

Harmonizing the Septic Shock Terminology: Need of the Hour

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Sepsis, a life-threatening illness, manifests considerable inter-patient variability with respect to the etiology, clinical course, and outcome. Talking of outcome, septic shock entails a peculiarly elevated mortality, accounting for a sizeable global disease burden. Although comprehensive guidelines have been framed and are time and again updated aimed at enabling clinicians to correctly identify and manage this deadly condition, there remain other pertinent concerns to be addressed in this subject. Herein, it is worth reflecting upon the use of vocabularies like refractory septic shock, catecholamine resistance, and high-dose norepinephrine often employed to connote circulatory failure across diverse research scenarios.^{1,2}

In this context, a recent systematic review by Antonucci et al. on the utilization of alternative wordings in septic shock deserves attention.¹ The group highlights that amidst catecholamine resistance underlining an attenuated vascular responsiveness to catecholamines and refractory septic shock characterizing a persistent hyperdynamic state of shock despite adequate fluid resuscitation and high-dose norepinephrine ($\geq 1 \mu\text{g}/\text{kg}/\text{min}$), there exists a discernible lack of well-established consensus definitions and dose thresholds to appropriately define the refractoriness. The inconsistencies were elucidated by the group following the inclusion of 8 studies (3 randomized controlled trials, 3 prospective and 2 retrospective studies) involving a total of 562 septic shock patients, which reported norepinephrine doses ranging from 0.2 to 3.8 $\mu\text{g}/\text{kg}/\text{min}$.¹ The former becomes more concerning when there is an ever-increasing impetus towards "precision" medicine, where implications of the practice variability constitute ardent debates.³

Specific to sepsis, it is imperative to acknowledge catecholamine resistance as a pathophysiological condition wherein the patients eventually culminate into refractory septic shock. The matter further compounds when the approach to defining such a clinical condition is intricately linked with the management approach such as the maximum norepinephrine dose, in this instance. Moreover, independent researchers additionally interrogate the isolated reliance on the vasopressor dose to characterize the aforesaid clinical state, in complex situations featuring the critically ill. Despite significant lacunae in defining refractory septic shock in the adult population, the European Society of Pediatric and Neonatal Intensive Care (ESPNIC) experts defined pediatric refractory septic shock as elevated serum lactate levels and myocardial dysfunction alongside hemodynamic support requirement. This definition was created using the Delphi questionnaire method and subsequently validated in a multicenter retrospective cohort study, by Morin et al.² Notably, the ESPNIC definition used vasoactive inotropic score

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(VIS) instead of absolute nor-epinephrine dosages as an estimate for the hemodynamic support dependency. The relevance of employing standardized scoring systems can also not be undermined in the current times propounding a multimodal strategy to mitigate vasodilation in septic shock, particularly with an escalating role of non-catecholamine agents.^{2,4}

Even from a strict research standpoint, the prevailing heterogeneity in the septic shock terminology is only expected to preclude the fraternity from drawing robust inferences from meta-analyses of the existing literature.⁵ Considering the ongoing interest in sepsis and septic shock across the critical care research, it is time to reassess our guard and simultaneously work concerted towards harmonizing the septic shock terminology which is indeed the need of the hour.

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