

## YEAR IN REVIEW

A year in review in *Minerva Anestesiologica* 2022:  
critical care

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## SARS-CoV-2 pandemic

In 2022, as in the previous year, the COVID-19 pandemic has been one of the most covered topics in scientific journals, and MA too has published several articles on this subject.

The COVID-19 pandemic put Italian hospitals and Intensive Care Units (ICUs) under prolonged and severe strain.<sup>1</sup> In a data analysis referred to the two consecutive pandemic waves in 2020, Nocchi *et al.* outlined the crucial role of the biggest hospitals (>300 beds) in terms of involvement in the pandemic response and provided benchmarks to understand ICU hospital response capacity better, highlighting the need for a more flexible approach to surge capacity definition.<sup>2</sup>

The availability of beds in ICUs has been a major problem in the phases of the pandemic's greatest upsurge,<sup>3</sup> and patient age has sometimes intervened in the decision to admit to intensive

care.<sup>4</sup> Kokkoris *et al.* carried out a single-center retrospective cohort study to investigate the prevalence, clinical features, and outcome of patients aged 70 years or more admitted to the COVID ICUs using disease severity as the only criterion for admission.<sup>5</sup> They found that elderly patients represented a considerable proportion (45%) of the ICU population and had the highest mortality. Age, illness severity, Charlson Comorbidity Index, obesity, and chronic pulmonary and renal disease were independent predictors of unfortunate outcomes.

About 14-17% of patients hospitalized for COVID-19 infection develops severe respiratory failure and many need mechanical ventilation.<sup>6,7</sup> In that setting, protective ventilation plays a vital role in minimizing barotrauma. Two articles dealt with this topic. Umbrello *et al.* systematically reviewed the literature to assess the incidence of barotrauma, the clinical characteristics,

and the influence on patient outcomes in mechanically-ventilated COVID-19 patients.<sup>8</sup> They found that barotrauma occurred in 11% of them compared with 2% of non-COVID patients and was associated with higher mortality and longer ICU length of stay. Asar *et al.* proposed a simplified equation to assess the mechanical power of mechanical ventilation in pressure control mode.<sup>9</sup> Such contribution may be precious given the usefulness of that parameter to evaluate the risk of barotrauma.<sup>10</sup>

Noninvasive ventilation has been largely used to treat COVID-19 related acute respiratory failure, particularly outside the ICU.<sup>11</sup> Facial masks and helmets provide advantages and disadvantages, and intensivists often base their choice on patients' preferences. Petrucci *et al.* compared the incidence of upper airways damages and bioptic findings in 30 patients ventilated with a facial mask and thirty ventilated with a helmet.<sup>12</sup> They found the use of facial masks more frequently associated with hyperemia (77% vs. 20%), laryngeal bleeding ulcerations (87% vs. 13%), and vocal cord edema with >50% narrowing of the tracheal lumen. Moreover, mucosal biopsies revealed more pronounced aspects of degenerative necrosis and inflammation in patients ventilated with facial masks. The Authors hypothesized that the observed differences might originate from inadequate air conditioning and higher airway pressure associated with the use of facial masks.

High mortality, around 40%, characterized the first phase of the COVID-19 pandemic.<sup>13, 14</sup> In patients who survived and were discharged from ICUs, postintensive care syndromes were frequently observed. Long COVID was defined as four weeks of persisting symptoms after the acute illness, while post-COVID syndrome and chronic COVID-19 were defined as symptoms lasting more than 12 weeks. These multifaceted clinical pictures confirm that COVID infection is a multisystem disease. An interesting review by Rasulo *et al.* offered readers a brief but exhaustive discussion of this problem that affects a growing number of patients.<sup>15</sup> In the accompanying editorial, Montini and Antonelli underlined the need for future studies to identify patients at risk precociously and include them in personalized recovery programs.<sup>16</sup>

COVID-19 patients are also at risk of thrombotic events.<sup>17, 18</sup> Consolo *et al.* aimed to characterize the platelet activation profile of sixteen COVID-19 patients at the initial stage of the disease using the platelet activation state assay.<sup>19</sup> Platelet activation was significantly higher in COVID-19 patients with respect to controls, suggesting that patient-specific platelet activation profile is a clinical marker to stratify COVID-19 patients at higher risk of poor clinical outcomes, who might benefit from antiplatelet therapy.

### Circulation

Last year, *Minerva Anestesiologica* published several exciting studies on the circulatory function in critically-ill patients. Among them, we point out two concerning fluid responsiveness assessment and two on echocardiography.

Passive leg raising is a simple and risk-free method to assess fluid responsiveness; however, the response to a fluid challenge remains the gold standard. Messina *et al.* investigated whether the concordance between passive leg raising and fluid load challenge was influenced by the methodology used to perform the fluid load challenge.<sup>20</sup> With a secondary analysis of the results of a multicenter study on 85 ICU patients with acute circulatory failure, they found that the two methods presented the best concordance when the effects of the fluid load were assessed ten minutes after the end of the infusion and not later, and an increase larger than 15% of the cardiac index or the stroke volume index was taken as the positivity threshold of the test. Once again, the results of that study pointed out that grey zones existed in the interpretation of diagnostic tests, and the final therapeutic decision should be based on global patient assessment.<sup>21</sup>

Ultrasounds provide some of the targets commonly utilized to assess fluid responsiveness after a fluid load challenge.<sup>22, 23</sup> Among them, the velocity-time integral (VTI) at the aortic annulus is strictly related to the cardiac output but is sometimes difficult to assess due to technical difficulties. Estimating blood velocity in the carotid artery is usually much easier. Pace *et al.* carried out a prospective, observational study to compare the carotid artery velocity-time integral (CVTI)

and the carotid Doppler peak velocity (CDPV) as ultrasound measures for assessing fluid responsiveness in 50 unstable patients under mechanical ventilation.<sup>24</sup> The increase of aortic VTI was utilized to differentiate responders to a fluid load challenge from non-responders. The formers showed significantly higher CVTI and CPDV before and after the fluid load, suggesting that carotid artery Doppler may provide an effective alternative to aortic VTI.

Type-one cardiorenal syndrome (CRS) consists of an acute kidney injury secondary to heart failure.<sup>25</sup> Geneix *et al.* investigated the echocardiographic parameters majorly associated with typing 1 CRS and potentially helpful in monitoring its clinical course.<sup>26</sup> In twenty-seven ICU patients affected by this syndrome, the echocardiographic findings at baseline consisted of right ventricular dysfunction and inferior vena cava dilation. The ratio between right and left ventricles diameters and the inferior vena cava size were the parameters that better mirrored the improvement of renal failure in response to therapy.

In the November issue, an exciting review by Sanfilippo *et al.* focused on left ventricular diastolic dysfunction and its anesthetic and intensive care implications. The Authors compared the left ventricle to a glass, whose shape and size varies with the disease's progress.<sup>27</sup> In the accompanying editorial, Tritapepe recommended that anesthesiologists and intensivists prioritize the evaluation of left ventricular diastolic function over the study of systolic function because they have much fewer therapeutic tools to deal with the former.<sup>28</sup>

### Critical emergency management

In 2020, an increase in the incidence of out-of-hospital (OHCA) and in-hospital (IHCA) cardiac arrests in comparison with the previous year was reported.<sup>29, 30</sup> In the July-August issue, MA published an article by Fontanelli *et al.* in which the Authors reviewed the literature on this topic.<sup>31</sup> The article examined patients' characteristics, treatment, and outcomes. They analyzed the mechanisms by which the COVID-19 pandemic could have influenced the cardiac arrest incidence directly in patients affected by the infec-

tion and indirectly in patients who were negative for the diagnostic tests for COVID-19.

Another exciting review by La Via *et al.* was published in October.<sup>32</sup> While it is pretty reasonable to use high oxygen inspiration fractions to ventilate patients during a cardiac arrest to provide the maximum oxygen delivery to tissues,<sup>33</sup> the results of a few studies suggest that hyperoxia may be detrimental to patients in the postresuscitation phase.<sup>34, 35</sup> The authors systematically reviewed the literature about the effects of hyperoxia and the potential damages in the first 36 hours after a cardiac arrest was successfully treated. The related meta-analysis pointed out that neurological outcomes and survival rates were significantly better in normoxic patients than in hyperoxic ones. Of note, early severe hyperoxia confined to the first six hours did not seem to affect neurologic recovery, possibly due to the shorter exposure to high oxygen concentration.<sup>36</sup>

### Respiration

Invasive mechanical ventilation (IMV) remains the most effective technique in the treatment of hypoxemic respiratory failure but is associated with several complications, including ventilator-associated pneumonia (VAP). Some very effective techniques allow us to avoid or at least delay IMV. High-flow nasal cannulas (HFNO), non-invasive mechanical ventilation (NIV) using a mask or helmet, and continuous positive airway pressure (CPAP) have all proven very effective in improving oxygenation in patients suffering from hypoxemic respiratory failure. However, some indefinite areas remain regarding the choice, timing, and possible association of those techniques.<sup>37, 38</sup> An interesting article by Urbina *et al.* was published in the July-August issue of MA.<sup>39</sup> The authors analyzed the course of 128 patients suffering from hypoxic respiratory failure from COVID-19 infection regarding the need for endotracheal intubation. They compared 88 patients treated with HFNO alone and 40 who alternated between HFNO and NIV. In the second group, the frequency of tracheal intubation, the primary outcome, was lower (38% vs. 60%;  $P=0.04$ ), and the days of IMV ( $P=0.015$ ), while

mortality showed no significant difference. This study had the merit of highlighting the synergism between two respiratory support techniques the alternation of which could make the treatment more effective and tolerable by the patient. Naturally, the limitations of a retrospective study on a heterogeneous population of patients remain, which calls for future controlled studies.<sup>40</sup>

A relatively frequent cause of NIV failure is patients' incapacity to tolerate the facemask pressure or the sense of isolation associated with helmet use. In critical patients presenting acute respiratory failure, delirium has a high incidence ranging up to 80% in those subjected to deep sedation and mechanical ventilation.<sup>41</sup> The onset of delirium certainly aggravates the patient's management difficulties and worsens their prognosis.<sup>42</sup> An interesting Italian multicenter study, published in the October issue, aimed to determine the incidence and timing of delirium in 90 patients treated with NIV for hypoxemic acute respiratory failure.<sup>43</sup> Delirium occurred in 32 patients (36%) after an average ICU stay of 48 hours. The relationship between NIV and delirium was evidenced by the higher incidence of the latter in subjects who used the helmet and tolerated the interface poorly; delirium occurrence was associated with a higher incidence of NIV failure.

Ultrasounds are a fundamental tool for diagnosing respiratory insufficiency, surpassing the traditional chest X-ray in sensitivity for many pathologies.<sup>44</sup> Furthermore, they offer the possibility of monitoring clinical severity through scores that have proved particularly useful during the COVID-19 pandemic.<sup>45</sup> To fully use their diagnostic potential, intensivists should be aware of the limitations of the technique and its potential errors, which have been increasingly codified thanks to interpretative software. In April, MA published an inspiring Experts' Opinion on the precautions needed to avoid ultrasound-related misdiagnosis in ten respiratory diseases.<sup>46</sup> The article, written by six experts in the field, offered the reader who was approaching the use of thoracic ultrasounds and the more advanced ones valuable advice for their clinical activity.

Finally, in the July-August issue, an article by Altinsoy *et al.* reported the data collected in a

randomized study that compared jet ventilation (HFJV), ventilation through a laryngeal mask, and ventilation through an endotracheal tube as respiratory support during percutaneous dilated tracheostomy.<sup>47</sup> The study, carried out on 75 patients treated with invasive mechanical ventilation for over a week, showed a significant shortening of the time required to perform the tracheostomy in the group supported with HFJV. Even more important was the observation that the number of complications and arterial desaturations was significantly lower than in the other two groups.

### Sepsis and infection

Sepsis-associated brain dysfunction (SHABD) is a complication developed by over 70% of septic patients but is sometimes less evident than the involvement of other vital functions.<sup>48</sup> In particular, the clinical symptoms are highly variable and may be affected by the failures of other organs.<sup>49</sup> In the May issue, El Boujdaini *et al.* evaluated the utility of repeated measurement of pupillometry to predict mortality and clinical severity in septic patients.<sup>50</sup> The authors retrospectively analyzed the data collected in the first five days of hospitalization of 75 patients and considered the worst daily value of the pupillary reflex response for each one. The answer was worse in patients who later died and those with higher SOFA scores, even if it was not an independent predictor of mortality at multivariate analysis. The authors concluded that further studies were needed to clarify the problem but that, for the time being, pupillometry was a simple and rapid method that could offer an essential aid in the neurophysiological monitoring of septic patients.<sup>51</sup>

The empiric antibiotic therapy to be administered to the septic patient pending the cultural tests' results should consider two needs. On the one hand, the need to limit as much as possible the use of antibiotics, such as carbapenems, that are potentially effective on bacterial strains resistant to other drugs, to prevent routine use from increasing the spectrum of antibiotic resistance. On the other hand, the risks of administering antibiotic therapy that may be ineffective until

culture results arrive. This problem is significant in the case of insidious pathologies characterized by a high mortality rate, such as secondary peritonitis, in which it is still unclear whether empirical antibiotic therapy efficacy is a prognostic factor of mortality.<sup>52-55</sup> In the May issue, there was an article by Georges *et al.* in which the authors reported their retrospective study on 131 critically-ill patients with secondary peritonitis admitted to a single ICU over six years.<sup>56</sup> In light of the peritoneal fluid culture results, initial empiric antibiotic therapy was ineffective in 35 patients (26.7%), but this finding was not associated with a significant increase in mortality, the need for a new surgery, or the length of stay in the ICU. Conversely, the prescription of carbapenem antibiotics was carried out in 29 patients but was justified in eight. The results of this study supported a more cautious use of some classes of antibiotics as the initial empiric therapy of peritonitis. In the accompanying editorial, Dalfino and Grasso underlined how these results should have also been interpreted based on the quality of the assistance, in particular, the control of the source of the infection, the local bacterial population, and the local degree of antibiotic resistance.<sup>57</sup> In this sense, the relatively low mortality reported by the French authors testifies to an exceptionally high level of care.

During the COVID-19 pandemic, early recognition of the most severe forms was critical. Procalcitonin (PCT) was one of the proposed markers based on the observation that deceased patients had higher PCT serum levels.<sup>58</sup> Zattera *et al.* performed a multicenter retrospective study in 36 Spanish ICUs in which they evaluated whether the value of serum PCT in the first 72 hours of hospitalization was predictive of mortality from COVID-19 infection.<sup>59</sup> The 777 patients included in the study were also divided into immunocompetent, subjected to chronic immunosuppression, and subjected to acute immunosuppression. The study confirmed that patients who died had higher PCT values, but the multivariate analysis did not demonstrate the PCT predictive value for fatal outcomes. The subgroup of patients acutely immunosuppressed by tocilizumab, steroids, or both had significantly lower serum PCT values.

## Neurocritical care

Cerebral imaging techniques are widely used to predict patients' trajectories after an acute brain injury. A large cohort of patients with mild head trauma, contusion, subarachnoid hemorrhage, or subdural hematoma at computerized tomography was associated with an incomplete neurological recovery one year after the injury. In contrast, intraventricular and petechial hemorrhage was related to unfavorable neurological outcomes.<sup>60</sup> More difficult but equally important would be predicting patients' capacity for neurological recovery after a cardiac arrest. In 37 patients admitted to a neurorehabilitation center about one month after a cardiac arrest, Rossato *et al.* correlated the results of positron emission tomography/computerized tomography scan (PET-CT) performed at the admission with the neurological improvement registered at the dismissal.<sup>61</sup> The Authors found that a too-high metabolic activity in the cerebellar Vermis compared with the cerebellar (V/C) hemisphere was an unfavorable marker. In particular, a ratio between the vermis and cerebellar (V/C) hemisphere higher than 1.5 predicted a poor neurological outcome.

Traumatic brain injury is a significant cause of mortality and disability, and since secondary neurological damage may play an essential role in its evolution, intensive care monitoring and treatment are of outstanding importance in managing these patients correctly.<sup>62, 63</sup> An Experts' Opinion by Picetti *et al.* was published in the May issue, in which the Authors revised this topic, focusing mainly on the management of severe TBI patients admitted to a spoke center and needing to be transferred to the hub center, the management of patients with intracranial hypertension/brain herniation awaiting for neurosurgery, and the neuromonitoring-oriented management in the immediate postoperative period.<sup>64</sup>

Finally, in the June issue, an Experts' Opinion by Mahendran *et al.* gave the reader ten tips and pearls to interpret head CT correctly.<sup>65</sup> This subject is undoubtedly helpful to intensivists to interact with radiologists and can help direct management, including when to proceed to more advanced modalities such as MR and conventional angiography.

## Pediatric intensive care

Airway management in children varies significantly in Europe. The choice of techniques and aids depends in part on the choices of the hospital or the individual anesthetist, as well as on the age range of the young patient.<sup>66, 67</sup> Saracoglu *et al.* performed a survey with a 20-question multiple-choice questionnaire sent to the members of the European Airway Management Society via a web-based platform.<sup>68</sup> They included in the analysis only the answers from one representative of the pediatric service of each hospital so that data from 143 hospitals were obtained. Among the aspects investigated were the routine use of direct or video laryngoscopy, straight or curved blades of the laryngoscope, and cuffed or uncuffed tracheal tubes. Of note, a considerable percentage of participants, primarily working in a hospital with no dedicated pediatric anesthesiologists, declared that they had no training in video laryngoscopy or flexible bronchoscopy.

In the last years, the use of cuffed tracheal tubes in children has increased because of the availability of high-volume, low-pressure tube cuffs.<sup>69, 70</sup> The choice between cuffed or uncuffed tubes was the subject of a study by Nacoti *et al.* in infants who underwent cardiac surgery.<sup>71</sup> The Authors compared the incidence of ventilator-associated pneumonia (VAP) and tracheobronchitis (VAT) registered in 121 children operated during a one-year period in which uncuffed tracheal tubes were used, with the incidence in 121 children operated during the following one-year period, in which cuffed tracheal tubes were adopted. The data collected showed that cuffed tubes markedly decreased VAP and VAT incidence.

## Ethics

The internet revolution has shown its effect on online health platforms and has become the most widely used source of health information.<sup>72</sup> The LIDA tool (Minervation Ltd., Oxford, UK) is an appraisal instrument developed to measure the quality of websites by evaluating accessibility, usability, and reliability.<sup>73</sup> Brain death is a crucial notion for contemporary medicine. However, it is a difficult concept for the public to understand,

resulting in a reliance on online resources for clarity. A Turkish cross-sectional study by Guven Kose *et al.* analyzed the quality and readability of the most searched public and medical websites providing information on brain death.<sup>74</sup> According to LIDA, median accessibility, usability, and reliability scores indicated moderate levels for both groups. The most ranked websites for brain death information exceed the National Institutes of Health's health-literacy recommendations. This study also demonstrated that the average readability level of online websites was difficult. We must provide appropriate and comprehensive sources of information about brain death, and website providers must be encouraged to improve the quality of information on this topic.

Communication between patients and staff is a challenging key issue in ICU. In this setting, establishing a patient-caregivers relationship is essential. However, intubated patients cannot speak because the tracheal tube prevents vocalization. Using alternative and augmentative communication tools could improve communication with intubated patients.<sup>75</sup> An interesting multicenter French study that included 151 patients showed that an eye-tracking, technology-based alternative communication device is easy to use for an intubated patient.<sup>76</sup> Although this device needs to be improved, patients, relatives, and caregivers showed high satisfaction utilizing that technology.

## Artificial Intelligence in Anesthesiology and Critical Care Medicine

As in many other fields, Artificial Intelligence (AI) rapidly expands its applications to improve quality and safety in anesthesiology and critical care.<sup>77</sup> The final purpose of this technique is to offer a support system to the physician to manage the increasing quantity of data that are continuously generated by our sophisticated monitoring and laboratory systems. MA dedicated an editorial and four experts' opinions to this topic.

The first article by Bellini *et al.* provided definitions like artificial intelligence, machine learning, deep learning, and telemedicine.<sup>78</sup> The

Authors reminded the reader of the five rights of decision support that machine learning must satisfy, which were providing the right information, to the right person, in the right format, through the right channel, at the right time in the workflow.<sup>79</sup>

In October, Villa and Romagnoli reviewed the topic of registers and biobanks in ICUs and anesthesia.<sup>80</sup> Electronic systems to manage anesthesia and critical care information are recently becoming an integrated component of enterprise-wide electronic medical records (EMRs).<sup>81</sup> The Authors examined the problems in creating and managing those enormous amounts of data and reviewed the multiple possible applications. Biobank research offers an important tool that could approach the value of prospective controlled and randomized studies, overcoming the limitations associated with too strict inclusion and exclusion criteria thanks to the potentially very high number of subjects enrolled.<sup>82</sup>

In November Pirracchio focused on AI application to safety and treatment in anesthesia and intensive care, explaining why complex modern modeling approaches were mainly superior to classical models thought to be applied by the anesthetist with a sheet of paper and a calculator.<sup>83</sup>

Finally, the last Experts' Opinion, by Montomoli *et al.*, dealt with the process of applying AI to ICUs. The three pillars that the authors believed were necessary for effective implementation were "the technological organization with appropriate infrastructure, data quality and quantity acquired by a process fully digitized able to produce reliable data, and last but not least, a digital culture and the right people able to lead the processes and leverage the results".<sup>84</sup>

### Miscellanea

Multiple-organ failure (MOF) is the primary cause of morbidity and mortality among ICU patients.<sup>85</sup> As such, MOF is an essential target for improving patient prognosis. In a retrospective, single-center cohort study, Jansson *et al.* assessed the changes in the incidence and outcomes of MOF over a decade (2008-2017).<sup>86</sup> The incidence and mortality of early-onset MOF de-

creased over time, while those of late-onset (>48 h after ICU admission) remained constant. Late-onset MOF is a resource-intensive and lethal condition and remains a focus for future research to improve the prognosis of MOF.

The proportion of elderly patients admitted to the ICU will increase in the coming decades because of the increased life expectancy in many countries.<sup>87</sup> Considering the need for better prognostic models in ICU patients over 80 years, Poole *et al.* conducted a multicenter cohort study including six Italian ICUs and 1189 patients.<sup>88</sup> Acute organ dysfunction was the leading cause of in-hospital death. However, chronic disease was a more important predictor of long-term outcomes in patients surviving hospital discharge. This study supports the idea of a time-limited trial of ICU for elderly patients to assess the response to treatment for potentially reversible acute organ failure while providing time to complete individual chronic risk stratification for longer-term outcomes.

Recent data suggest a connection between post-traumatic stress disorder (PTSD) and burnout in emergency healthcare workers (HCWs).<sup>89</sup> Carmassi *et al.* evaluated the incidence and impact of PTSD and burnout symptoms on the quality of life in 137 emergency HCWs in an Italian University hospital before the COVID-19 pandemic.<sup>90</sup> Using the DSM-5 PTSD criteria, 24.6% reported partial (meeting 2-3 criteria) and 14.3% reported full PTSD (meeting all criteria). HCWs with full PTSD reported significantly higher burnout, compassion fatigue scores, and global functioning impairment than those without PTSD. These data highlight the need for institutions to develop and implement mental health assessment, support, and treatment services to mitigate the impact of stressful and work-related traumatic events on HCWs.

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