Myocardial Dysfunction in Pediatric Septic Shock

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Objective To evaluate the prevalence and significance of myocardial dysfunction in children with septic shock.
Study design Thirty patients with septic shock were evaluated by transthoracic echocardiography within 24 hours of admission to a pediatric critical care unit. Transthoracic echocardiography evaluation included left ventricular (LV) size and function, mitral valve inflow velocities in early and late diastole, mitral valve annular velocities in systole and early and late diastole, and LV myocardial performance index. LV systolic dysfunction was defined as an ejection fraction or shortening fraction *z*-score <−2, and LV diastolic dysfunction was defined as a mitral valve inflow velocity/annular velocity in early diastole ratio *z*-score >2. Secondary outcomes included troponin I concentration, acute kidney injury, and 28-day mechanical ventilation–free duration.
Results Mortality for the 30 patients (mean age, 9.5 ± 7 years) was 7%. The prevalence of LV systolic and/or diastolic dysfunction was 53% (16 of 30). Eleven patients (37%) had systolic dysfunction, 10 (33%) had diastolic dysfunction, and 5 (17%) had both. Systolic and/or diastolic dysfunction was significantly associated with troponin I level (P = .007) and acute kidney injury (P = .02), but not with ventilation-free duration (P = .12). Kaplan-Meier analyses for pediatric critical care unit and hospital length of stay identified no differences between patients with and those without myocardial dysfunction.
Conclusion Myocardial dysfunction occurs frequently in children with septic shock but might not affect hospital length of stay. *(J Pediatr 2014;164:72-7)*.

Septic shock is defined as sepsis with cardiovascular organ dysfunction or sepsis-induced hypotension that persists despite adequate fluid resuscitation.[1] Important components of the clinical progression from systemic inflammation to death in these patients are circulatory instability and myocardial dysfunction. Mortality is higher in adults with septic shock and myocardial dysfunction compared with those without myocardial dysfunction.[2,3] Recent studies of septic shock, mostly in adults, have used echocardiography to evaluate myocardial function in both systole and diastole.[4-6] Unlike adults in septic shock, who are more likely to have vasomotor dysfunction and to require vasopressor therapy, children in septic shock frequently respond to both inotropic and vasodilating agents, suggesting that myocardial dysfunction may play a more significant role in children than in adults.[3]

Quantitative assessment of myocardial function in pediatric septic shock can be quite challenging, given the confounding effects of loading conditions and rapid heart rates on functional indices. Studies in children with septic shock have shown reversible impairment of left ventricular (LV) contractility, an inverse correlation of ejection fraction (EF) and fractional shortening with admission troponin I concentration, and myocardial wall motion abnormalities.[7-9] Although mortality from septic shock has declined significantly since the advent of goal-directed therapy, there remains a paucity of comprehensive data on myocardial function in children, especially during the early phase when acoustic interference from the lungs during mechanical ventilation often precludes accurate echocardiographic quantification of myocardial function.

In this prospective cohort study, we examined the prevalence and pattern of LV systolic and diastolic dysfunction in pediatric septic shock. In addition, we used several measures of clinical status in the pediatric critical care unit (PCCU) to evaluate the association between echocardiographic functional measures and morbidity in children with septic shock, including the Pediatric Logistic Organ Dysfunction (PELOD) score, which has been used previously to quantify multiorgan dysfunction in the PCCU setting.[10]

A	Mitral valve inflow velocity in late diastole	LV	Left ventricular
á	Mitral valve annular velocity in late diastole	MPI	Myocardial performance index
E	Mitral valve inflow velocity in early diastole	PCCU	Pediatric critical care unit
é	Mitral valve annular velocity in early diastole	PELOD	Pediatric Logistic Organ Dysfunction
EF	Ejection fraction	pRIFLE	Pediatric Risk, Injury, Failure, Loss, and End-Stage Kidney Disease
IVA	Mitral valve annular acceleration during isovolumic contraction	ś	Mitral valve annular velocity during systole
		RV	Right ventricular
		TTE	Transthoracic echocardiography

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Methods

This prospective cohort study, approved by the Institutional Review Board of Montefiore Medical Center, was conducted in the PCCU of The Children's Hospital at Montefiore between July 2011 and September 2012. Fluid-refractory septic shock was defined as shock persisting despite ≥60 mL/kg of fluid resuscitation (when appropriate) using the American College of Critical Care Medicine's definition, and standard noninvasive and invasive monitoring and laboratory testing techniques were used in all patients.[1] Patients aged 1 month to 21 years with suspected sepsis and fluid-refractory shock were eligible for study participation on admission to the PCCU after informed consent was obtained. Exclusion criteria included primary conditions associated with myocardial ischemia or cell injury (eg, myocarditis, cardiomyopathy), cardiothoracic surgery or trauma within the previous 14 days, pregnancy, Kawasaki disease, congenital heart disease, and cardiopulmonary resuscitation (cardioversion and defibrillation) within the previous 14 days. All patients who met the inclusion criteria and who did not have any exclusion criteria were enrolled regardless of race, ethnicity, sex, or socioeconomic status.

Overall morbidity in the setting of septic shock was evaluated using the PELOD scores at the time of admission and daily during the entire PCCU stay; 28-day mechanical ventilation–free duration; pediatric Risk, Injury, Failure, Loss, and End-Stage Kidney Disease (pRIFLE) score to assess acute kidney injury[11]; troponin I level; and PCCU and hospital length of stay.

Transthoracic echocardiography (TTE) was performed with the Philips IE33 system (Philips, Andover, Massachusetts) in all eligible patients within 24 hours of admission for septic shock or within 24 hours of development of septic shock during hospitalization. All TTE studies included 2-dimensional and M-mode echocardiography, as well as blood flow and tissue Doppler analysis. Images were stored digitally for offline review and analysis. Evaluation of systolic function included measures of LV size and function as well as tissue Doppler evaluation of medial and lateral mitral valve annular velocities in systole (ś) and mitral valve annular acceleration during isovolumic contraction (IVA). Evaluation of LV diastolic function included mitral valve inflow velocities by blood flow Doppler analysis in early (E) and late (A) diastole and mitral valve annular velocities by tissue Doppler analysis in early (é) and late (á) diastole. The LV myocardial performance index (MPI) for assessing combined systolic and diastolic function was calculated as the sum of isovolumic contraction and relaxation times divided by ejection time as assessed by tissue Doppler evaluation.

LV systolic dysfunction was defined as an EF or shortening fraction z-score <-2. LV diastolic dysfunction was defined as a mitral valve medial E/é z-score or lateral E/é z-score >2. Myocardial dysfunction was considered present when the patient had LV systolic dysfunction, LV diastolic dysfunction, or both. Optimization techniques for imaging as well as morphometric and Doppler evaluation were used as described previously.[12] All Doppler measurements were averaged over 3 consecutive cardiac cycles to account for respiratory variation, especially because most of the patients were supported with mechanical ventilation. One patient treated with high-frequency oscillatory ventilation had poor echocardiographic windows, and TTE was performed on the day after the onset of septic shock when he was changed to conventional mechanical ventilation.

All offline measurements were performed independently by 2 investigators under the supervision of the Medical Director of the Pediatric Echocardiography Laboratory at The Children's Hospital at Montefiore who were blinded to the clinical data and management for each patient. Interobserver variability was assessed as the percent variance of individual variables from the mean of 2 measurements. Statistical analyses were performed using SPSS version 17.0 (SPSS Inc, Chicago, Illinois). Descriptive analysis was applied for demographic and clinical variables, such as age, sex, and source of sepsis. All variables were evaluated for normality and equal variance. To account for the effects of body size and age, all TTE data were expressed as z-scores based on available normal values in children.[13] The median and IQR of normal values from resting children were used for the analysis of IVA.[14] The association between mitral valve ś and MPI in the setting of systolic and diastolic dysfunction was analyzed using the Pearson χ^2 test or Fisher exact test. For data showing a non-Gaussian distribution, comparisons were made using the Mann-Whitney U test, with a significance level of $P = .05$ (2-tailed). Correlations between myocardial dysfunction and secondary outcome measures were calculated using the 2-tailed Spearman coefficient for nonparametric correlations. Multiple binary logistic regression was used to calculate the effect of multiple predictor variables (eg, PELOD, pRIFLE) on the dichotomous outcome of presence or absence of myocardial dysfunction. Kaplan-Meier analysis was used to evaluate the influence of myocardial dysfunction on time-to-event data, including 28-day PCCU stay and 60-day hospital stay.

Results

Thirty patients were eligible for inclusion into the study (**Figure 1**; available at www.jpeds.com). The demographic and clinical characteristics of the study cohort are presented in **Table I**. The mean patient age was 9.5 ± 7 years (range, 1 month to 21 years); 6 patients were aged <1 year and 24 were aged >1 year. Two of the 30 patients died (6.7%).

Positive bacterial cultures from blood, urine, trachea, and/or other soft tissues were documented within the first 72 hours of admission in 22 patients (73%). In these 22 patients with septic shock and a positive bacterial source, methicillin-resistant *Staphylococcus aureus* (n = 6) and *Klebsiella pneumoniae* (n = 5) were the most common organisms detected. Other organisms identified included *Pseudomonas aeruginosa*

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