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Improved ICU outcomes in ARDS patients: implication on long-term outcomes

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The primary goal of intensive care medicine is to prevent short-term mortality by developing innovative and efficient interventions. This task has been achieved in many clinical conditions, one of which is ARDS. The ARDS network [1] showed that using lower tidal volume increases survival. More recently, a short course of neuromuscular blocking agents [2] and the use of prone position [3] have been proven to significantly improve survival in ARDS patients with severity criteria. As the practice of intensive care medicine has reached high levels of efficiency, caregivers and researchers have recently turned their efforts towards the assessment of the long-term outcomes of the patient, beyond the ICU discharge. As an example, it was found in ARDS patients surviving the ICU stay that the physical, but not the mental, quality of life decreased in the very long term [4]. In patients with acute kidney injury requiring (AKI) hemodialysis during the hospital stay as compared to patients without AKI, the long-term (up to 10 years) mortality was not different but the dialysis requirement

for end-stage kidney disease was considerably increased [5]. The implications of not dying in the ICU on long-term outcomes are schematically drawn in Fig. 1.

Wang et al. [6] re-analyzed the data of a prospective large cohort of early acute respiratory distress syndrome (ARDS) patients and found that 1-year mortality was clinically significantly higher than short-term mortality, i.e. at hospital discharge, and largely depended on previous comorbidities and age, but not on severity of the acute illness. The fact that mortality increases as time is running and age is going up is a basic tenet in epidemiology; eventually, all patients die. The fact that acute illness severity was not a marker of long-term mortality is not surprising because these indicators were originally developed to predict hospital mortality. Using them for predicting long-term outcome is not validated, and subject for further research. Actually, as Wang et al. split their study into two epochs, the rate of mortality was similar across them, 24 % from ICU admission to hospital discharge and 22 % from hospital discharge to 1-year after ICU admission. The finding that previous comorbidities affect long-term mortality in ARDS is not unexpected but quite new and clinically relevant. Indeed, in the most recent RCT on ARDS [2, 3, 7], patients with preexisting conditions with expected death within 6–12 months were excluded. However, it is known that prior quality of life in patients admitted to ICU is lower than in the general population [8], and that this worst preexisting health status impacts on long-term survival in acute kidney injury [9].

The common decision-making to accept a patient into an ICU precludes taking into account patient's age, comorbidities, and functional status, including ADL. However, at the time a patient is referred to the ICU, the diagnosis of ARDS has usually not yet been made. Furthermore, the assessment of ARDS 12–24 h after the initial diagnosis may be highly relevant to start interventions with important benefits [3] and to define a more

Fig. 1 Patient's trajectory after ICU discharge alive

reliable prognosis [10]. Therefore, should age and comorbidities play a role in end-of-life decisions in patients with ARDS, this could be done after a few days of management and not at the time of ICU admission. Thus, age and comorbidities associated with ARDS cannot easily be used to decide on the eventual futility of an ICU admission. Wang et al. tell us, however, that age and comorbidities influence the long-term prognosis in ARDS. Should this finding then be used to set the level of care during the ICU stay? It may be difficult for a clinician to cope with such a long-term perspective if the patient becomes stabilized and/or some improvement in the acute illness can be anticipated, and the given evidence-based treatment improves short-term survival. In cancer patients, several recent reports have shown that the short-term outcome was improved when early interventions were carried out [11]. Pène et al. [12] have found that, in patients with hematological malignancies admitted with multiple organ failure, the short-term mortality does not depend on previous health status. Azoulay et al. [13] recently made a comprehensive and relevant summary for the policy regarding ICU admission in patients with serious underlying disease. The main message of this review is to not restrict ICU admission to patients with cancer and hematological malignancies, and by contrast to admit those patients as early as possible into the ICU. Whether this policy should also apply to patients with cancer or hematological malignancies and ARDS remains to be established. Treatment of ARDS will not cure the underlying disease and severe co-morbidities. But it is of value to know that the treatment of ARDS is so successful that it allows patients to die—at a later stage—of their underlying or original disease. Adding time to life, even months, can be of high value. In this respect, noninvasive

ventilation is of value in patients with acute respiratory failure, who have declined intubation [14], leading to the concept of palliative noninvasive ventilation [15].

The findings from the study by Wang et al. should encourage better defining and assessing of previous comorbidities in a way that could be relevant for the ICU. The burden of comorbidity is commonly assessed by using the Charlson's approach or global scores like APACHE III or SAPS III. The Charlson index is very important but has been validated over a 10-year follow-up. Such a long-term follow-up may be irrelevant for patients discharged alive after an ICU stay. Furthermore, it has been developed more than a quarter of a century ago. The relative importance of each component should henceforth be updated. Global scores like SAPS III include age, physiology, severity of the acute illness, and comorbidity. Therefore, entering age, comorbidity score, and global score together into a multivariate analysis would promote multicollinearity. Finally, any specific comorbidity can be better described. As an example, COPD can be more precisely defined from the GOLD classification. Chronic kidney disease can be staged according to the baseline glomerular filtration rate. HIV infection can be staged into three clinical categories and three levels of CD4 count.

The study of Wang et al. performed a sensitivity analysis based upon the recent Berlin proposal for ARDS [16]. They found that, to meet the Berlin criteria for ARDS, 14.7 % of ARDS patients had to be excluded, a rate which is close to what we found in a recent prospective survey [17]. ARDS is a syndrome, not a disease. The experts apparently did not incorporate into the Berlin definition the fundamental pathophysiological impairments, such as higher extra-vascular lung water, higher

lung permeability, lung recruitability, and size of the “baby lung”. We are left with ARDS severity staged from the intensity of hypoxemia taking into account the level of PEEP, used as a threshold and not at a fixed value. The results by Wang et al. provide us with an additional puzzle piece to understand the heterogeneity in outcome of ARDS patients. This kind of information is easier to implement than its pathophysiological counterpart. In line with COPD phenotypes [18], phenotyping ARDS taking

into account comorbidities could be a way to better understand and to better manage ARDS patients and to reduce the heterogeneity in this syndrome.

The findings by Wang et al. stress the need of further larger multicenter surveys, specifically addressing the issue of defining comorbidity.

Conflicts of interest No author declares any conflict of interest.

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