Editorial

Critical Care Medicine 2017: Bigger Picture, Better Future

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A lot of new progress has been made in critical care medicine during 2016, including the new definition of Sepsis-3, the fourth revision of the *Surviving Sepsis Guidelines* presenting, increasing using of point-of-care ultrasonography and so on. Furthermore, the critical care fields trend to be more precise, more evidence-based.

In January 2017, the fourth revision of the *Surviving Sepsis Guideline* was presented at the 46th annual Society of Critical Care Medicine meeting and published online jointly in *Critical Care Medicine*[1] and *Intensive Care Medicine*.[2] In which, the guideline redefined the Sepsis-3, presented organ failure assessment (SOFA) score instead of systemic inflammatory response syndrome (SIRS), limited the early goal-directed therapy (EGDT), and emphasized the hemodynamic monitoring (HM).

But with my concern that as the advent of Sepsis-3, it is important to consider whether there is still a place for the SIRS. However, sepsis is a global concern so the definition should be applicable across the spectrum of health-care systems. The complexity of the Sepsis-3 definition with the need for SOFA score determination of organ dysfunction/failure may not be readily available in some low- and medium-income countries, such as China. I think the advantages of a new definition would have to be substantial to warrant a tiered set of definitions dependent on resources.

EGDT is another significant change in the fourth surviving sepsis campaign version which was limited by the ProCESS, Australasia ARISE, and England ProMISe. Recently, Prof. Qiu published a meta-analysis, which demonstrated that a nonsignificant trend toward reduction in the longest all-cause mortality in patients resuscitated with EGDT was noted.[3] However, EGDT significantly reduced Intensive Care Unit (ICU) mortality in severe sepsis and septic shock patients. Hence, the Rivers *et al*.'s[4] work was still very useful as it provided us a construct on how to understand resuscitation, such as start therapy early, correct hypovolemia, and restore perfusion pressure. These concepts are as important today as they ever were. Therefore, we can say that: what we hold, IS the concept, NOT idiographic index, especially the index is hysteretic.

HM in critically ill patients is advocated more frequently in 2016. But still, the rational recommendation in this field was a lack of evidence which depending on the inherent limitations of randomized controlled trials (RCTs) in ICU patients and the HM itself. That may make them inferior to well-designed observational studies for a variety of research questions. The monitoring of cardiac output (CO), for instance, may be crucial in many instances of hemodynamic instability. However, the CO value in and by itself may not necessarily lead to the "correct" therapeutic decision, since the optimal CO cannot always be determined: a high CO may not be high enough, and a low CO does not tell us what to do. In addition, HM may increase the tendency to normalize (or even maximize) the measured physiological variables, although "normaly" of hemodynamic variables does not necessarily mean "adequacy." Anyway, HM supplies invaluable insights about the patient's hemodynamic status and is essential for the correct individual management of critically ill patients. The paucity of formal evidence showing that HM is improving patient outcome may be explained by both the shortcomings of evidence-based medicine and HM itself. The honest and open acknowledgment of these shortcomings should become an integral part of the education of clinicians who take care of critically ill patients.

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The landmark study with acute respiratory distress syndrome (ARDS) patients was in Brazil. Amato *et al*.[5] found that the driving pressure (DP) during the first 36 h was independently associated with high mortality. This was the first time that a possible relationship between high-DP and worse outcomes had been found.

A high-DP results in more "energy trauma" and as such is a key mediator of ventilator-induced lung injury (VILI) in positive pressure ventilation. We are in need of clinical studies that show the best way to limit DPs and RCTs that test whether strategies aiming for low DPs truly affect the outcome of patients with ARDS and maybe even those with uninjured lungs. Now, more and more studies demonstrated that the greater the power, the greater the likelihood of lung injury. Vt, respiratory rate, PEEP, DP, as well as the patients' compliance and airways resistance all had an impact on lung injury. Hence, the prediction of risk of dying is determined by multiple variables in ARDS patients.

When we mention to the VILI, we should not avoid the problem of the ICU acquired respiratory muscle weakness which is associated with prolonged mechanical ventilation and increased risk of ICU and hospital readmission. Future studies should reveal the optimal monitoring techniques and the precise goals of monitoring. In patients who have developed ICU-acquired respiratory muscle weakness, no intervention has been shown to improve outcome. Nevertheless, several studies have demonstrated that inspiratory muscle strength training improves strength. No drug has been approved to improve respiratory muscle function. As respiratory muscle weakness has detrimental effects on patient outcomes, clinically effective treatment strategies are urgently needed.

Extracorporeal membrane oxygenation (ECMO) now is arisen and advanced using in ICU. With a steady rise since 2009 in the number of ECMO-treated critically ill patients and number of centers providing ECMO support, either overseas or in China, there are many aspects should be concerned. The complex changes in drug pharmacokinetics and pharmacodynamics that occur with the addition of an ECMO circuit to the management of a critically ill patient are the most important things which the intensivists should be considered. Although data are limited regarding the optimal regimen and dosing of sedatives and analgesics for critically ill patients receiving ECMO support, with the existing literature suggesting that, in many cases, higher amounts of analgosedation may be necessary to achieve therapeutic levels than would be expected for critically ill patients not receiving ECMO. Certain classes of antimicrobials may likewise be affected by ECMO, potentially leading to subtherapeutic drug concentrations if usual dosing regimens are used. Now, the evidence is building, and according to the Analgesia, Sedation, and Antibiotic Pharmacokinetics (ASAP) during ECMO trial,[6] we believe the future ECMO support in ICU with the medicating patients will be given us more stronger confidence.

Finally, the precision medicine in ICU should be placed on the research agenda. In the ICU, a deluge of data accompanies the tremendous complexity and heterogeneity of critical illness. These conditions make critical care fertile ground for an exploration of precision medicine approaches to research and practice. Change may be incremental rather than wholesale, in which small proof-of-concept studies demonstrate the viability of precision critical care. Till now, the Australia and New Zealand Intensive Care Society (ANZICS) registry contains detailed clinical data on some 1.3 million admissions from more than 140 ICUs. The ANZICS owned the most excellent registry system and perfect database which make their RCTs more convinced. However, it is discouraging that the Chinese ICU registry system is established not so well, and our future direction must be the precision medicine directed therapy which must be based on the big data and perfect registry system. Novel trial designs will be needed to more efficiently enroll patients with narrowly defined syndrome subtypes. Both genomic and nongenomic data must be coopted to derive new insights into critical care endotypes and rapidly identify patients at the bedside. These tasks must be supported by a robust data infrastructure developed by clinicians, researchers, and data scientists.

We harvested a lot in many fields last year, but there are also many challenges waiting us to solve. Still, some large RCT studies are underway which will lead to the important directions to us. Besides, discovering critical illness trajectories using clinical phenotypes with big data and the precision medicine directed therapy are also an astonishing and amazing trend. All of these will provide more convinced and evidenced-based outcome in the future of critical care medicine.

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