EDITORIAL

Ultrasound in Refractory Septic Shock: Have We Pitched and Pictured It Correctly Yet?

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Pediatric septic shock contributes to most deaths in a pediatric intensive care unit (PICU). In high-income countries, mortality due to septic shock is in the range of 10–50% among children; the mortality is four-fold higher in low- and middle-income countries (LMIC).[1] Refractory septic shock (RSS) is described as a specific entity responsible for most deaths in pediatric septic shock.[2] Several recommendations and algorithms are in place to guide the management of sepsis and septic shock in children, well known among them is the Surviving Sepsis Campaign Guidelines, first released in 2004 and the latest update was published in 2020.[3] The objectives of these recommendations are to standardize the care of children with septic shock and thus help in reducing the mortality from septic shock. In settings where intensive care units (ICUs) are available, the guidelines recommend initial fluid resuscitation (up to about 40 mL/kg) over the first hour while monitoring for (a) improvement in markers of cardiac output (CO) and (b) features of fluid overload. Fluid resuscitation is essential to maintain adequate atrial filling pressure so that CO as well as tissue perfusion is maintained. When features of perfusion abnormality persist, the recommendation is to start on vasoactive agent infusion. Either epinephrine or norepinephrine can be used as first-line agents depending on clinician preference and individual patient physiology. Although stronger evidence is lacking to confirm the various components of these recommendations, these guidelines represent the best current clinical practice.

Compliance with the recommendations has proven to decrease mortality in pediatric septic shock patients as highlighted in a study that showed a reduction in mortality from 38 to 8%.[4] Nevertheless, there are barriers that make it difficult to adhere to the presently available guidelines. Firstly, the unique problems that are associated with resource limitations in our settings are not well-represented in these frameworks. These include lack of early detection of septic shock as well as delay in treatment, limited availability of healthcare providers, ignorance about the goals and treatment protocols, and limited access to pediatric intensive care beds. The second, the more generalizable one, is the lack of evidence base and clear guidelines on the management of persistent or refractory shock at advanced stages. It is in this context that the paper published in the current issue of this journal on tiered approach including point-of-care ultrasound (POCUS) in the management of persistent septic shock assumes significance.[5]

The surviving sepsis campaign guidelines do not advocate any particular method of hemodynamic monitoring of children with septic shock; however, there is a suggestion to use advanced hemodynamic monitoring, when available, in addition to bedside clinical variables to guide the management of children

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with septic shock and sepsis-associated organ dysfunction. Serial echocardiographic assessment does find mention in the guidelines, suggesting that the addition of this could recognize myocardial dysfunction and hypovolemia that is not apparent on clinical examination. In fact, at many centers, POCUS and echocardiographic assessment of fluid deficit or adequacy, cardiac contractility, and the adverse effects of excess fluid (fluid overload) is a routine in the management of children with septic shock.

The authors have compiled and presented the data of 10 patients admitted to PICU with persistent or RSS. In the initial management of shock, POCUS was performed within 60 minutes of the first fluid bolus (FB), aiming to rapidly screen for tamponade, cardiac function, and inferior vena cava (IVC) dimensions with respirophasic variations along with lung ultrasound to gauge fluid tolerance and guide FB decisions. Patients who did not respond to therapy based on the unit shock management protocol and this examination were managed with the guidance of POCUS and noninvasive CO monitoring. These assessments were done in a tiered manner, progressing from evaluation of right ventricular function and diastolic dysfunction (tier 1), noninvasive CO monitoring using a bioimpedance device (tier 2) and assessment of venous congestion using venous Doppler (tier 3). The information obtained from the sequential assessment in complement to clinical examination was used to categorize children based on physiological derangements and guide management decisions including fluid titration, vasoactive agent selection, and initiation of diuresis or dialysis. The authors found that their stepwise assessment contributed positively to the management of persistent shock with 8 out of 10 children benefitting to have a favorable outcome.

This case series, with the limitation of small sample size, throws light on two important aspects of pediatric septic shock management. Firstly, it sensitizes the readers about the evolving utility of POCUS on comprehensive hemodynamic assessment at the bedside. Quantification of right ventricular dysfunction, assessment of diastolic dysfunction, and venous excess ultrasound (VExUS) are some of the desirable skills in transthoracic echocardiogram that has the potential to help physicians in caring for the hemodynamically unstable patients.[6]

Recent guidelines are available on performing comprehensive echocardiogram that goes beyond simple hemodynamic assessment in adult patients.[7,8] These are set as training standards or competencies for accreditation; however, the expertise is not widespread currently to gain acceptance as a routine practice at the ICU bedside. In addition to the subjectivity and the required learning curve for these advanced techniques, its performance in PICU can be limited by the small size of the patients and the need for an evidence-based list of normal and abnormal values in children for correct interpretation. Similarly, thoracic bioimpedance devices commonly employed in pediatric postoperative care studies for CO measurement have their share of issues with accuracy and validity in pediatric septic shock.

Secondly and most importantly, the authors brought out the clinical uncertainties in managing children with septic shock and elucidated the competing physiological abnormalities existing in the same patient. In children, fluid-RSS was reported to have heterogeneous hemodynamic alterations. Ceneviva et al. reported that out of 50 children with community-acquired infections, majority (58%) with fluid-refractory/dopamine-resistant shock had low CO and high systemic vascular resistance (SVR) and only 22% had low CO and low SVR state.[9] These hemodynamic states progressed rapidly and changed more frequently during the first 48 hours. In contrast, children with catheter-associated bloodstream infections had hemodynamic changes similar to adults' fluid-refractory warm shock with high cardiac index and low SVR. Thus, the hemodynamic pattern of septic shock may be cause-dependent and quite dynamic. Sepsis-induced myocardial dysfunction has been reported to occur in a high fraction (25–50%) of children with septic shock.[10] Indeed, the recent attempt at a definition of RSS in children describes RSS as a state of circulatory failure due to septic cardiomyopathy with or without vasoplegia. A score based on blood lactate, vasoactive inotrope score, and echocardiographic assessment of cardiac function could discriminate nonsurvivors early; however, there is not enough evidence to construct a management algorithm that works and improves the outcome of such patients with highest risk of death.[11] The present report by Natraj et al. is a welcome concept; however, larger studies, preferably in a randomized design, are required in this specific population of persistent or refractory shock patients to understand the role of advanced hemodynamic assessment tools and quantify the effect of tiered assessment-based management strategies on clinical outcome.

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