ischemic encephalopathy (HIE), elevated intracranial pressure, status epilepticus, and other brain injuries. Shivering complicates TTM, and the associated energy burden and its response to treatment are poorly understood. We describe the pattern of shivering and response to neuromuscular blockade in a series of patients undergoing TTM after cardiac arrest using continuous indirect calorimetry.

Methods With IRB approval, we studied 16 patients undergoing TTM for HIE with continuous calorimetry during their treatment. The calorimeter measures inspired and expired oxygen and carbon dioxide, which are used in the Weir equation to calculate resting energy expenditure (REE). We excluded patients known to be actively seizing, requiring FiO_2 >0.5, with early spasticity, or who did not shiver. All patients received counterwarming, moderate analgosedation, and bolused vecuronium in response to visible shivering, measured hourly by nurses using the Bedside Shivering Assessment Scale.

Results Sixteen patients of average age 57 included 12 men. Twelve patients had CPC of 1 to 3 on hospital discharge. Sixteen shivering events were monitored with calorimetry among the 12 patients. The average rate of energy expenditure (without shivering) leading up to and following paralytic treatment was 1,425 kcal/hour (± 489 kcal/hour) and 1,386 kcal/hour (± 235 kcal/hour). This was significantly greater than the predicted basal energy expenditure (1,089 ± 222 kcal; $P = 0.007$ and $P < 0.001$). Time from a change in baseline energy expenditure to recognition and treatment of clinical shivering was 57 (± 64) minutes, and from treatment with neuromuscular blockade to baseline energy expenditure was 30 (± 20) minutes. This accounts for a total difference of 15,223 kcal (± 10,997 kcal) before treatment and 7,113 kcal (± 3,706 kcal) after treatment for each shivering episode compared with baseline ($P = 0.01$ and $P = 0.003$).
Conclusion The energy burden of shivering is underestimated by standard nutritional formulas in patients undergoing TTM after cardiac arrest. Subclinical shivering is associated with increased energy expenditure. Clinical recognition occurs long after the increase in metabolic activity, and persists for a significant period of time after treatment. These findings should influence how shivering is monitored and treated during TTM.

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Temperature management following cardiac arrest: introducing a protocol improves compliance with targets

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Introduction We audited the achievement of therapeutic hypothermia (TH) before and after the introduction of a cooling protocol. Instituting TH is recommended following the return of spontaneous circulation (ROSC) for many patients who survive a cardiac arrest [1,2]. The key intervention may be the avoidance of hyperthermia rather than cooling [3].
Methods We conducted a chart review of all patients admitted to the Department of Critical Care (DCC) at our hospital following cardiac arrest over 2 years in 2010 to 2012 (Group 1). We recorded compliance with key recommendations produced by the Royal College of Anaesthetists [4] although we defined post-ROSC hyperthermia as >37.2°C rather than >38°C. A TH protocol was designed and personnel in the emergency department and DCC educated as to its use. Recommended practice was the infusion of cold i.v. normal saline (1 to 2 l) followed by the use of an intravascular cooling device (Alsius CoolGard™). Data collection was then undertaken after introduction of the protocol for all patients admitted to the DCC following cardiac arrest in November 2012 to 2013 (Group 2).
Results Forty-three patients were admitted in Group 1, 28 in Group 2. Of these, 42% in both groups were following out-of-hospital (OOH) VF arrests. Cooling was attempted in 88% and 82% of OOH VF patients respectively. For patients with either in-hospital or non-VF/VT cardiac arrests, the numbers cooled were 16% and 12.5%. Cooling initiation within 1 hour increased from 27 to 50%. Achievement of a target temperature of 32 to 34°C within 4 hours of ROSC was 55% and 50% respectively. Target maintenance for 12 to 24 hours after ROSC increased 79% to 100%. Avoidance of hypothermia <31°C for 48 hours after ROSC improved 95% to 100%. Slow rewarming at 0.25 to 0.5°C/hour to 37°C was achieved in 76% and 90%. Avoidance of temperature >37.2°C for 48 hours after ROSC increased 84 to 100%. Of the patients cooled, survival with good neurological outcome was achieved in 52% in Group 1 and 88% in Group 2.
Conclusion The institution of a temperature management protocol improved compliance with recommended goals, both in achieving hypothermia and in the avoidance of hyperthermia.
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P500

Factors involved in prolonged effect of neuromuscular blockade in therapeutic hypothermia

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Introduction Therapeutic hypothermia (TH) following out-of-hospital cardiac arrest (OHCA) improves neurological outcomes in such patients. During TH, neuromuscular blockade is used to control shivering in the patient. In our hospital, we use vecuronium as a neuromuscular blocker. However, occasionally, prolonged effects of vecuronium delay accurate evaluation of patients' neurological function or extubation. Unfortunately, the factors involved in the prolonged effect of vecuronium in TH remain unclear.
Methods We conducted a retrospective cohort study of patients managed with TH following OHCA at our institution from April 2010 to September 2013. We defined full-muscle reaction to train-of-four stimulation (TOF) as the end of effects of vecuronium. In this study, the time from the end of vecuronium administration to full-muscle reaction to TOF was evaluated as the outcome. We calculated the adjusted hazard ratio (HR) for the outcome using Cox regression analysis after adjustment for age, gender, albumin levels, estimated glomerular filtration rate, temperature at the end of vecuronium administration, and total amount of vecuronium per kilogram of body weight.
Results In total, 52 patients were evaluated in this study (86.5% male; average age, 55.2 years). The median time from the end of vecuronium administration to full-muscle reaction to TOF was 660 minutes (maximum: 10,363 minutes; minimum: 72 minutes). Blood albumin levels on admission decreased the time (adjusted HR: 2.31, 95% CI: 1.073 to 5.004; $P < 0.05$). However, other factors had no significant difference on the time. The amount of vecuronium per kilogram of weight had no significant differences (adjusted HR: 1.073, 95% CI: 0.869 to 1.325; $P = 0.511$).
Conclusion The time from the end of vecuronium administration to full-muscle reaction to TOF decreased in relation to blood albumin levels on admission. Other factors had no significant difference on the outcome time. Taken together, the outcome time may be determined by albumin levels and not by the administered amount of vecuronium per kilogram of body weight. Based on this result, we suggest that blood albumin levels on admission should be taken into consideration for appropriate use of vecuronium in TH.
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P501

Serum phosphate concentration during the rewarming period after deep hypothermic circulatory arrest

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Introduction Short-term neuropsychologic dysfunction (SND) is often observed during the postoperative period of open total arch repair (TAR) under deep hypothermic circulatory arrest (DHCA). We supposed that there might be a large consumption of high-energy phosphates during the rewarming period, and this might be associated with awakening and SND. Due to difficulty in measuring such high-energy phosphates at the bedside, we measured the serum phosphate concentration (P) as a substitute, and assessed its influence on awakening and postoperative SND.
Methods Twenty patients with a mean age of 68 ± 11 years who underwent open TAR under DHCA applied at a temperature of 20°C, with antegrade cerebral perfusion (ACP) or retrograde cerebral perfusion (RCP), were enrolled. Arterial blood gas lactate concentration (ALac), $ScvO_2$, and P were measured at 2, 4, 6, and 10 hours after weaning from cardiopulmonary bypass (CPB). We also measured time to confirm M6 on the Glasgow Coma Scale (GCS), and incidence of SND.

Occurrence of SND was defined as neurological disarrangement such as irritability, confusion, or delirium within 48 hours after operation.
Results Durations of CPB, aortic clamp, and circulatory arrest were 194 ± 51, 136 ± 53, and 70 ± 17 minutes respectively. Nine patients underwent ACP (89 ± 26 minutes) and 11 patients underwent RCP (56 ± 25 minutes). Concentration of ALac, $ScvO_2$, and P changed at 2, 4, 6, 10 hours after CPB as follows: ALac 4.0 ± 1.9, 5.1 ± 2.6, 5.3 ± 3.3, 4.0 ± 2.8 mmol/l, $ScvO_2$ 71 ± 6.7, 67 ± 10, 67 ± 9.7, 65 ± 11%, and P 2.9 ± 0.9, 2.4 ± 0.7, 2.2 ± 1.0, 1.8 ± 0.8 mg/dl, respectively. Serum P recovered to 2.6 ± 1.4 at 18 hours after CPB. The incidence of hypophosphatemia (<2.6 mg/dl) and SND in our series were 18/20 (90%) and 14/20(70%) respectively. There was a correlation between minimum P and time to confirm M6 on the GCS ($P = 0.508$, Fisher r-to-z transformation), but no significant correlation between SND. The mortality rate during the first 28 days was 5% (1/20).
Conclusion Serum phosphate decreased dramatically during the rewarming period after deep hypothermic circulatory arrest. There was a moderate correlation between minimum phosphate concentration and time to confirm M6 on the GCS. Monitoring phosphate concentration might predict neurological recovery after deep hypothermic circulatory arrest.

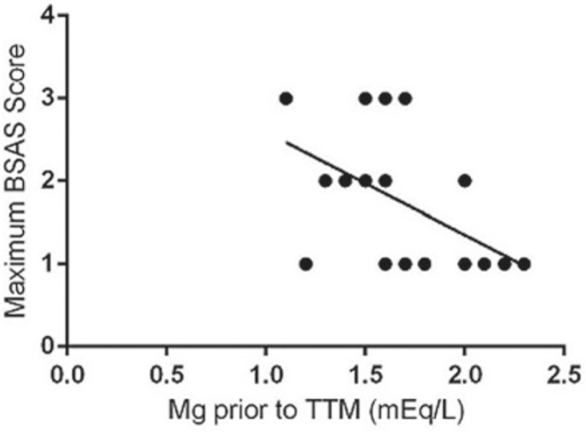

Figure 1 (abstract P502).

P502

Influence of baseline magnesium concentrations on shivering in therapeutic temperature modulation

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Introduction Therapeutic temperature modulation (TTM) is widely used in the care setting to improve outcomes of patients with traumatic brain injury (TBI). Through fever prevention, both oxygen utilization and caloric expenditure are reduced, so metabolic efficiency can be maximized [1]. However, patient cooling is not without consequences and shivering is experienced by more than 70% of patients achieving TTM. Because shivering triggers an increase in metabolic demand, causing additional oxygen consumption and the promotion of catabolism, its prevention is ideal [2]. We set out to review the data surrounding the anti-shivering component of a normothermia protocol in the surgical ICU (SICU) of one Minnesota hospital.
Methods A retrospective review was conducted looking at SICU patients managed with a normothermia protocol, with particular attention paid to the anti-shivering portion of the protocol. Serum magnesium (Mg) levels were assessed prior to initiation of TTM and Bedside Shivering Assessment Scale (BSAS) scores were collected.
Results Twenty patients receiving TTM for TBI were evaluated (March to October 2013). One-half of the patients maintained targeted BSAS scores <1 for the full duration of TTM ($n = 10$ of 20). Serum Mg levels at the initiation of TTM were observed to negatively correlate with the level of shivering, as indicated by the BSAS scoring system ($P = 0.02$). See Figure 1.
Conclusion The literature suggests the positive impact of TTM on patient outcomes can be maximized with shivering prevention [2]. Current SICU practices provide a similar Mg loading dose for all patients, regardless of baseline Mg levels. In our observed patients, achieving a baseline serum Mg level >2 was associated with lower shivering scores throughout the TTM course. This supports the hypothesis that serum Mg concentrations prior to TTM are important predictors of shivering reduction, and suggests that loading doses of Mg should be tailored to the individual patient to achieve such levels.

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