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YEAR IN REVIEW

A year in review in *Minerva Anestesiologica* 2021. Critical care

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SARS-CoV-2 pandemic

In 2021, MA published numerous original articles and reviews on the COVID-19 pandemic.

Gattinoni *et al.* reviewed 213 COVID-19 patients with PaO_2/FiO_2 ratio <300 mmHg and found silent hypoxemia at hospital admission in more than 30%.[1] In particular, dyspnea was absent in 18% of patients with PaO_2/FiO_2 ranging from 50 to 150 mmHg and in 25% of those presenting marked chest X-ray abnormalities.

The best clinical management for COVID-19 respiratory failure is still debated. In early phases, noninvasive ventilation (NIV) may improve oxygenation, but most authors agree that intensivists should promptly identify patients at high risk of disease progression and treat them with early tracheal intubation and invasive ventilation.[2] Chiumello *et al.* carried out a scoping review on patient respiratory management worldwide.[3] They found that invasive ventilation was the most frequently used respiratory modality, but NIV and CPAP were also broadly applied; prolonged invasive ventilation was associated with higher mortality; tracheostomy was performed often and with great caution to minimize the risk of viral transmission.[4]

Invasive mechanical ventilation is associated with an increased risk of barotrauma originating from parenchymal inhomogeneity due to diffuse alveolar injury and exuberant fibrosis.[5] An electronic survey performed among the intensivists of the COVID-19 Lombardy Intensive Care Unit network showed that about 7% of 2041 COVID-19 patients presented signs of lung barotrauma while on invasive mechanical ventilation.[6] Only in a few cases, the barotrauma was attributable to non-protective ventilatory settings.

Recent evidence supports the use of lung ultrasound as an easy-to-use, quick, and reproducible tool for lung morphologic assessment at the patient bedside.[7] Biasucci *et al.* used a comprehensive score to assess the initial lung involvement in 85 COVID-19 patients; they reported that the score was a good predictor of the need for mechanical ventilation and NIV failure.[8]

Treatment with low-dose dexamethasone and tocilizumab, a humanized monoclonal antibody against the IL-6 receptor, may decrease mortality among COVID-19 patients receiving mechanical ventilation.[9, 10] In the September issue, Romano *et al.* reviewed the literature on corticosteroid use in COVID-19 patients and concluded that treatment should be limited to severe forms of ARDS and last 7-10 days.[11] Yet, timing is crucial because corticosteroids may expose patients to the risk of significant viral replication and superinfections if given too early and immune response deregulation if given too late. Indeed, the frequent occurrence of severe opportunistic superinfections such as pulmonary mucormycosis highlights the impairment of immune response caused by COVID-19.[12] Montini *et al.* performed a prospective observational study on 105 consecutive adult patients admitted to the intensive care unit with laboratory-confirmed COVID-19 and fulfilling ARDS criteria.[13] Of them, 62% were treated with tocilizumab and 21% with sarilumab, a humanized monoclonal antibody against IL-6. In the multivariable Cox proportional regression hazards model, patients who received the monoclonal antibodies had a lower risk of death. Conversely, Monti *et al.* observed no statistically significant benefit with the use of tocilizumab or anakinra in 61 mechanically-ventilated, COVID-19 patients.[14]

The COVID-19 pandemic has raised unprecedented challenges for healthcare and hospital organizations, including bed availability, care protocols, supply shortage, and unexpected complications. Consequently, adaptive systems operating in an unstable environment with exhausted medical and non-medical personal were required, and regional health systems found new solutions to optimize intensive care for COVID-19 patients.[15] In Lombardy, which was the epicenter of the COVID-19 pandemic in Italy, a regional law redesigned the hub-and-spoke system during the first pandemic wave to allocate resources better. In particular, the neuro-ICUs admitted patients with trauma, stroke, and neurosurgical emergencies requiring specialized interventions, while non-specialized ICUs received COVID-19 entries. In the October issue, Chieregato *et al.* reported how those changes impacted the central hospital in Lombardy.[16] Meanwhile, Belgium managed patient overflow (*i.e.*, the number of patients exceeding the available beds) with new COVID-19 specific ICU beds.[17] Patients were redistributed all over the country to keep a homogenous proportion of COVID-19 patients in all ICUs.

Unfortunately, the COVID-19 pandemic negatively influenced the epidemiology of out-of-hospital cardiac arrest (OHCA). A systematic review pointed out that, compared to the pre-pandemic period, there was an increase in pooled annual OHCA incidence and fatal case rate, and a decrease in the survival rate after hospital admission and in the occurrence of shockable rhythms.[18] Jansen *et al.* investigated whether the integration of Advanced Life Support (ALS) protocols with precautions to prevent Covid-19 transmission to healthcare workers could have influenced ALS effectiveness.[19] They found that integration resulted in delayed chest compressions and prolonged no-flow time. The reduced resuscitation quality might hypothetically contribute to the increase in OHCA mortality.

International recommendations for intraoperative management of COVID-19 patients included dedicated operating rooms and anesthetic machines, adequate respiratory monitoring, protocolized protections for healthcare personnel, and particular attention to potentially life-threatening events, such as severe hemorrhage and thrombosis.[20] Minimization of the risk of infection and anesthesia safety were the subject of an Expert Opinion by Saracoglu *et al.* published in May.[21] In the delivery room, psychological support is recommended for COVID-19 mothers after delivery, and strict isolation for newborns.[22]

According to a study by Chiesa *et al.* published in December, 41% of critically ill, mechanically ventilated COVID-19 patients developed deep venous thrombosis, the majority being catheter-related and occurring under pharmacologic thromboprophylaxis.[23] Of note, an initial strategy of therapeutic anticoagulation with heparin does not increase the probability of survival of these patients but is associated with a high risk of bleeding.[24, 25] Acute kidney injury is also frequent in critically ill COVID-19 patients and often requires continuous venovenous hemofiltration (CVVHF). Ryan *et al.* compared renal replacement therapy and renal recovery before and during the COVID-19 pandemic and found that hospital mortality and the rate of renal recovery was similar in COVID-19 and non-COVID 19 patients.[26]

Finally, Marinangeli *et al.* reviewed chronic pain treatment during the COVID-19 pandemic in the July issue.[27] In particular, the authors stressed the risk that chronic pain management is deprioritized. Inadequate analgesia treatment may favor the occurrence of self-medication, adverse events, and even treatment discontinuation.

Circulation

Nearly all critically-ill patients present phases of hemodynamic instability during critical illness, and it is now clearly proved that delayed or inappropriate treatment increases mortality.[28] Therefore, the main challenge to the intensivist is identifying high-risk patients, performing adequate monitoring, and choosing effective pharmacological and mechanical support strategies.[29] MA published three interesting reviews on the topic. In June, an article authored by a panel of 16 experts provided helpful indications on the use of vasopressors and inotropes.[30] The authors stressed the concept that tissue hypoperfusion should be recognized and treated as soon as possible. The document included three sections on: 1) initial assessment, monitoring, and routes of infusion; 2) septic shock; 3) cardiogenic shock. A second expert opinion by Pinsky *et al.* dealt with the management of cardiovascular insufficiency.[31] The Authors proposed an original, step-by-step approach that included: 1) the ultrasound assessment of heart function; 2) the evaluation of arterial and ventricular elastances; 3) a volume load test by leg raising; 4) a reasoned approach to treatment. They summarized it with the acronym BEAT (browse the heart, elastances, assess volume status, and treat). Finally, Brandi *et al.* reviewed current indications and contraindications to Extra Corporeal Life Support (ECLS) by performing systematic research on guidelines, consensus statements, and position papers.[32] They collected 13 cardiac and 13 pulmonary indications and 23 cardiac and 14 pulmonary contraindications but remarked no common consensus among the authors. Furthermore, available resources strongly influence applying ECLS while benefits (or harms) are often uncertain.[33, 34]

Right ventricular insufficiency is relatively common in critically ill patients and is associated with increased mortality.[35, 36] The tricuspid annular plane systolic excursion (TAPSE) is the main echocardiographic parameter to evaluate right ventricle function and is traditionally measured through the apical four-chamber view often unavailable in critically-ill patients. Škulec *et al.* investigated the feasibility and effectiveness of measuring TAPSE through the subcostal view (sTAPSE), which proved to be a reliable parameter of right ventricular systolic function and impairment in those patients.[37]

Securing an intravenous infusion route is essential for critically ill patients. In some cases, however, this task can be challenging even if ultrasound has dramatically facilitated the placement of intravascular catheters. Two articles dealt with this topic. Lee *et al.* randomized 142 patients to undergo internal jugular catheterization with ultrasound by Dynamic Needle Tip Positioning (DNTP) or conventional long-axis in-plane technique.[38, 39] DNTP resulted in significantly higher success rates on the first attempt and less frequent needle redirections during the procedure. Van Loon *et al.* compared the dilator effect of the electrical stimulation with a commercially-available device and the application of a tourniquet on upper limb veins.[40, 41] DNTP performance was better than tourniquet, but the authors obtained the best effect by combining the two techniques.

Critical emergency medicine (CREM)

Prognostication after cardiac arrest and successful cardiopulmonary resuscitation (CPR) remains challenging.[42] The model for end-stage liver disease (MELD) Score modified by Heuman *et al.* by excluding INR (MELD – XI) proved to be an effective predictor of mortality in critically ill patients even in the absence of severe liver failure.[43, 44] In an article published in September, Rezar *et al.* aimed to evaluate its prognostic value for estimating mortality after CPR.[45] In 106 patients, the new score combined with serum lactate had higher predictive ability than the more complex SOFA-score. A high rate of severe neurological sequelae characterizes cardiac arrest (CA) since only 8.4% of survived patients had an optimal neurological outcome.[46] Khazanova *et al.* reviewed the literature on EEG monitoring for neurological prognostication after cardiac arrest.[47] The authors highlighted that temporal evolution was a fundamental aspect of EEG interpretation because patterns associated with irreversible brain injury were occasionally observed in patients who achieved a good outcome. Indeed, EEG monitoring acquired greater value if incorporated into a multimodal prognostication approach.[48] Myocardial dysfunction is another complication that can affect post-resuscitation care and outcome.[49] In the March issue, Babini *et al.* highlighted the prognostic importance of identifying two phenotypes of myocardial dysfunction after cardiac arrest.[50] Intensivists should distinguish benign and malign forms based on clinical and hemodynamic variables, such as diuresis, plasma lactate, heart rate, arterial pressure, cardiac output, central/mixed venous saturation, and the need for vasopressor support.

Extracorporeal cardiopulmonary resuscitation (eCPR) with venoarterial extracorporeal membrane oxygenation (ECMO) provides blood flow and oxygenation in cardiac arrest.[51] In an expert opinion published in January, Lotz *et al.* reviewed the eCPR potential to improve cardiac arrest outcomes, dealing with organizational, technical, and ethical issues.[52]

Supraglottic devices are an interesting alternative to tracheal intubation for advanced airway management during CPR because of their more effortless and faster positioning, particularly by inexperienced rescuers. Hinkelbein *et al.* reviewed the current data on the laryngeal tube (LT) used for this purpose.[53] Their meta-analysis pointed out that that device improved CPR quality. Compared with other airways, LT use improved short-term survival but was associated with worse long-term survival.

Simulation-based education and training in CREN are of paramount importance for acquiring technical skills (TS) and behavioral non-technical skills (NTS). The SIAARTI-Academy-CREM group evaluated the efficacy of its course in comparison to traditional learning programs in terms of acquisition of TS and NTS skills in 327 trainees in anesthesia and intensive care.[54] The Authors found that TS and NTS improved significantly and remained over time in trainees who received the course material and joined the course compared to trainees who received only the course material and trainees who served as controls.

Respiration

In the July issue, a meta-analysis by Longobardo *et al.* focused on the therapies of severe ARDS performed in "non-specialist" intensive care units (ICUs), *i.e.*, those with extracorporeal support facilities.[55] The Authors reviewed all the trials published after the guidelines on ARDS management published in 2019, including the recently published PETAL trial.[56-58] They found that only low tidal volume (TV) ventilation and prone position for more than 12 hours/day improved mortality, while lung recruitment maneuvers (LRM), higher PEEP levels, neuromuscular blockers (NMB) use, corticosteroid therapy, and "liberal" *vs*. "conservative fluid management" did not. In the March issue, a meta-analysis by Lyu *et al.* evaluated NMB's role in treating mild to moderate ARDS.[59] They found that NMBs decreased mortality during ICU stay, but not at 28 and 90 days. Of note, NMB use was not associated with an increased incidence of neuromuscular weakness. The somewhat disappointing conclusions of these two meta-analyses should probably not lead to the abandonment of therapies that have shown some efficacy but no effect on mortality. Instead, further trials are necessary to evaluate more tailored approaches to high PEEP, LRMs, NMBs, corticosteroids, and "conservative" fluid management.

Lung-protective ventilation strategy (LPVS) consists of low TV values, moderate PEEP levels, and frequent LRMs to minimize end-inspiratory alveolar wall stretch and atelectrauma during general anesthesia.[60] According to the available evidence, LPVS may significantly decrease postoperative pulmonary complications.[61] In the June issue, Fu *et al.* nicely showed that LPVS prevented postoperative lung aeration loss (as assessed through lung ultrasound), minimized the unplanned need for oxygen supplementation, and decreased hospital stay in patients who underwent general anesthesia for major abdominal surgery.[62]

Mechanical assistance to spontaneous ventilation (assisted mechanical ventilation) can improve patient comfort, oxygenation, and hemodynamics and favor weaning from mechanical ventilation. However, the quality of mechanical assistance is critically dependent on good patient-ventilation interaction. Patient-ventilator asynchronies may arise for various reasons: inadequate assistance level, too high or too low patient ventilatory drive, and dynamic hyperinflation. In the March issue, Di Nardo *et al.* showed that the detection of asynchronies improves significantly when the diaphragmatic electrical activity-time (EAdi/t) waveform is available on the ventilator screen.[63] In the accompanying editorial, Ventre stressed the detrimental impact of asynchronies on the weaning process.[64]

Finally, the assessment of diaphragmatic thickness (DT) with ultrasound has recently gained popularity among intensivists because it proved to be a good index of diaphragmatic trophism. In the April issue, Corradi *et al.* showed that in 77 patients admitted to the hospital for COVID-19 infection, a worse outcome, *i.e.*, the need for invasive mechanical ventilation (IMV) or patient death, was significantly associated with a thin diaphragm at baseline measurement.[65]

Sepsis and infection

Current literature highlights the importance of early diagnosis and treatment of sepsis to reduce patient mortality and hospital length of stay.[66] On this basis, accurate biological indicators of sepsis are undoubtedly helpful in choosing the correct level of monitoring and treatment. In the October issue, Li *et al.* authored an interesting systematic review on the diagnostic value of mid-regional pro-adrenomedullin (MR-proADM), which directly reflected the levels of adrenomedullin, a vasodilator peptide involved in the regulation of vascular tone and endothelial permeability.[67] The authors included 11 studies and found out that MR-proADM was an excellent biomarker for the diagnosis of sepsis, with high sensitivity and specificity (0.83 and 0.90, respectively) at the best cut-off value of 1-1,5 nmol/L. Leptin has immunomodulatory actions and may play a protective role in sepsis.[68-70] Karampela *et al.* compared plasma leptin in 102 septic patients and 102 healthy controls and found that leptin, its soluble receptor (sOB-R), and the Free Leptin Index (FLI) increased significantly during the first 48h from sepsis onset and decreased one week later.[71] They also found that baseline leptin was an independent predictor of 28-day survival. Finally, estrogen is another hormone involved in the immune response to sepsis.[72, 73] In the May issue, Findikli *et al.* evaluated the prognostic value of the GPER-1 receptor (serum G protein-coupled estrogen receptor-1) in 160 septic patients. They showed that a value >2.58 pg/mL was an independent prognostic factor to predict 28-day mortality with 85.7% sensitivity and 72.1% specificity.[74]

Inflammation, organ dysfunction, and platelet activation affect platelet morphology in critically-ill patients.[75-77] Fogagnolo *et al.* investigated the prognostic values of platelets distribution width (PDW) and mean platelet value (MPV) in critically ill patients.[78] The main finding was that the accuracy of platelet indices to predict 90-day mortality was significant in septic patients but not in non-septic ones. In addition, in the septic group, survivors had lower PDW and MPV than non-survivors, while changes in platelets indices after 24-48 hours were associated with higher mortality.

A severe coagulopathy is frequent in sepsis and should be recognized and treated as soon as possible.[79, 80] In the January issue, Fan *et al.* investigated the association between dynamic changes of red cell distribution width (RDW) and disseminated intravascular coagulopathy in septic patients.[81] They reported that RDW standard deviation (RDW-SD) and increase were independent predictors of 28-day mortality and sepsis-related DIC morbidity.

Renal care

Creatinine clearance calculated from serum creatinine with standard formulas overestimates the glomerular filtration rate and is a late marker of acute kidney injury (AKI).[82] A prospective, observational study carried out by Bolgiaghi *et al.* in 40 mechanically-ventilated ICU patients showed that the response to furosemide stress test (FST) in terms of diuresis and electrolytes secretion, associated with ultrasound assessment of Renal Index is a better tool to evaluate kidney function in critically ill patients.[83] As stated by Ostermann and Lumlertgul, these results add to the growing evidence supporting the use of FST and ultrasound imaging in clinical practice.[84-86] Predicting the future is difficult, especially in the field of AKI, but knowing which patient will develop AKI and which sub-phenotype will be invaluable information for clinicians.[87]

AKI is frequent after brain injury and substantially impacts mortality and neurological outcome.[88] A stimulating paper by Pesonen *et al.* reviewed AKI epidemiology after brain injury and examined the potential mechanisms involved in a causal relationship between the two entities.[89] Hypothetically, cerebral lesions might alter renal function through a neuro-endocrine pathway, combining the activation of sympathetic, renin-angiotensin-aldosterone, and glucocorticoid systems, which all impair renal autoregulation. Cerebral lesions might also lead to a systemic inflammatory response, making the kidney vulnerable to dysfunction. Finally, direct lesions of specific brain areas might also lead to vasomotor changes and AKI.

Approximately 4% of patients admitted to ICUs have severe metabolic imbalance due to AKI and need continuous renal replacement therapy (CRRT), during which anticoagulation is necessary.[90] Nowadays, regional citrate anticoagulation (RCA) is generally preferred to unfractionated heparin mainly because associated with a more extended filter–circuit lifespan, fewer CRRT interruptions, lower bleeding risk, and costs.[91] A Swiss prospective single-center study by Cassina *et al.* compared two CRRT modalities (continuous hemodialysis, RCA-CVVHD, versus continuous venovenous hemofiltration, RCACVVH) in safety, workload, effectiveness, and costs.[92] Their findings show that RCA-CVVHD yields longer filter patency and improves depuration effectiveness but causes metabolic alkalosis and increases nursing interventions and cost. However, specialized ICU nurses can perform and manage RCA-RRT modalities with high competency levels.

Neurocritical care

MA published three interesting reviews on neurological monitoring in critically ill patients. The first, published in May, concerned non-invasive brain oximetry in adult patients without primary brain injury.[93] This review is particularly important because the appearance of neurological dysfunction is widespread in ICU patients, even in the absence of lesions directly affecting the central nervous system, such as intracranial hemorrhages or traumatic lesions.[94] This neurological dysfunction is often difficult to diagnose based on clinical symptoms due to sedation and analgesia. The authors examined several fields of NIRS application in the ICU, such as ECMO, delirium, cardiac arrest, and septic shock. In the corresponding editorial, Simeone and Bruder stressed that NIRS is only part of the neurological evaluation in the critically ill because the pathogenesis of secondary brain damage is complicated, and hypoxia is only one of the possible causes.[95] The second review concerned continuous electroencephalographic monitoring in critically ill patients, which has increased in the last years because recommended by scientific societies.[96-98] Rossetti and Lee reviewed the evidence supporting the use of continuous EEG monitoring and concluded that it is still weak even if the rationale is reasonable. The third review was published in April. Akim *et al.* investigated the concordance between transcranial sonography and cerebral computed tomography to detect brain midline shift in adult patients.[99] They concluded that sonography was reliable and offered the advantage of bedside, real-time evaluation.

Finally, an expert opinion by Taccone *et al.* published in December dealt with refractory intracranial hypertension, focusing on the role of therapeutic hypothermia, barbiturates, and decompressive craniectomy.[100]

Pediatric critical care

In May, MA published the Italian guidelines on managing pediatric severe traumatic brain injury.[101] The document, which updated the previous guidelines, included 25 evidence-based recommendations and five research recommendations.[102] This topic is of the utmost importance since cerebral trauma is the leading cause of death and disability in children. The Authors extensively reviewed the literature and concluded that the quantity and quality of evidence remained low even if clinical output improved in the last years. In the editorial, Piastra and Visconti reiterated the importance of having updated guidelines to standardize treatments.[103] In this sense, it would also be essential to have centers specialized in treating pediatric head trauma throughout the national territory and identify a unitary training course for pediatric intensivists.

In September, MA published an engaging experts' opinion by Metha *et al.* on metabolism and energy delivery in critically ill children. The authors started by examining the effects of the stress response on protein, carbohydrate, and lipid metabolism to propose a pragmatic approach to artificial nutrition in critically ill children.[104]

Finally, intensivists frequently utilize ultrasound to assess the amount of aerated lung in adult patients.[105-107] In critically-ill children, lung ultrasound score (LUS) has been recently used but not yet fully validated. Fochi *et al.* compared the lung ultrasound score with computed tomography (CT) in ten children.[108] They found that the score significantly correlated with lung density and the percentage of hypoaerated lung areas at CT. Moreover, they registered moderate interobserver variability in ultrasound scoring, which is noteworthy because an acknowledged ultrasound limit is the operator dependency.

Ethics

The SARS-CoV-2 virus pandemic has severely tested the health systems worldwide, creating a condition of scarcity of life-saving health resources for the first time since the "Spanish" flu epidemic (1918-1920). In an exciting and in-depth opinion paper about the SIAARTI Guidelines for allocating scarce intensive care resources,[109] Sulmasy pointed out that "in responding to a pandemic, our ethics do not change. We apply our principles and act virtuously in all circumstances, including crisis situations."[110] Thus, it is not that there is one set of ethics for "ordinary" times and another for "extraordinary" times. The drama and complexity of events cannot upset the order of principles and reference values, nor does it justify coming up with new reference points *ad hoc*.

Giannini highlighted that bioethics had offered many different ways to address the challenging topic of scarce resource allocation, each the expression of a particular school of thought and supported by different sets of arguments.[111] In his opinion, the most significant value is the "prognostic criterion," based on which priority is given to those for whom treatment has the greater probability of success.[112] This criterion completes the principle of proportionality of care and allows us to achieve what is, in practical terms, the "possibly good" in the specific and dramatic circumstances confronting us.[113] Moreover, he emphasized that applying criteria for rationing resources is justifiable and ethically acceptable only after all parties involved (at local, regional, and national levels) have made every possible effort to increase the availability of resources (for example, the number of ICUs beds), and after evaluating every possibility of transferring patients to centers with the capacity to care them.

Miscellanea

Delirium is an acute brain disorder affecting 30% to 80% of the critically ill.[114] Liu *et al.* conducted a systematic review and meta-analysis to evaluate dexmedetomidine effectiveness and safety to treat it.[115] They included ten RCTs and five non-RCTs on 1017 patients. The results showed that dexmedetomidine promotes delirium resolution at sedative dosages. However, when compared with other drugs, the occurrence of bradycardia increases. In the accompanying editorial, Sperotto and Amigoni noted that, differently to what was previously reported,[116] this meta-analysis did not confirm dexmedetomidine effectiveness in reducing the length of invasive mechanical ventilation and ICU stay.[117] Postoperative delirium is particularly frequent after liver transplantation, but no comprehensive meta-analysis on risk factors has been conducted in this population.[118] This gap has been filled by Zhou *et al.*, who found that postoperative delirium after liver transplantation was frequent, with 30% incidence and multifactorial etiology.[119] In ICU patients, sleep disorders are risk factors for delirium.[120] Boots *et al.* investigated whether core body temperature rhythm can be a surrogate for the presence of sleep-wake circadian rhythms and nighttime sleep quality in a prospective cohort study on 20 critically ill patients in the weaning stage from mechanical ventilation.[121] Their results did not support that hypothesis. Indeed, the authors found no association between temperature rhythmicity and sleep stages, illness severity scores, and TISS, nor was the relationship with time awake significant. Even if the study was negative, the authors underlined that their results had potential implications for care plans that attempt to normalize sleep patterns and promote the return to circadian homeostasis.

A growing body of evidence shows that stress situations affect healthcare workers employed in emergencies and lead to post-traumatic stress disorder (PTSD).[122] In a prospective study on 137 health care workers (HCWs) in the Emergency Room and Intensive Care Unit of an Italian University Hospital, Carmassi, *et al.* registered that 14.3% of HCWs presented a full symptomatological DSM-5 PTSD and 24.6% a partial PTSD.[123] Full and partial PTSD were associated with severe work and social impairment and positively correlated with burnout and post-traumatic stress symptoms. Those data highlighted the need for a more profound assessment of work-related trauma and post-traumatic stress in HCWs, with great potential for well-being and burnout prevention.

Multiple-organ failure (MOF) is the leading cause of morbidity, mortality, and resource utilization in patients with sepsis, multiple trauma, and severe burns.[124] In a retrospective, single-center study on 13270 ICU patients over ten years (2008-2017), Jansson *et al.* registered MOF incidence and mortality per year. The authors observed a significant reduction of the incidence and mortality of early-onset MOF (first 48 hours), while those of late-onset MOF remained constant over the years. The length of ICU (P=0.024) and hospital (P=0.032) stays also decreased while the duration of mechanical ventilation remained constant.[125] The authors presented other exciting data showing that intensive care improved substantially in those years, but MOF remained a resource-consuming and lethal condition.[126]

In a retrospective monocentric cohort analysis of 72 critically ill COVID-19 patients, Peluso *et al.* described the characteristics of those who developed fever and the effects of temperature control on hemodynamic and respiratory variables.[127] They found that male gender and severe baseline oxygenation impairment were independently associated with fever. Treating fever reduced heart and respiratory rate and improved systemic oxygenation in spontaneously breathing patients.

Finally, Schizodimos *et al.* provided a comprehensive review of the literature published in the last twenty years on venous thromboembolism and thromboprophylaxis in ICU.[128] They outlined that: 1) the use of thromboprophylaxis was mandatory in all critically ill patients; 2) in critically ill patients, the balance between thrombotic and bleeding risk should be assessed daily; 3) thromboprophylaxis should be planned based on the risk of bleeding and mechanical prophylaxis preferred in case of high risk.

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