# **Evaluation of Bedside Echocardiography in Children with Septic Shock in the Pediatric Intensive Care Unit**

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#### ABSTRACT

Objective: We analyzed the echocardiographic findings of children with septic shock who have a high mortality rate in pediatric intensive care units (PICU).

**Methods:** The study was conducted in the 3<sup>rd</sup> step PICU as a prospective observational study. Children aged 1 month-18 years, who were followed up with septic shock and started vasoactive medication, were included in the study. Echocardiography was performed within the first hour at the latest in patients diagnosed with septic shock. Echocardiographic findings were compared in non-surviving and surviving patients.

**Results:** There were 39 (38% female) children diagnosed with septic shock in this study. The median age of the patients was 20 months. The vasoactive medication was started in all patients. There was no statistically significant difference between the patients who non-surviving and those who survived in terms of echocardiographic findings. The ejection fraction (EF) of the patients who died was median 71.5% [minimum (min.) 40, maximum (max.) 79], and the EF of the surviving patients was 72.5 (min. 53, max. 81; p>0.05). The shortening fraction of non-surviving patients was 39.5 (min. 18, max. 46), and 40 (min. 26, max. 48) in surviving patients (p>0.05).

**Conclusion:** The reason why there is no difference between the echocardiographic findings of the patients who non-surviving and survived septic shock, may be due to the functioning of the compensation mechanisms in septic shock or the immediate initiation of vasoactive drug therapy. Prospective, multi-center, more comprehensive studies with a larger number of patients are needed to obtain clearer information on this subject.

Keywords: Septic shock, echocardiography, pediatric intensive care unit, vasoactive drug, ejection fraction, shortening fraction

## **INTRODUCTION**

Sepsis includes a spectrum of diseases resulting from infections with microorganisms such as bacteria, viruses, fungi, or parasites or their toxic products.<sup>1,2</sup> In the International Pediatric Consensus Conference in 2005, definitions related to sepsis and organ failure in children were put forward. Accordingly, sepsis was defined as the presence of two or more criteria for systemic inflammatory response syndrome (SIRS) with suspected or proven infection. SIRS is a common inflammatory response of the host to infection-

related or non-infection-related trauma, chemical, malignancy, autoimmune, or idiopathic conditions.

SIRS criteria are body temperature >38.5 °C or <36 °C as measured by oral, bladder, rectal or central probe, mean heart rate tachycardia > two standard deviations above normal for age or, in children younger than one year, the mean heart rate for age bradycardia <10<sup>th</sup> percentile, mean respiratory rate tachypnea > two standard deviations above normal for age, or the need for non-elective mechanical ventilation, increased or decreased leukocyte count for age, or more than 10 percent of immature

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neutrophils. To define SIRS, one of these criteria must be either an abnormal leukocyte count or abnormal body temperature, and 2 or more of the other criteria are required. Septic shock is the development of cardiovascular dysfunction in the presence of sepsis.<sup>3</sup> Although these definitions are up-to-date at the time of writing of this article, studies on definitions are ongoing.

The host response to infection begins with the recognition and attachment of microbial components by innate immune cells, particularly macrophages. With the balance between pro-inflammatory and anti-inflammatory mediators, the infection is localized, bacterial invasion is prevented, damaged tissues are repaired and healing occurs. If the balance is disturbed in favor of proinflammatory mediators, a generalized inflammatory response occurs and sepsis develops.<sup>4,5</sup>

In the last conference of the Podium (The Pediatric Organ Dysfunction Information Update Mandate) in January 2022, organ dysfunction and criteria in critically ill children were re-evaluated and the current scoring systems were developed.<sup>6</sup> Accordingly, cardiovascular dysfunction in critically sick children was defined by 9 elements, 4 of which were indicative of severe cardiovascular dysfunction. These were defined as cardiopulmonary arrest lasting longer than 5 min (>5 min) or the need for mechanical circulatory support or the presence of at least 2 abnormal findings of findings of tachycardia, hypotension central venous oxygen saturation, vasoactive inotropic score, troponin-I, lactate or left ventricular ejection fraction on echocardiography.<sup>3,7-9</sup> Inclusion of echocardiographic ejection fraction measurement among the criteria for the diagnosis of cardiovascular dysfunction seems important in terms of diagnosis, treatment and follow-up.

Mortality and morbidity of sepsis and septic shock are high worldwide.<sup>10</sup> In a meta-analysis by Menon et al.<sup>11</sup> in children, mortality was reported to be 10.9% in sepsis and 36.8% in septic shock. To reduce mortality and morbidity, sepsis surviving campaign suggested that septic shock should be recognized within 1 h and sepsis within 3 h.<sup>8</sup>

Sepsis causes haemodynamic instability in children due to myocardial dysfunction, capillary leak, and vasodilation. Initially, it may be only one of these findings, and other findings may be added or changed over time. The early recognition and treatment of patients with septic shock is life-saving. Early antibiotic therapy, appropriate haemodynamic correction, and control of the source of infection reduce morbidity and mortality.<sup>3</sup>

Clinical signs of septic shock include fever, toxic appearance, edema (due to increased vascular permeability), respiratory distress, altered consciousness, myocardial dysfunction, and inadequate tissue perfusion. While septic shock was previously categorized as warm or cold, this classification has been sidelined recently, considering that it does not accurately reflect the underlying pathophysiology of sepsis.<sup>6</sup> For this reason, further monitoring such as echocardiography, may be necessary for children who do not respond immediately to the initial treatment to make a correct diagnosis. In previous studies, bedside echocardiography was shown to be a valuable tool in the evaluation of the hemodynamic status of children with septic shock.<sup>12</sup> Echocardiography is also useful in imaging the heart, evaluating the condition of the aorta and pulmonary arteries, and diagnosing congenital and acquired heart diseases. It also allows functional evaluation of the heart.<sup>13</sup> Transthoracic echocardiography is invasive and should be performed early in septic shock. It is a valuable guide for physicians in the diagnosis and management of treatment, the determination of fluid resuscitation, and the evaluation of cardiac function in patients with septic shock.<sup>14</sup>

Echocardiographic measurements are becoming increasingly common in patients with septic shock. In this study, we investigated the role of echocardiography in the diagnosis and treatment of children with septic shock, who were followed up in a pediatric intensive care unit (PICU), by evaluating cardiac functions with echocardiography.

# **MATERIALS AND METHODS**

#### **Study Design and Patients**

This study was conducted in a 3<sup>rd</sup> stage PICU between June 2021 and March 2022. The study was initiated with the approval of the Kahramanmaraş Sütçü İmam University, Faculty of Medicine Non-Invasive Clinical Trials local ethics committee (decision no: 05 session: 2021/08).

Patients aged 1 month to 18 years who were diagnosed with septic shock were included in this study. Consent for this study was obtained from the patients or their families.

The diagnostic sepsis was made when 2 or more of the SIRS criteria were met in the presence of a proven or suspected infection.<sup>3</sup>

The diagnosis of septic shock was diagnosed when sepsis was accompanied by cardiovascular dysfunction. Cardiovascular dysfunction was defined when our patients developed hypotension or the need for a vasoactive drug to maintain blood pressure, or when two of the findings of increased arterial-lactate level, metabolic acidosis, prolonged capillary refill, or oliguria developed.<sup>3,8</sup> Patients who were administered vasoactive drugs were included in this study.

Patients with congenital or acquired heart disease were excluded from this study.

## **Echocardiographic Evaluation**

Echocardiography of septic shock patients admitted to the PICU were performed at the bedside with a two-dimensional, M-mode, and color Doppler echocardiography device. Echocardiographic were examined using an Affiniti 50 echocardiography machine (Philips Medical Systems, Andover, MA, USA) using 4-2 mhz and 8-3 mhz sector probes suitable for the age and weight of patients by the same experienced pediatric cardiologist. Echocardiographic measurements were assessed according to the American Echocardiography Association Pediatric Echocardiography Guideline.<sup>15</sup> Ejection fraction (EF) and shortening fraction (FS)

were calculated using formulations as EF (%)=[left ventricle enddiastolic diameter (LVEDD)<sup>3</sup>-LV end-systolic diameter (LVESD)<sup>3</sup>]/ LVEDD<sup>3</sup>x100 and FS=(LVEDD-LVESD)/LVEDDx100. Images and real-time heart movements were acquired in the short and long axes of the heart. Systemic arterial pressure, mean pulmonary arterial pressure, right ventricular dilatation and hypertrophy, right atrium size, presence of pericardial fluid, left atrium (LA), left ventricle (LV), interventricular septum thickness, LVEDD, LVESD, left ventricular posterior wall thickness, left ventricular mass, EF, FS, intracardiac mass, tumor, and thrombus were evaluated.

In this study, echocardiography was performed within 1 h of when sepsis and septic shock were suspected. Echocardiography was performed by a pediatric cardiologist. When cardiovascular dysfunction developed, vasoactive drug was started without waiting for echocardiography. In other words, vasoactive medication was initiated either before echocardiography or concurrently with echocardiography.

#### **Statistical Analysis**

Statistical analysis were performed using SPSS for Microsoft Windows, version 25.0 (IBM Corp., NY, USA). The data are presented as mean, standard deviation, frequency and percentage distributions as statistics. The conformity of the data to the normal distribution was evaluated with the Kolmogorov-Smirnov test. Normally distributed data are expressed as mean ± standard deviation, non-normally distributed data are expressed as median [minimum (min.)-maximum (max.)]. Student's t-test was used in the analysis of numerical data that met the parametric test assumptions, and the chi-square test was used in the analysis of categorical data. The Mann-Whitney U test was used for the analysis of non-normally distributed data. Test results were considered significant if p<0.05.

## RESULTS

In total, there were 39 (38% female) pediatric patients who developed septic shock and were administered vasoactive drugs. The ages of the pediatric patients ranged from 1 month to 204 months, and their median age was 20 months. In this study, echocardiography was performed within 1 h of when sepsis and septic shock were suspected. Echocardiography was performed by a pediatric cardiologist at the bedside in the PICU. When cardiovascular dysfunction developed in the patients, vasoactive drug was administered without waiting for echocardiography. In other words, patients were given vasoactive drugs either before echocardiography or started simultaneously with echocardiography. The demographic and echocardiographic findings of the children are given in Table 1. There was no statistically significant difference in terms of gender, age, height and weight of the patients who died compared with the survivors. While all the patients who died were intubated and provided with mechanical ventilator support, 38% of the surviving patients were intubated. The EF values of the patients who died were 71.5% (min. 40, max. 79), and the EF values of the surviving patients were 72.5% (min. 53, max. 81) (p>0.05). The FS for the patients who died was 39.5% (min. 18, max. 46), and 40% (min. 26, max. 48) for the surviving patients (p>0.05). There was no statistical difference in terms of other echocardiographic findings (Table 2).

The laboratory findings of the patients are presented in Table 3.

# **DISCUSSION**

In our study, we evaluated the echocardiographic findings of patients who were followed up with the diagnosis of septic shock and who took vasoactive drugs, at the time of diagnosis or within 1 h of diagnosis in our PICU.

Even in the best intensive care units, the most common cause of death is multiple organ failure syndrome.<sup>16</sup> One of the common causes of multi-organ failure is sepsis and septic shock.<sup>3,6</sup> Severe sepsis and septic shock is a serious disease group that accounts for approximately 33% of PICU hospitalizations all over the world, with a mortality rate of between 21% and 41%.<sup>10,11,17</sup> The death rate for male children is higher than for female children.<sup>11</sup> In our study, 30.7% of our patients who were followed up with the diagnosis of septic shock and who were administered vasoactive drugs died, and for our patients who died, the mortality was higher in male children than in female children, which is in line with the literature.

It is not always possible to evaluate myocardial contraction and intravascular volume by clinical examination of patients with sepsis and septic shock. Therefore, echocardiographic

Table 1. Demographic and echocardiographic findings ofchildren diagnosed with septic shock			
	Patients n=39		
Sex (female)(%)	%38		
Age (month)*	20 (1, 204)		
Weight (kg)*	9.45 (2.4, 60)		
Height (cm)*	78 (50, 155)		
IVSd*	5 (3, 9)		
IVSd zs*	0.55 (-1.19, 1.49)		
LVEDD*	27 (18, 40)		
LVEDD zs*	-0.11 (-1.82, 2.64)		
LVPW*	4 (3, 7)		
LVPW zs*	0.55 (-1.3, 1.97)		
LVESD*	18 (11, 26)		
LVESD zs*	0 (-2.2, 3.45)		
EF*	72.5 (40, 81)		
KF*	40 (18, 48)		

\*median (min.-max.)

LVEDD: Left ventricular end-diastolic diameter, LVPW: Left ventricular posterior wall thickness, LVESD: Left ventricular end-systolic diameter, EF: Ejection fraction, zs: Z-score, IVSd: Interventricular septum end-diastolic wall thickness

Table 2. Demographical and echocardiographical findings ofchildren who died and surviving with septic shock				
	Ex n=12	Surviving n=27	р	
Sex (female/ male)	3/9	12/15	0.25*	
Age (month)	28 (4, 123)	13 (1, 204)	0.69+	
Weight (kg)	9.2 (2.4, 34)	9.45 (2.8, 60)	0.77*	
Height (cm)	82 (50, 131)	75.5 (51, 155)	0.98*	
IVSd	5 (4, 7)	5 (3, 9)	0.75 <sup>+</sup>	
IVSd zs	0.61 (-0.46, 1.49)	0.52 (-1.19, 1.31)	0.6+	
LVEDD	27.5 (19, 40)	27 (18, 40)	0.9*	
LVEDD zs	-0.10 (-1.82, 1.6)	-0.10 (-1.66, 2.64)	0.6+	
LVPW	4.5 (4, 6)	4 (3, 7)	0.37*	
LVPW zs	0.91 (-0.57, 1.77)	0.47 (-1.3, 1.97)	0.38 <sup>+</sup>	
LVESD	18.5 (11, 24)	16 (11, 26)	0.56+	
LVESD zs	-0.23 (-2.2, 3.45)	0.035 (-1.77, 2.09)	0.87*	
EF	71.5 (40, 79)	72.5 (53, 81)	0.54+	
FS	39.5 (18, 46)	40 (26, 48)	0.61*	

\*Chi-square test, \*Mann-Whitney U test, median (min.-max.)

LVEDD: Left ventricular end-diastolic diameter, LVPW: Left ventricular posterior wall thickness, LVESD: Left ventricular end-systolic diameter, EF: Ejection fraction, FS: Shortening fraction, zs: Z-score; IVSd: Interventricular septum end-diastolic wall thickness

evaluation may guide the patient's fluid needs and the initiation of other supportive treatments such as vasoactive medication. Regarding this, Ranjit et al.<sup>18</sup>, in their study, suggested that the echocardiographic evaluation of pediatric patients with septic shock resistant to fluid and inotropic therapy provided valuable information to determine the cause of low cardiac output that could not be detected by physical examination, and they reported

that the most common finding in most patients was insufficient fluid volume. Additionally, in another study conducted in a PICU in our country, it was reported that echocardiography in pediatric patients followed up with diagnoses such as acute respiratory distress syndrome, pulmonary edema, cardiogenic shock and septic shock is a guide for initiating fluid, vasoactive and inotropic agents in the management of these patients.<sup>19</sup>

Feng et al.<sup>20</sup>, in a study conducted with adult sepsis patients in intensive care units, showed that echocardiography was associated with a decrease in 28 day mortality. Accordingly, they reported that more fluid, dobutamine, mechanical ventilator support, other inotropic and vasopressor drugs, and sedative drugs were given to patients who underwent echocardiography. They attributed this to the fact that echocardiography provides useful information in patient management.<sup>20</sup> In a study by Rato et al.<sup>21</sup> on pediatric intensive care patients, they mentioned the benefits of bedside echocardiography. 38% of their patients were respiratory tract infection and 21% were septic shock patients. They mentioned that their echocardiography changed the clinical follow-up and treatment plans in most patients, and they emphasized that echocardiography is valuable as a diagnostic and hemodynamic monitoring tool in the PICU<sup>21</sup> In a study by Baranwal et al.<sup>22</sup> in pediatric patients with sepsis in India, they detected myocardial dysfunction via echocardiography in 55% of the patients who experienced septic shock, and systolic dysfunction was found in half of the them and diastolic dysfunction was found in 1/8 of them. No myocardial dysfunction was detected via echocardiography in any sepsis patient who did not develop shock.<sup>22</sup> We present studies reporting that echocardiographic evaluation is beneficial in terms of diagnosis, treatment and follow-up in septic shock patients. In our study, in our pediatric patients with septic shock, the median value of the ejection fraction was 72.5% and the median FS value was 40%, which is within normal limits compared to the general population.13

Table 3. Laboratory findings of children who died and surviving with septic shock				
	Ex n=12	Surviving n=27	р	
WBC (10 <sup>9</sup> /L)	7.37 (0.67, 14.48)	12.99(2.61, 29.41)	0.076 *	
Neutrophil (10º/L)	5.260 (0.0030, 11.59)	7.42 (1.61, 26.11)	0.264	
Lymphocyte (10º/L)	1.230 (0.450, 5.910)	3.625 (0.320, 10.850)	0.123 *	
Hb (g/dL)	10.4 (7.5, 16.4)	10.1 (8, 18.1)	0.77 *	
PLT (10 <sup>9</sup> /L)	163 (5, 480)	251 (41, 683)	0.28	
Prokalsitonin (μg/L)	43.1 (1.85, 325)	2.27 (0.12, 423)	0.01 *	
CRP (mg/L)	81 (2, 446)	23 (1, 425)	0.032 *	
Troponin-I (μg/L)	0.005 (0.005,0.37)	0.01 (0.005,0.548)	0.41	
AST (IU/L)	70 (22, 795)	33 (16, 109)	0.034 +	

WBC: White blood cell, PLT: Platelet, Hb: Hemoglobin, CRP: C-reactive protein, AST: Aspartate transaminase

Additionally, no difference was found in terms of the echocardiographic findings in patients who died and those who survived. Sanfilippo et al.<sup>23</sup> investigated the prognostic value of echocardiographic evaluation in their meta-analysis and review study on pediatric patients with sepsis. Accordingly, they reported that they could not find any relationship between the left ventricular systolic or right ventricular function measurements of echocardiographic parameters in pediatric sepsis and mortality. However, they suggested that there is a relationship between mortality and impaired left ventricular diastolic dysfunction.<sup>23</sup>

Patients with fluid-resistant septic shock may have low, normal, or high cardiac output. Hemodynamics may be variable and may improve with vasoactive drug support. The hemodynamic parameters of systemic vascular resistance are heterogeneous and develop over time in response to inotropic and vasopressor support.<sup>24,25</sup> In our study, there was no significant difference between the echocardiographic findings in any patient who developed septic shock compared to the population, and there was no difference between the echocardiographic findings of those patients who died and those who survived, which may be due to the initiation of vasoactive drug support without waiting for echocardiography. Additionally, the initial hyperdynamic cardiac response to compensate for septic shock may also cause this.

# CONCLUSION

Undoubtedly, echocardiography is a useful non-invasive method in the determination of diagnosis, follow-up and treatment of sepsis and septic shock in PICUs. However, there was no difference between the echocardiographic findings of those patients who died and those who survived in our study. This may be due to the functioning of the compensatory mechanisms in septic shock or the immediate initiation of vasoactive drug therapy. To obtain clearer results on this subject, more comprehensive, multicenter, prospective studies with a larger number of patients are needed.

### Ethics

**Ethics Committee Approval:** The study was initiated with the approval of the Kahramanmaraş Sütçü İmam University, Faculty of Medicine Non-Invasive Clinical Trials local ethics committee (decision no: 05 session: 2021/08).

**Informed Consent:** Consent for this study was obtained from the patients or their families.

## Peer-reviewed:

#### **Authorship Contributions**

Surgical and Medical Practices: S.İ., U.U.G., Concept: U.U.G., Design: U.U.G., Data Collection or Processing: S.İ., U.U.G., Analysis or Interpretation: S.İ., Literature Search: S.İ., U.U.G., Writing: S.İ.

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