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Araştırma / *Research Article*

Risk Factors for Sepsis Following Congenital Heart Surgery

Konjenital Kalp Cerrahisi Sonrası Sepsiste Risk Faktörleri

Yasemin Yavuz
Nurgül Yurtseven
Numan Ali Aydemir
Oktay Korun
Serap Şimşek-Yavuz

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ABSTRACT

Objective: *This study aims to evaluate the incidence and risk factors associated with sepsis in pediatric patients who underwent congenital heart surgery.*
Method: *A total of 289 patients were prospectively enrolled in this study. Patients were divided into two groups according to the Society of Critical Care Medicine (SSCM) diagnostic criteria as Group I including 28 patients who fulfilled the criteria for sepsis and Group II including 261 patients without diagnosis of sepsis. Demographic information, type of operation, complexity, duration of preoperative hospitalization (>5 days) and intensive care unit (ICU) stay, requirement for mechanical ventilation (MV), history of pulmonary hypertension (PHT), and requirement for emergency surgery, total cardiopulmonary bypass (CPB) and aortic cross-clamp (ACC) times. During the postoperative period delayed sternal closure, duration of mechanical ventilation, the need for reintubation, and need for reoperation were also recorded.*
Results: *The incidence of sepsis was 4.74%. The mortality rate in septic patients was 32%. Factors associated with sepsis were younger age, low body weight, duration of preoperative hospitalization and ICU stay, preoperative requirement for MV, palliative and emergency interventions, history of PHT, prolonged MV, reintubation, and reoperation. Multivariate analysis identified reintubation and duration of MV as the major risk factors for sepsis.*
Conclusion: *Serious infectious problems, such as sepsis, are encountered due to inadequate development of immune resistance mechanisms in pediatric patients. Appropriate preoperative preparation of patients for surgery, reducing the length of stay in the hospital and in the ICU, and reducing the need for reintubation by extubating the patients for an optimal period, would reduce the mortality rate due to sepsis.*

Keywords: *sepsis, congenital heart surgery, risk factors*

ÖZ

Amaç: *Bu çalışmada konjenital kalp cerrahisi yapılan pediyatrik hastalarda sepsis sıklığı ve sepsis ile ilişkili risk faktörleri değerlendirildi.*
Yöntem: *Bu çalışmaya 289 hasta prospektif olarak alındı. Hastalar, Society of Critical Care Medicine (SSCM) tanı ölçütlerine göre Grup I'de, sepsis kriterlerini sağlayan 28 hasta ve Grup II'de sepsis tanısı almayan 261 hasta olmak üzere 2 gruba ayrıldı. Demografik bilgiler, ameliyat tipi, kompleksite, preoperatif hastanede yatış süresi (> 5 gün) ve yoğun bakım ünitesinde (YBÜ) kalış, mekanik ventilasyon gereksinimi (MV), pulmoner hipertansiyon öyküsü (PHT) ve acil cerrahi girişim gereksinimi, toplam kardiyopulmoner baypas (KPB) ve aortik kros klemp(AKK) süreleri kaydedildi. Postoperatif dönemde gecikmiş sternum kapanması, mekanik ventilasyon süresi, reentübasyon ve reoperasyon gereksinimi kaydedildi.*
Bulgular: *Sepsis insidansı %4.74 idi. Septik hastalarda mortalite oranı %32 idi. Sepsis ile ilişkili faktörler genç yaş, düşük vücut ağırlığı, preoperatif hastanede yatış süresi ve YBÜ kalış süresi, preoperatif MV, palyatif girişimler, acil cerrahi, PHT öyküsü, uzun süreli MV, reentübasyon ve reoperasyon idi. Çok değişkenli analiz, reintubasyon ve entübasyon süresini sepsis için majör risk faktörü olarak tanımlandı*
Sonuç: *Pediatrik hastalarda sepsis gibi ciddi infeksiyon sorunları, bağışıklık mekanizmalarının yetersiz gelişmesi nedeniyle rastlanmaktadır. Ameliyat için hastaların uygun preoperatif hazırlıkları, hastanede ve YBÜ'de kalma sürelerinin azaltılması ve hastaların optimal bir süre için ekstübasyona tabi tutulmasıyla tekrar entübasyon gereksiniminin azaltılması sepsis nedeniyle ölüm oranını azaltacaktır.*

Anahtar kelimeler: *sepsis, konjenital kardiyak cerrahi, risk faktörleri*

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Nurgül Yurtseven
SBÜ. Dr. Siyami Ersek
Göğüs Kalp Damar Cerrahisi EAH
Anestezi ve Reanimasyon Anabilim Dalı
İstanbul - Türkiye
nurgulyurtseven@hotmail.com
ORCİD: 0000-0001-9991-2859

Y. Yavuz 0000-0003-0506-6474
SBÜ. Koşuyolu EAH
Anestezi ve Reanimasyon Anabilim Dalı
İstanbul - Türkiye

N. A. Aydemir 0000-0002-9276-1979
O. Korun 0000-0002-5776-6993
SBÜ. Dr. Siyami Ersek
Göğüs Kalp Damar Cerrahisi EAH
Pediatrik Kalp Cerrahisi Anabilim Dalı
İstanbul - Türkiye

S. Şimşek-Yavuz 0000-0002-4675-169X
İ. Ü. İstanbul Tıp Fakültesi
Enfeksiyon Hastalıkları Anabilim Dalı
İstanbul - Türkiye

INTRODUCTION

Infections and sepsis are among the most common problems encountered by physicians in the pediatric ICU. While in adults, urinary tract infections and pneumonia are more commonly encountered after cardiac operations, the most common nosocomial infection after pediatric cardiac surgery is sepsis [1]. The development of conjugated vaccines has not substantially decreased the incidence of sepsis since the number patients who undergo surgery before they can develop a complete immune response has increased. This condition may be attributed to several factors including decreased incidence of sepsis, with resultant increases in the survival of premature babies and patients with immune insufficiency, the success rates of complicated surgical interventions, and the use of interventional management modalities. Despite a decrease in the mortality rate of childhood sepsis from 97% to 9% in the last 40 years, sepsis remains among the most important causes for mortality. This may be attributed to the fact that sepsis is a complex syndrome and the lack of well-established diagnostic criteria [2]. The early diagnosis of sepsis is important since delayed initiation of therapy can be fatal. Although the success rate is high when treated in early stages, this might not be possible because of difficulties in definitive diagnosis and high index of suspicion [3,4].

We designed our study to determine the incidence, etiology, main risk factors, and outcome of sepsis for postoperative cardiac pediatric patients admitted to the pediatric cardiac intensive care unit (PCICU).

MATERIALS and METHODS

A total of 289 sequential patients who underwent elective cardiac surgery at the Pediatric Cardiovascular Surgery Department of Siyami Ersek Cardiovascular and Thoracic Surgery Training and Research Hospital were prospectively enrolled in the study. This study was approved by the Research, Planning and Coordination Department of the Ministry of Health. Patients who were diagnosed with sepsis according to the SSCM diagnostic criteria in the postoperative period during the intensive care unit stay formed the Group I (n:28) and the remaining 261 patients formed the Group II.

Variables collected were age, gender, duration of hospitalization (if >5 days) and ICU length of stay, requirement for MV, history of PHT, and emergency status of the surgery, whether or not open-heart surgery had been performed, and if performed, the duration of CPB and ACC times, and also the need for total circulatory arrest (TCA). The surgical risk was calculated for each patient according to the Aristotle Complexity Score. Data regarding delayed sternal closure, MV time, the need for reintubation, or reoperations (other than delayed sternal closure) were recorded postoperatively.

Statistical Analyses

Statistical analysis was performed using the Statistical Package for Social Sciences for Windows version 15.0 (SPSS Inc., Chicago, Illinois, USA). Group comparisons were performed using a Student's t-test and a Mann-Whitney U test for normally and non-normally distributed data, respectively. Comparison of qualitative data was performed using chi-square and Fisher's exact tests. Logistic regression method was used to evaluate risk factors of sepsis. The results obtained were analyzed within a 95% confidence interval and $p<0.05$ was accepted as statistically significant.

RESULTS

The incidence of sepsis was 4.74%. The demographic and preoperative characteristics of the groups are presented in Table I. There was no significant difference between the groups with respect to gender, whereas the mean age and weight of patients in Group I were significantly lower ($p<0.01$). Aristotle risk scores of the groups were similar. In Group I preoperative hospitalization was longer, preoperative requirement for MV and ICU increased and PHT was more frequently seen.

Table I. Comparision of patient demographics and preoperative parameters.

	Group I	Group II	p
Age (Mean±SD), (month)	10.42±12.1	38.31±45.6	0.001**
Weight (Mean±SD), (kg)	4.3±2.6	11.2±8.9	0.001**
Female, n (%)	7 (25.9)	113 (43.3)	ns
Male, n (%)	20 (74.1)	148 (56.7)	
Aristotle score (Mean±SD)	7.81±2.33	7.50±2.05	ns
Preoperative hospitalization for >5 days, n (%)	21 (75.0)	98 (37.5)	0.001**
Preoperative requirement of mechanical ventilation, n (%)	5 (17.9)	7 (2.7)	0.001**
Preoperative requirement of ICU, n (%)	7 (25.0)	25 (9.6)	0.013*
PHT, n (%)	15 (53.6)	61 (23.4)	0.001**

*[a] Student t test; *p<0.05, **p<0.01, ns: Not significant; n: number, SD: standard deviation, PHT: Pulmonary hypertension*

Table 2. Causative micro-organism of sepsis.

Causative microorganism	Number
Klebsiella pneumonia	7
Candida albicans	5
Pseudomonas aeroginosa	3
Serratia marcescens	2
Proteus spp.	2
Enterococcus	2
Candida parapisilosis	2
Coagulase + Staphilacoccus	1
Staphilacoccus Epidermis	1
Acinetobacter baumannii	1
Acinetobacter lwoffii	1
Burkholderia cepacia	1

Causative microorganisms of sepsis are shown in Table 2. Gram- negative microorganisms are more common and the most common microorganism was *Klebsiella pneumonia* (7 of 28).

Intergroup comparisons of other variables are presented in Table 3. The rate of palliative repair was significantly higher in Group I compared to Group II (p<0.05). A significantly higher number of patients in Group I underwent CPB and ACC compared to Group II (p<0.05). CPB and ACC times were not different between two groups (p>0.05). The diagnosis of sepsis was more frequently made in reoperated and

Table 3. Comparision of patient peroperative and postoperative parameters.

	Group I	Group II	p
Palliative; n (%)	14 (50.0)	75 (28.0)	<0.05*,[a]
Emergency surgery, n (%)	4 (14.3)	3 (1.1)	0.001**
Pulmonary band, n (%)	7 (25.0)	6 (2.3)	0.001**
Use of CPB; n (%)	18 (64.3)	215 (82.4)	0.021*,[a]
CPB time, (Mean±SD)	97.16±30.46	97.4±37.8	ns[b]
Use of Aortic CC; n (%)	16 (57.1)	204 (78.2)	0.013*,[a]
CC time, (Mean±SD)	71.75±30.28	69.57±34.42	ns[b]
TCA; n (%)	1 (3.6)	3 (1.1)	ns[a]
Duration of mechanical ventilation, Mean±SD	900.2±792.4	83.8±141.6	0.001**
Open sternum, n (%)	4 (14.3)	18 (6.9)	ns
Reoperation, n (%)	10 (35.7)	25 (9.6)	0.001**
Reintubation, n (%)	24 (85.7%)	23 (8.8)	0.001**

[a] Chi-square test;
[b] Student t test;
**p<0.05; **p<0.01,*
SD: Standard deviation, ns: Not significant, n: number. CPB: Cardiopulmonary bypass,
ACC: Aortic Cross-clamp, TCA: Total circulatory arrest, ICU: Intensive Care Unit, PHT: Pulmonary hypertension,

reintubated patients, in cases under prolonged MV (longer than 96 hours), and in pulmonary artery banding surgery (p<0.05). There was a significant intergroup difference as for mortality rates (p<0.01). The mortality rate in the Group I was 32.1% compared with 6.8 % in Goup II. The variables which were related to sepsis in univariate analysis were included in the multivariate analysis. Accordingly, the logistic regression model was significant (p<0.001), the Negelkerke R-square value was 0.671, and the explication coefficient of the model was 95.8 percent. Only factors correlated with sepsis including duration of MV (odds ratio: 1.01) and the need for reintubation (odds ratio: 11.15) were significantly correlated with the development of sepsis (p<0.01) (Table 4).

Table 4. Evaluation of risk factors of sepsis by the logistic regression method.

	p	**ODDS** (95% CI)
Type of surgical repair	0.898	1.110 (0.2-5.5)
Duration of intubation	0.001**	1.005 (1.0-1.01)
Preoperative hospitalization for >5 days	0.449	1.701 (0.43-6.73)
Preoperative mechanical ventilation	0.800	0.688 (0.03-12.40)
Preoperative ICU stay	0.217	0.153 (0.01-3.0)
Reoperation	0.789	1.232 (0.26-5.70)
The need for re-intubation	0.004**	11.155 (2.20-56.42)
PHT	0.993	1.00 (0.20-4.90)

ICU: Intensive care unit; PHT: Pulmonary hypertension;
ODDS: Odds ratio;
*CI: Confidence interval; **p<0.01*

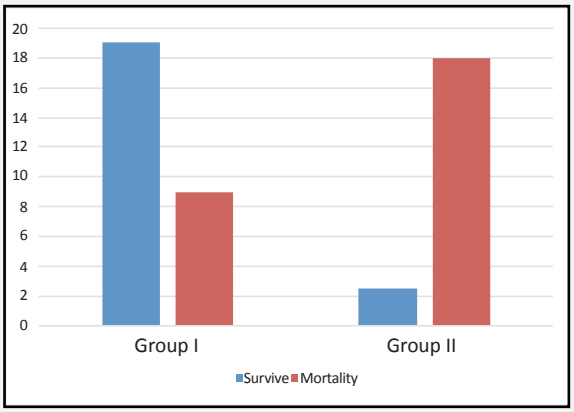
DISCUSSION

Sepsis is the major cause of pediatric ICU admissions and hospital-acquired infections worldwide. Sepsis is encountered in 23% of patients in pediatric ICUs, and ranks fourth among the causes of infant mortality, following congenital anomalies, prematurity, and sudden infant death syndrome [6].

Studies have reported that the incidence of sepsis in pediatric ICUs varies distinctly from 1-8 in every 1000 live births to 2%-30 percent [7]. In the present study, the incidence of sepsis was 4.74 percent. Sepsis is a pathologic state with a very high mortality rate worldwide, which is reported in many studies to range between 5% and 80 percent. Sepsis- related mortality rates in pediatric patients has fallen from nearly 100% in 1960s to 5%-10% in recent years [8]. With the increased number of pediatric ICUs, greater number of newborns are treated and the reasons of mortality in newborns treated in these ICUs are mostly nosocomial infections and sepsis, which occur most commonly due to invasive interventions as well as surgical procedures performed on newborns [9]. The mortality rate is high especially in candida infections [10]. In the present study the mortality rates among septic, and nonseptic patients were 32.1% , and 6.8% , respectively..

Elella et al. [11] reported that Gram-negative organisms were responsible for 67% of the bloodstream infections in the pediatric cardiac ICU, with pseudomonas spp. (28%) and enterobacter spp. (22%) as the main causative organisms. In this study Gram-negative organisms were responsible for 67.8% of the bloodstream infections and the main causative organisms were *Klebsiella pneumoniae* (25%).

Pediatric patients, particularly newborns, are susceptible to infection and thus sepsis due to their inadequately developed immune system and defense mechanisms [12]. Bacterial colonization, and consequently the risk for sepsis, is increased in this group of patients due to immaturity of their immune systems. Additionally the underlying disease conditions, medications and surgical interventions, other invasive routines of the ICU (placement of nasogastric tubes, endotracheal intubation tubes, central and peripheral catheters, and urinary drainage tubes and catheters), and complications associated with surgery, further disrupt the already weakened defense mechanism and increase the susceptibility of patients to infection, and thus sepsis [8]. Wolfler et al. [12] reported that the mortality rate from sepsis was higher among patients with severe concomitant diseases compared with those without. Policies to follow-up critically ill children only in well-equipped



*Chi-square test , **p<0.01*

Figure 1. Comparison of the mortality between groups.

and well-experienced centers may result in decreased mortality rate as observed in this patient group; however, sepsis remains a major problem and a treatment target.

Various scoring systems are still being used in pediatric cardiac surgery. Among these, most widely the Risk Adjustment for Congenital Heart Surgery (RACHS-1) and Aristotle score are being used [13]. In the comparative study conducted by Kang et al. [14] in which both scoring systems were used, no difference was found between the two systems; however, they demonstrated that there was a weak association between postoperative mortality and Aristotle scoring system. In the present study, the Aristotle scoring system was used and no relationship was established between sepsis and Aristotle scoring system. Diagnosis of sepsis was more frequent in patients undergoing a palliative repair compared to total correction. This can be attributed to the increased length of stay in the ICU of these patients. Palliative repair patients generally require more time on MV and in the ICU in general to adapt to their new physiology which consequently increases the risk for infection.

Age has been shown to be an important risk factor for the development of infection in previous studies [15,16]. The natural defense mechanisms of the body are less developed in younger patients. During congenital cardiac surgery, the unavoidable use of devices, such as intra-arterial and central catheters, further disrupts the already weakened immune defense and increases susceptibility to infection. This assumption is supported by the relatively lower mean age of patients who developed sepsis in the present study. In a study conducted by Chang at al. [17] on pediatric cardiac surgery patients, gender was shown to be a risk factor for mortality which was higher among females. Seifert [18] demonstrated that in addition to female gender, mortality rate was also higher in younger patients and those with PHT. On the other hand, Chen [19] emphasized the importance of PHT in patients with congenital heart diseases, and reported that the need for postoperative ventilator support increased, and postoperative complications were more frequent in such patients. In the present study, no significant difference was observed with respect to gender. Presence of PHT was related to sepsis in univariate analysis, yet there was no correlation in multivariate analysis. Similar to the above-mentioned studies, a significant relationship was found between sepsis and prolonged postoperative ventilation. The incidence of sepsis was demonstrated to be higher particularly in pediatric cardiac surgery patients with a prolonged length of preoperative hospital stay, in patients who required pre-operative mechanical ventilation, and preoperative hospitalisation in intensive care [20]. Such patients were colonized with resistant organisms of the ICU, so they were inappropriately prepared for surgery and their already weakened immune systems became more prone to infection through the effect of so many factors. In the present study, in univariate analysis this condition was also supported by the higher incidence of prolonged length of preoperative hospital stay, preoperative need for MV, preoperative ICU stay, and emergency surgery in the sepsis group.

Reintubation is a risk factor, especially for pneumonia [21]. However, the prolonged duration of MV and ICU stay in patients with nosocomial pneumonia, together with the need for invasive monitoring

observed in this group of patients also explains the higher incidence of sepsis. Bakshi at al. found that reintubation increased blood-borne infections by 7-fold [22]. Reintubation and prolonged duration of MV increases the rate of invasive vehicle use, which increases the risk of infection. In our study, reintubation and duration of MV support were found to be factors that increased the risk of sepsis. Valere [23] reported that the risk for infection was higher in patients whose sternums were left open and those who underwent reoperation. Reoperation was only a risk factor in the univariate analysis in the present study. Brown et al. [24] reported that a prolonged duration of ICU stay increased the incidence of sepsis by 50% within 30 days.

Slonim et al. [25] reported that patients who stayed in the ICU for a longer period were of a younger age; and these patients were reported to have a greater need for preoperative MV and had more preoperative problems. They also stated that the postoperative complication score of those patients was higher since they underwent more complex surgical procedures. A prolonged duration of ICU stay was associated with an increase in the incidence of sepsis [19,25].

Sepsis is an important reason for mortality of patients treated in the postoperative cardiac ICU. Based on the findings of this cohort and the current literature, implementation of management policies to optimize the duration of MV and reduce the need for reintubation can be a treatment target to reduce the incidence of sepsis in these patients.

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