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A comparison of very old patients admitted to intensive care unit after acute versus elective surgery or intervention

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ABSTRACT

Background: We aimed to evaluate differences in outcome between patients admitted to intensive care unit (ICU) after elective versus acute surgery in a multinational cohort of very old patients (≥80 years; VIP). Predictors of mortality, with special emphasis on frailty, were assessed.
Methods: In total, 5063 VIPs were included in this analysis, 922 were admitted after elective surgery or intervention, 4141 acutely, with 402 after acute surgery. Differences were calculated using Mann-Whitney-*U* test and Wilcoxon test. Univariate and multivariable logistic regression were used to assess associations with mortality.
Results: Compared patients admitted after acute surgery, patients admitted after elective surgery suffered less often from frailty as defined as CFS (28% vs 46%; $p < 0.001$), evidenced lower SOFA scores (4 ± 5 vs 7 ± 7; $p < 0.001$). Presence of frailty (CFS >4) was associated with significantly increased mortality both in elective surgery patients (7% vs 12%; $p = 0.01$), in acute surgery (7% vs 12%; $p = 0.02$).
Conclusions: VIPs admitted to ICU after elective surgery evidenced favorable outcome over patients after acute surgery even after correction for relevant confounders. Frailty might be used to guide clinicians in risk stratification in both patients admitted after elective and acute surgery.
Trial registration: NCT03134807. Registered 1st May 2017.

1. Introduction

Patients 80 years and older are admitted to the intensive care unit (ICU) for various reasons. However, patients admitted electively after planned surgery differ from patients who are admitted acutely [1]. Elective admission to ICU has been associated with favorable outcome in the elderly compared to acute patients and it is questionable if these patient sub-groups can be compared with regard to outcomes and risk prediction [1-4].

Mortality of such very old intensive Patients (VIP) admitted to an ICU remains high and post-ICU morbidity causes relevant health costs and leads to human suffering [5]. Further, due to cost pressures on health systems, the question which patients should receive maximal therapy and which patients might benefit primarily from conservative medical therapy arose [6,7]. In one randomized controlled trial, systematic admission to ICU even failed to improve outcomes at 6-month in patients 75 years and older [8].

Several clinical scores are available to guide clinicians in the intensive care setting. Currently, the most commonly used and most thoroughly tested models are the Sequential Organ Failure Assessment score (SOFA), the Acute Physiology And Chronic Health Evaluation II (APACHE II) and Simplified Acute Physiology Score 2 (SAPS2) score [9-11]. Recently, the Clinical Frailty Scale (CFS), assessing frailty through a simple clinical assessment, has been successfully used to risk-stratify elderly patients [5,12].

Patients admitted after elective surgery versus after acute surgery might differ significantly with regards to characteristics, outcomes and predictors of outcomes. We therefore aimed to compare admitted after elective surgery or intervention versus after acute surgery or intervention in a large, multinational collective of VIPs admitted to an ICU with regards to outcome and predictors of mortality with special emphasis on frailty.

2. Methods

2.1. Study subjects

VIP1 is a prospective multicenter study, registered on ClinicalTrials.gov (ID: NTC03134807). These patients were already investigated in another context and methods and patients have been described in previous publications [5,12,13]. In summary, each participating ICU could either include consecutive patients during a three-month period or the first 20 consecutive patients fulfilling the inclusion criteria (all patients aged 80 years or older admitted to a participating ICU). Data were collected between October 2016 and February 2017. Patients with prior elective surgery or intervention before admission to ICU were considered elective, all others acute. Patients after elective surgery or intervention were admitted for post-operative management including troubleshooting of perioperative complications.

In this study all patients with reported age, sex, frailty score and SOFA score and data on ICU mortality were included. Data on 30-day mortality was available in 820 elective and in 3830 acute patients.

2.2. Statistical analysis

Continuous data points are expressed as median ± interquartile range (IQR). Differences between independent groups were calculated using Mann-Whitney *U* test for non-paired data and Wilcoxon test for paired data. Categorical data are expressed as numbers (percentage). Chi-square test was applied to calculate differences between groups and McNemar's test for paired data. Univariate and multivariable logistic regression analysis was performed to assess associations with mortality and calculate odds ratios (OR). For the multivariable regression model, confounders with a p-value <0.10 in the univariate analysis were included. Elimination criterion was a p-value of >0.10. Predictiveness was evaluated calculating area under the curve (AUC) and an optimal cut-off was calculated by means of the Youden Index. A p-value of <0.05 was considered statistically significant.

2.3. Matched-paired analysis

296 patients admitted after acute surgery or intervention were matched for age, sex, frailty and SOFA score (perfect-match) to 296 patients admitted after elective surgery or intervention. Paired analysis was applied as described above. SPSS version 22.0 (IBM, USA) and MedCalc Statistical Software version 18.6 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2018) were used for all statistical analyses.

3. Results

3.1. Study population

Admission diagnoses and baseline characteristics are presented in Table 1. Compared to patients admitted after acute surgery or intervention, patients admitted after elective surgery or intervention were younger (83 ± 5 vs 84 ± 5 years; $p < 0.001$), suffered less often from frailty as defined as CFS (28% vs 46%; $p < 0.001$), evidenced lower SOFA scores (4 ± 5 vs 7 ± 7; $p < 0.001$) and had a shorter ICU length of stay (1.2 ± 2 vs 2.1 ± 5.4 days; $p < 0.001$). In patients admitted after elective surgery, both treatment withdrawal (5% vs 15%; $p < 0.001$) and withholding (2% vs 8%; $p < 0.001$) were less frequent. Patients admitted after elective

Table 1
Baseline characteristics in the overall cohort.

	Acute medical	Trauma	Acute surgery	Elective surgery	p-value
n=	3484	255	402	922	
Age					
Median (IQR)	84 (81–86)	84 (81–86)	84 (82–87)	83 (81–86)	<0.001
Frailty score					
Median (IQR)	4 (3–6)	4 (3–6)	4 (3–5)	4 (3–5)	<0.001
SOFA score					
Median (IQR)	7 (4–11)	7 (4–11)	7 (4–11)	4 (2–7)	<0.001
ICU length of stay					
Median (IQR)	2.9 (1.1–6.6)	2.9 (1.1–6.6)	2.1 (1.0–6.0)	1.2 (0.9–2.9)	<0.001
Female sex	1686 (48%)	108 (42%)	212 (47%)	414 (45%)	0.01
Treatment withdrawn	983 (28%)	68 (27%)	59 (15%)	43 (5%)	<0.001
Treatment withhold	515 (15)	51 (20%)	31 (8%)	15 (2%)	<0.001
NIV	981 (28%)	32 (13%)	62 (15%)	86 (9%)	0.002
Intubation	1753 (50%)	167 (65%)	213 (53%)	412 (45%)	0.006
Renal replacement therapy	383 (11%)	10 (4%)	36 (9%)	40 (4%)	0.002
Vasoactive drugs	1925 (55%)	129 (51%)	250 (62%)	326 (35%)	<0.001

IQR – inter-quartile range; SOFA - sequential organ failure assessment score; ICU – intensive care uni; NIV – non-invasive ventilation.

surgery less often needed renal replacement therapy 4% vs 9%; ($p < 0.001$), vasoactive drugs 35% vs 62% ($p < 0.001$) and were intubated less often (45% vs 53%; $p < 0.001$). In patients after acute surgery, 274 of 402 patients were admitted from out-of-hospital.

3.2. Survival analysis

Compared to patients admitted after acute surgery both ICU (3% vs 14%; $p < 0.001$) and 30-day mortality (8% vs 26%; $p < 0.001$) were lower in patients admitted after elective surgery, even after correction for frailty, age, sex and SOFA score (30-day-mortality; OR 0.39 95%CI 0.24–0.63; $p < 0.001$). Again, after exclusion of patients in whom treatment was withdrawn or withhold, patients admitted after elective surgery evidenced lower intra-ICU (1% vs 7%; $p < 0.001$) and 30-day mortality (6% vs 13%; $p < 0.001$) compared to patients admitted after acute surgery.

Predictors of 30-day-mortality are given in Table 2. Presence of frailty (CFS >4) was associated with significantly increased mortality both in patients admitted after elective surgery (7% vs 12%; OR 1.96 95%CI 1.17–3.27; $p = 0.01$), in patients after acute surgery (2% vs 34%; OR 1.82 95%CI 1.15–2.89; $p = 0.01$) as well in all acute (36% vs 49%; OR 1.70 95%CI 1.50–1.94; $p < 0.001$) patients. Frailty was moderately predictive for survival at one month (AUC 0.61), an optimal cut-off was exactly at the frailty level of ≤4 points.

In patients admitted after acute surgery, patients admitted from out-of-hospital evidenced worse outcome both intra ICU (20% vs 11%; $p = 0.01$) and at one month (34% vs 23%; $p = 0.02$).

Table 2
Association of relevant factors with 30-day mortality in elective surgery and acute surgery patients.

	Univariate			Multivariate		
A - acute surgery	HR	95%CI	p-value	HR	95%CI	p-value
Age	1.05	0.99–1.11	0.13			
Frailty score	1.21	1.05–1.39	0.007	1.26	1.09–1.46	0.002
SOFA score	1.14	1.08–1.20	<0.001	1.15	1.09–1.21	<0.001
Female sex	1.28	0.81–2.03	0.30			
B - elective surgery	HR	95%CI	p-value	HR	95%CI	p-value
Age	1.04	0.97–1.11	0.30			
Frailty score	1.33	1.13–1.56	0.001	1.32	1.12–1.55	0.001
SOFA score	1.15	1.09–1.22	<0.001	1.15	1.08–1.22	<0.001
Female sex	1.04	0.63–1.71	0.89			

SOFA - sequential organ failure assessment score.

Table 3
Baseline characteristics in the matched-paired cohort (n = 655 patients for each group).

	Elective surgery	Acute surgery	p-value
n=	296	296	
Age			
Median (IQR)	83 (81–86)	83 (81–86)	n/a
Frailty score			
Median (IQR)	4 (3–5)	4 (3–5)	n/a
SOFA score			
Median (IQR)	6 (3—10)	6 (3–10)	n/a
ICU length of stay			
Median (IQR)	1.5 (1.00–2.00)	2.00 (0.93–5.39)	<0.001
Female sex	148 (50%)	148 (50%)	n/a
ICU death	14 (5%)	29 (10%)	
30-day death	28 (10%)	60 (20%)	
Treatment withdrawn	4 (1%)	19 (6%)	<0.01
Treatment withhold	14 (5%)	37 (13%)	<0.01
NIV	34 (12%)	48 (16%)	0.11
Intubation	153 (52%)	138 (47%)	0.21
Renal replacement therapy	15 (5%)	25 (8%)	0.15
Vasoactive drugs	133 (45%)	165 (56%)	<0.01

IQR – inter-quartile range; SOFA - sequential organ failure assessment score; ICU – intensive care unit; NIV – non-invasive ventilation.

3.3. Matched-pair analysis

In the two cohorts (n = 296 each from patients admitted after elective surgery versus patients after acute surgery, Table 3) matched for age, gender, frailty and SOFA score, there both ICU mortality (mean difference 5.07%; 9.37–0.76%; $p = 0.03$) and 30-day mortality (mean difference 10.12%; 3.58–16.65%; $p < 0.01$) was lower in patients admitted after elective surgery.

4. Discussion

Here we have shown that in patients 80 years and older admitted to ICU, compared to patients admitted after acute surgery or intervention [1] patients admitted after elective surgery or intervention were clinically less sick, younger and less frail as assessed by CFS, [2] even after correction for relevant confounders and in a matched-pair analysis, patients admitted after elective surgery had a shorter ICU length of stay and lower mortality. Further, [3] frailty assessed by CFS was associated with 30-day mortality both in patients admitted after elective and acute surgery.

A growing proportion of VIP is admitted to ICUs and how to risk stratify these patients is of relevance but unclear [14,15]. In our study, patients admitted electively after surgery evidenced better prognosis compared to patients admitted after acute surgery even after correction for age, frailty and organ failure at admission as assessed by CFS and SOFA score, respectively. This is in accordance to studies showing elective ICU admission after surgery being associated with better outcome [1]. Still, compared to patients from European Surgical Outcome Study (EuSOS), mortality in this cohort was higher but seems in line as patients in this cohorts were older and all of them admitted to ICU compared to only 8% in EuSOS [16]. Of note, differences in comorbidities, known to be associated with outcome, were not systematically reported in this study and might influence the outcome [17]. Parameters assessing dynamics of disease course such as lactate clearance might improve our ability to predict risk of death [18,19]. Still, frailty, a condition characterized by deteriorated physiologic reserves and vulnerability to high morbidity due to falls, cognitive decline and hence need for special care, might add insight over biomarkers and intensive care

scores, which were not specifically developed for VIPs [20,21]. In our study, frailty was assessed by CSF, which has successfully been tested against other tools [22]. Other methods to measure frailty such as (modified) frailty index and hospital frailty risk score were proposed, but not available in this study [23-25]. Still, compared to CFS, these scores primarily assess comorbidities and deviate from the multidimensional frailty concept [26]. Multidimensional score models including frailty might help for better risk prediction: in a study of 275 patients aged 65 years or more undergoing intermediate or high-risk elective surgery, a multidimensional frailty score model (composed of the Charlson Comorbidity Index, dependence in activities of daily living, dementia, risk of delirium, short mid-arm circumference and malnutrition) predicted mortality rates more accurately than the ASA classification [27].

In patients admitted after elective surgery, frailty was associated with higher mortality. We therefore think that before elective surgery VIPs should undergo structured frailty screening. The indication for surgery should undergo rigorous examination if a patient is deemed frail. In VIPs before any elective intervention modifiable risk factors should be reduced. Studies investigating effects of specific measures tailored to minimize the effect of frailty on mortality are warranted [28,29]. Inclusion of geriatric consultancy has proven valuable in other areas of medicine. Studies have documented that for post-operative elderly patients, mainly after hip fracture, geriatric unit admission offers a benefit as compared to surgical unit admission: In Boddaert et al.'s study, postoperative admission to a dedicated geriatric unit reduced both readmission rate (14% versus 29%, $P = 0.007$) and 6-month mortality (15% versus 24%, $P = 0.04$). After adjustment for comorbidities, risk ratio of death at 6 months was 0.43 (95%CI 0.25 to 0.73, $P = 0.002$) [30]. Of note, frailty might specifically result in an inability to tolerate or survive perioperative adverse events. Of note, in our study, in elective patients, frailty assessed by CFS was associated with increased one-month mortality, but not with ICU mortality (data not shown). Frailty might specifically be suited to predict longer-term mortality. In this regard the recently started VIP2 study (NCT03370692) will bring further evidence.

Admissions of VIPs to an ICU bring up both economic and ethical issues [31]. In our study patients admitted acutely evidenced high one-month-mortality. Costs of VIPs admitted to ICUs were previously shown to be high [6,32]. Further, relevant proportion of surviving VIPs might suffer from high morbidity, although other studies found comparable levels of quality of life to matched non-ICU patients [33-35]. Therefore, a thorough pre-admission assessment is necessary not only in elective but also in acutely admitted VIPs. Therapy goals and possible restrictions should be formulated and communicated early [36,37]. Especially in VIPs an “intensive care trial” of 24 to 72 h duration should be undertaken. During this time frailty should be assessed and realistic treatment goals in consent with patients and their relatives formulated and critically evaluated [7,38-40]. For these “intensive care trials” in VIPs the concept of “geriatric ICU” with intensive care medicine specialists as well as geriatric specialists is intriguing. Once a “curative” approach is established, geriatric rehabilitation could be planned to reduce long-term morbidity [36].

4.1. Strengths and limitations

In our study detailed information about the type of surgery was unavailable. Further, no information in acute or elective patients about a possible delay between decision for surgery/ICU admission and actual surgery/admission in ICU was collected. No information about an early rehabilitation program post-surgery contributing to low one-month mortality was available for analysis. No information about perioperative complications was available. However, strength is that an analysis of a very large, multicenter, multinational cohort with prospectively collected data was available in VIPs.

5. Conclusion

VIPs admitted to ICU after elective surgery were younger and clinically less severley ill, resulting in a more favorable outcome compared to patients admitted after acute surgery, even after correction for relevant confounders. Frailty might be used to guide clinicians in risk stratification in both patients admitted after elective and acute surgery.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcrc.2019.04.020.

Competing interests

The authors declare that they have no competing interests.

Author contributions

BW and CJ analyzed the data and wrote the first draft of the manuscript. HF and BG and DL and IS contributed to statistical analysis and improved the paper. JM and MK and AB and AM and FA and AA and BG and MC and SC and LF and JF and ML and BM and RM and SO and CÖ and BP and WS and AV and CW and TZ gave guidance and improved the paper. All authors read and approved the final manuscript.

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Ethics Approval and consent to participate

A study protocol was provided to participating centers. Every participating center obtained ethics approval according to local legislation. A copy of the ethics approval was sent to the study coordinator before start of the study.

Consent for publication

Written informed consent was obtained of all included subjects.

Availability of data and materials

All data relevant for this study will be given by the authors upon specific request.

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