

Postoperative Fever and Major Infections after Pediatric Cardiac Surgery

Chodchanok Vijarnsorn MD*, Gornmiga Winijkul MD**,
Duangmanee Laohaprasitiporn MD*, Paweena Chungsomprasong MD*, Prakul Chanthong MD*,
Kritvikrom Durongpisitkul MD*, Jarupim Soonswang MD*, Apichart Nana MD*,
Thaworn Subtaweesin MD***, Somchai Sriyoschati MD***, Julaporn Pooliam MSc****

* Division of Pediatric Cardiology, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Bangkok, Thailand

** Division of Ambulatory and Toxicology, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Bangkok, Thailand

*** Division of Cardio Vascular Thoracic Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Bangkok, Thailand

**** Research and Statistics Consultant, Faculty of Medicine Siriraj Hospital, Bangkok, Thailand

Objective: 1) to identify the current status of major infections and other etiologies of postoperative fever from pediatric cardiac surgery, 2) to determine the risk factors of major infections.

Material and Method: Databases of pediatric cardiac surgery patients in 2005 were retrospectively reviewed. The main outcomes of interest were postoperative fever and its etiologies. Potential predictors were analyzed by comparing patients who developed or did not have infections.

Results: Two hundred thirty patients, 43% ($n = 99$) developed postoperative fever. Major infections occurred in 13.5% ($n = 31$), and postpericardiotomy syndrome (PPS) was seen in 8.7% ($n = 20$) of the patients. The infection rate was 16.9/100 procedures, including pneumonia (29 episodes) and blood stream infection (6 episodes). Risk factors were infancy, prolonged ventilator support > 2 days, hospital length of stay (LOS) > 14 days, intensive care unit (ICU) LOS > 3 days, re-open procedure, and extubation failure rate. Conversely, cyanosis and high complexity operations were not associated. Positive erythrocyte sedimentation rate was related to infections or to PPS (the area under the ROC = 0.72).

Conclusion: Following pediatric cardiac surgery, major infections are still problematic. The risks increase with infancy, prolonged ventilator support, prolonged hospital and ICU LOS, re-open procedure, and extubation failure.

Keywords: Heart defects, Congenital, Postoperative complications, Cross infections, Postpericardiotomy syndrome

J Med Assoc Thai 2012; 95 (6): 761-70

Full text. e-Journal: <http://jmat.mat.or.th>

Fever above 38°C is common in the first few days after cardiovascular thoracic surgery in children⁽¹⁾. Most intermediate postoperative fever results from cytokines, including interleukin (IL)-1, IL-6, IL-10, tumor necrotic factor-alpha (TNF- α), and interferon-gamma (IF- γ), which are released in response to the systemic inflammatory response (SIR) after tissue trauma, transfusion, blood loss, or hypothermia^(2,3). In addition, cardiopulmonary bypass (CPB) can activate the immune system by leukocyte interaction with foreign surfaces of the circuits that aggravate non-specific SIRS in some patients⁽⁴⁾. Conversely, acute and subacute postoperative fever is typically caused

by infections, such as surgical site infection (SSI), blood stream infection (BSI), urinary tract infection (UTI), and pneumonia⁽⁵⁻⁷⁾. Some reports indicate that the infection rate among pediatric patients undergoing cardiac surgery is between 13 and 30.8%^(6,8-13). Furthermore, non-infectious causes of fever, according to some studies, may be due to postpericardiotomy syndrome (PPS), which is associated with autoimmune processes initiated by pericardial cell damage and blood in the pericardial sac⁽¹⁴⁾.

Health care associated infection (HAI) is still reported frequently during the postoperative period and can greatly affect surgical outcomes, for example, by increasing hospital length of stay (LOS) and costs. Prior studies^(9,12,15,16) documented the potential risk factors for HAI, such as younger age, preoperative hospitalization > 2 days, high complexity score, longer hospital LOS, cyanotic heart disease, open chest post-surgery, preoperative ventilator support,

Correspondence to:

Vijarnsorn C, Division of Pediatric Cardiology, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

Phone: 0-2419-7000 ext. 5672, Fax: 0-2948-9371
E-mail: cvijarnsorn@yahoo.com, chodchan@ualberta.ca

preoperative leukocyte band form, presence of genetic syndrome, and postoperative hyperglycemia. Nevertheless, the traditional risk index by wound classification, calculated from the American Society of Anesthesiologist's Physical Status Classification (ASA) with a clean to contaminated operation, is limited for predicting SSI in cardiac surgery. So far, few reports refer to the surveillance of major infections after pediatric cardiac surgical procedures in a developing country.

Siriraj Hospital is a tertiary university hospital and the main referral hospital for congenital cardiac surgery in Thailand. Case volumes of congenital cardiac surgery are 300 to 400 cases/year, with up to 70% for patients in the pediatric age group. The surveillance of mortality and complications in pediatric cardiac surgery patients using the risk adjustment for congenital heart surgery (RACHS-1) classification⁽¹⁷⁾ and the Aristotle Basic Complexity score (ABC score)⁽¹⁸⁾ was performed preliminarily in the center based on database in 2005⁽¹⁹⁾. A high rate of postoperative fever was documented⁽¹⁹⁾. Consequently, the objectives of the present study were to: 1) identify the current status of major infections and other etiologies of postoperative fever in pediatric congenital cardiac surgery patients, and 2) determine the risk factors for serious HAI after cardiac operation, using the preliminary survey data.

Material and Method

Data sources

After receiving approval from the Siriraj Institutional Review Board and Ethics Committee, the authors retrospectively reviewed the medical records of all pediatric patients, aged 0 to 15 years old, who underwent cardiac surgery in Siriraj Hospital between January 1 and December 31, 2005, who had developed postoperative fever with a body temperature above 38°C within 7 days after the congenital cardiac operation. Preterm babies were excluded from the present study, because of the concern for their individual response to environmental temperature. Adolescents, between 15-18 years of age, were excluded because of the institute's unique limitations, which registers them in adult care units in that period. Demographic data, including age, gender, presence of genetic syndrome, diagnosis of congenital heart disease; and intraoperative data, including type of operation, total operative time (time in operating theatre), cardiopulmonary bypass time (CPB time), and aortic cross clamp time (AoX time) were obtained. The risk adjustment for congenital

heart surgery (RACHS-1) method and the Aristotle Basic Complexity (ABC) scoring system was applied to account for case complexity. A retrospective analysis of the variables and a statistic analysis were conducted of the preoperative and intraoperative factors, and the surgical outcomes. Total length of stay was defined as the number of days spent as an inpatient receiving any service, from the day of that admission until the ultimate discharge home or death. In particular, the mortality rate, length of stay in the ICU, duration of use of ventilator, and duration of use of intravenously inotropic drugs were recorded as effects.

Study variables

Definitions of serious infection (BSI, SSI, pneumonia, or UTI) were based on the CDC's guidelines for preventing SSI^(7,20). Onset of fever, peak temperature, test variables; white blood cell (WBC) count, absolute neutrophil count (ANC), levels of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were used to determine the sensitivity and specificity to major infection group. Typically, levels of ESR and CRP were measured after the first three postoperative days, for these cases.

Data analysis

The patients' baseline characteristics and potential confounders were summarized using descriptive statistics that are presented as percentage, mean, and standard deviation. Proportion of infection was calculated and illustrated with other etiologies of postoperative fever and non-infectious afebrile patients. Mortality rate was calculated as a ratio between groups. The LOS and other durations, which were continuous outcomes, were presented as a mean with standard deviation. The association between potential risk factors and the health care-associated infection was assessed by a univariate analysis. Continuous variable were assessed with the Wilcoxon rank sum test and the categorical variables were evaluated by the Fisher's exact test. The multivariate analysis was performed with a step-wise logistic regression, and finally combined for each outcome. The p-value of less than 0.05 was considered statistical significance. The validation of clinical signs and laboratory variables that are expected to help in diagnosing serious infections were calculated as sensitivity, specificity, and area under the receiver operating curve (ROC). The statistical analysis was performed with SPSS 10.0 for Windows (SPSS. Inc., Chicago, IL, USA).

Results

Patients' characteristics

During the 12-month study period, 230 patients met the eligibility criteria. In terms of gender, 126 males and 104 females (ratio of 55:45) were included. The mean age was 4.28 years. Of the patients, 2.6% ($n = 6$) were under 30 days of age and 23.9% ($n = 55$) were between 30 days and 1 year on the day of operation. Definite genetic syndromes were presented in 3.04% of the patients (6 cases of Down syndrome,

1 case of VATER association). Most of the procedures were stratified into RACHS-1 risk categories 1 and 2, and into ABC levels 1-2, which comprised 60.9% and 56.1%, respectively, of the total procedures. Postoperatively, 99 patients (43%) developed fever. Major infections were found in 13.5% ($n = 31$). PPS was diagnosed in 8.7% ($n = 20$), and fever without evidence of major infection or that did not meet the criteria for diagnosis of PPS was found in 20.8% ($n = 48$) of the patients.

Table 1. Characteristics of patients, for the postoperative fever group and the afebrile group

Characteristics	Total (n = 230)	Postoperative fever patients (n = 99)			Afebrile patients (n = 131)
		Major infection (n = 31)	PPS (n = 20)	Without PPS and major infection (n = 48)	
Male:Female	126:104	8:13	11:9	23:25	74:57
Open:close heart surgery	188:42	28:3	20:0	44:4	97:34
Cyanosis:acyanosis	127:103	14:17	9:11	28:20	76:55
Age at surgery (years) (mean \pm SD)	4.28 ± 3.9	3.2 ± 4.2	4.4 ± 3.5	3.7 ± 3.7	4.6 ± 3.9
< 1	61 (26.5)	13	1	16	31
1-15	196 (73.5)	18	19	32	100
Definite genetic syndrome	7 (3.04)	2	0	0	5
RACH-1 level; n (% in group)					
Level 1	22 (9.6)	2	1	3	16
Level 2	118 (51.3)	17	15	24	62
Level 3	81 (35.2)	12	4	17	48
Level 4	8 (3.5)	0	0	4	4
Level 5	1 (0.4)	0	0	0	1
ABC level; n (% in group)					
Level 1	23 (10)	2	1	3	17
Level 2	106 (46.1)	16	10	22	58
Level 3	80 (34.8)	11	6	17	46
Level 4	21 (9.1)	2	3	6	10
Procedural time (min)	221.2	225.2 ± 88.6	212.7 ± 93.2	234.2 ± 98.4	198.7 ± 78.4
Bypass time (min)	84.8	86.5 ± 52.1	95.2 ± 51.5	101.5 ± 61.5	77.5 ± 72.7
Cross clamp time (min)	45.6	54.6 ± 31.2	55.2 ± 36.4	52.7 ± 38.2	31.8 ± 32.2
Hospital LOS (day)	18.2 (2-142)	33.4 ± 30.8	12.4 ± 20.0	15.7 ± 17.1	2.9 ± 7.8
ICU LOS (day)	4.1 (0-87)	33.9 ± 31.4	2.1 ± 1.5	3.1 ± 3.6	15.9 ± 17.4
Ventilator support duration (day)	3.3 (0-87)	11.1 ± 18.9	1.8 ± 1.4	2.4 ± 3.1	1.84 ± 2.7
Open chest procedure; n (% in group)	22 (10.2)	9 (29)	0 (0)	7 (14.5)	9 (6.8)
Failure extubation; n (% in group)	12 (5.6)	5 (16.6)	1 (5.1)	2 (3.9)	4 (3.1)
Discharge mortality; n (% in total cases)	14 (6.1)	4 (1.7)	0 (0)	2 (0.8)	8 (3.4)

Values are expressed as mean \pm SD, and n (%)

The demographic data of the patients is shown in Table 1. The authors categorized the patients into four groups, according to the cause of infection: postoperative major infection (I), PPS (II), patients who developed fever without major infection or PPS (III), and an afebrile group (IV). Patients in groups II, III, and IV were defined as patients who did not have a major infection ($n = 199$). Of the patients who were diagnosed with a major infection, 41% were under one-year of age. In addition, their operations were entirely classified in RACHS-1 levels 1-3. Mean hospital LOS, ICU LOS, and days of ventilator support for patients who had major infections was longer than those for the other three groups. In addition, the other postoperative outcomes, such as the rates of re-open sternotomy and re-intubation rate, and mortality discharge seemed to be highest in the group of patients with major infections.

Postoperative major infections

With regards to the pathogens of infection, 39 events of major infections were reported in 31 patients (Table 2, Fig. 1). Three patients were diagnosed with a serious HAI with more than one episode. The most common site of infection was pneumonia (29 episodes). Twenty-four sputum culture specimens were obtained from the endotracheal tube.

Table 2. Events of major infections and pathogens

Causes of major infections	Number of events (%)
Blood stream infection (BSI)	6 (2.6)
<i>Acinetobacter baumanii</i>	1
<i>Pseudomonas aeruginosa</i>	1
Methicillin resistant <i>Staphylococcus aureus</i> (MRSA)	1
Methicillin sensitive <i>Staphylococcus aureus</i> (MSSA)	1
Gram negative pathogen (unidentified)	1
Candida albican	1
Pneumonia	29 (12.6)
<i>Acinetobacter baumanii</i>	4
Methicillin resistant <i>Staphylococcus aureus</i> (MRSA)	1
Gram negative rod	1
Urinary tract infection	2 (0.8)
<i>Citrobacter</i>	1
Candida albican	1
Deep surgical site infection (MRSA)	1 (0.4)
Superficial surgical site infection	1 (0.4)
Total	39

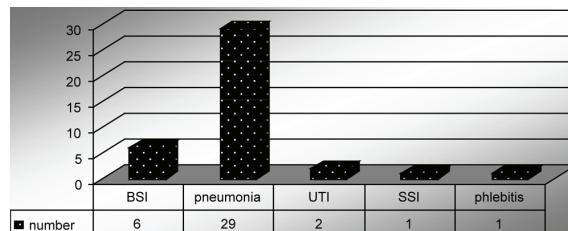


Fig. 1 Sources of postoperative major infections

In addition, BSI with positive hemoculture was found in four patients, revealing *Acinetobacter baumanii*, *Pseudomonas aeruginosa*, gram negative rod, MSSA, MRSA, and *Candida albicans*. Two patients developed bacteremia with more than one episode (Fig. 1). The overall in-hospital major infection rate (NIR) was 16.9 per 100 procedures.

Risk analysis of major infection

The association between the potential risks of major infections by univariate and multivariate models is presented in Table 3. The gender, cyanotic heart disease, higher complexity of congenital heart disease (RACHS-1 levels 4-6 and ABC levels 3-4) revealed almost a negative correlation with major infections (odds ratio = 0.9, 95% CI = 0.4-1.9). In contrast, younger age (< 1 year-old), longer ventilator

support > 2 days, ICU LOS > 3 days, hospital LOS > 14 days, rate of reopen procedure, and rate of postoperative extubation failure showed positive associations with the major infections (significant odds ratio, 95% CI and p-value). The open-heart procedures, presence of genetic syndrome, time of operation, cardiopulmonary bypass, and cross clamp times revealed an odds ratio > 1, though 95% CI and p-value showed no significant predictor of major infections. To clarify the role of variables and interrelations, the multiple regression is shown in Table 3.

In terms of hard outcomes, the mortality discharge was scrutinized (Table 4). The risk mortality of patients with postoperative major infections was 2.6 times greater than the non-infectious group, though

it was not statistically significant (95% CI = 0.9-9.5, p-value 0.08). Some variables, such as hospital LOS > 14 days, ICU LOS > 3 days, use of ventilator support > 2 days, and rate of reintubation could be considered as crucial outcomes. As a result, the relative risks were high for the outcomes in patients who developed postoperative major infections.

To study the patterns of fever and major infections, the authors explored the variables that may enhance the diagnoses (Table 5). With the small number of patients available for comparing the independent risk variables, the ESR levels in patients who had major infection (group I) and PPS (group II) tended to be higher than patients who had not (group III). A statistical difference was demonstrated between PPS

Table 3. Results of multivariable analysis to determine risk factors for major infections

Variable	Crude OR (95% CI)	p-value [#]	Adjusted OR (95% CI)	p-value ^{##}
Male	1.2 (0.5-2.5)	0.841		
Age < 1 year-old	2.3 (1.1-4.9)	0.048*		
Cyanotic heart disease	0.6 (0.3-1.3)	0.239	0.2 (0.1-0.6)	0.002*
Open heart procedure	2.2 (0.6-7.6)	0.307		
Definite genetic syndrome	2.7 (0.5-14.4)	0.240		
Complexity of RACH-1 level ≥ 4	-	0.613		
Complexity of ABC level ≥ 3	0.9 (0.4-1.9)	0.811		
Procedural time >260 min	1.4 (0.6-3.2)	0.534		
CPB time > 85 min	1.6 (0.7-3.5)	0.290		
Cross clamp time > 60 min	1.5 (0.7-3.5)	0.416		
Ventilator support > 2 days	5.1 (2.3-11.3)	<0.001*	4.8 (1.8-12.3)	0.001*
ICU LOS > 3 days	4.1 (1.9-9.2)	0.001*		
Hospital LOS > 14 days	7.9 (3.3-18.8)	<0.001*	8.7 (3.3-23.3)	<0.001*
Re open chest procedure	4.7 (1.8-11.8)	0.002*		
Reintubation	5.3 (1.6-17.8)	0.013*		

[#]Univariate analysis by chi-square test, Fisher's exact test

^{##}Multivariate analysis by forward step-wise logistic regression

* Statistical significance at p-value < 0.05

Table 4. Comparison of relative risks for major infections and worse outcomes

Outcomes	Relative risk (95% CI)	p-value
Mortality	2.6 (0.9-9.5)	0.08
Hospital LOS > 14 days	2.7 (2.0-3.7)	<0.001*
Prolong ventilator support > 2 days	2.8 (1.8-4.4)	<0.001*
ICU LOS > 3 days	2.7 (1.6-4.4)	<0.001*
Required reintubation	4.5 (1.5-13.2)	0.003*

* Statistical significance at p-value < 0.05

and non-serious causes of fever (*p*-value 0.03). To determine the differences between serious diagnosis (group I; major infection and group II; PPS) and non-serious causes of fever (group III), parameters such as WBC count > 15,000 cells/mm³, ANC count > 10,000 cells/mm³, and positive ESR value > 23 mm/hour were analyzed. The authors found that positive ESR value was likely to be useful for enhancing the diagnosis, with the area under the ROC = 0.72, sensitivity = 0.78, and specificity = 0.72 (Table 6).

Discussion

The present study is the first preliminary report focusing on postoperative fever and major infection, following pediatric congenital cardiac surgery, in Thailand. The results demonstrate that postoperative fever, especially those caused by infections, is still a problematic issue. Several independent factors: younger age (< 1 year-old), longer ventilator support (more than 2 days), ICU LOS > 3 days, hospital LOS > 14 days, rate of reopen procedure, and rate of postoperative extubation failure are significant

risks of postoperative major infections. ESR levels may also be useful predictive markers for diagnosing postoperative infections and PPS.

In the present study, the in-hospital major HAI patient ratio after pediatric cardiac surgery was 13.5. The overall in-hospital major infection rate (NIR) was 16.9 per 100 procedures, which is similar to recent findings from Finland (12.9%), Israel (16.9%), and Canada (25.2%)^(6,9,11,21). Typically, NIR varies across institutes due to individual infrastructure care. Grisaruso-Soen et al⁽¹¹⁾ reported a high NIR (38.3%) that was suggested to be due to understaffing (the nurse:patient ratio was 1:2-3), while, in Siriraj Hospital, the ratio was 1:2. Recently, in a large multi-center cohort study from the US, the authors reported a dramatic decrease in major infections rate (to 2.8%)⁽¹²⁾. Nevertheless, in the present study, major infections were defined as septicemia, mediastinitis, and endocarditis. Other infections, such as pneumonia, UTI, and phlebitis, were not included. In contrast, the present study did not exclude these etiologies and the authors found that the majority of postoperative infections were pneumonia.

Table 5. Results of observational events and laboratory tests for a diagnosed cause of postoperative fever

Variables	(I) Febrile with major infection (n = 31)	(II) Febrile with PPS (n = 20)	(III) Febrile without non-PPS and major infection (n = 48)	p-value [#]
Peak temperature (°C) (mean ± SD)	38.9 ± 0.8	38.5 ± 0.7	38.5 ± 0.6	0.105
Onset PO fever (mean ± SD)	2.1 ± 2.3	3.1 ± 2.4	2.2 ± 2.3	0.006*
Duration of fever (day) (mean ± SD)	5.7 ± 8.1	2.6 ± 1.7	3.1 ± 8.2	0.084
WBC (cells/mm ³) (mean ± SD)	15,730.0 ± 5,480.0	13,707.0 ± 4,564.0	14,415.0 ± 5,398.0	0.374
ANC (cells/mm ³) (mean ± SD)	11,250.0 ± 5,317.0	9,197.0 ± 4,004.0	10,384.0 ± 5,015.0	0.361
ESR (mm/hr) (mean ± SD)	40.5 ± 35.3 (n = 11)	44.6 ± 24.2 (n = 17)	23.0 ± 20.0 (n = 10)	0.135**
CRP (mg/L) (mean ± SD)	Positive (n = 1/1) 153	Positive (n = 6/6) 21.5 ± 15.1	NA	

[#] One-Way ANOVA, Kruskal-Wallis test

* Statistical significance between groups II & III (*p*-value = 0.004) by Mann-Whitney U test

** Statistical significance between groups II & III (*p*-value = 0.03) by Mann-Whitney U test

Table 6. Area under the ROC, sensitivity, specificity, and odds ratio of laboratory investigations for major infections or PPS, compared to control group, in postoperative febrile patients

Investigations	Area under the ROC	Sensitivity	Specificity	p-value	OR (95% CI)
WBC > 15,000 cells/mm ³	0.592	0.44	0.63	0.452	1.30 (0.6-3.1)
ANC > 10,000 cells/mm ³	0.607	0.42	0.56	0.975	0.98 (0.4-2.2)
ESR positive (> 23 mm/hr)	0.721	0.78	0.72	0.005*	11.00 (1.7-69)

* Statistical significance at *p*-value < 0.05

Consequently, the present results showed a higher rate of postoperative infection.

Looking at BSI and SSI, several studies reported rates of 6-8.6% and 2.3-5%, respectively^(8-10,12,13,15,16). By comparison, the present survey showed BSI and SSI rates of only 1.7% and 0.8%, respectively. As possible explanations, first, the post-discharge follow-up had not been completed in the authors' cross-sectional study. Second, the eligible patients in the present study had excluded some patients who were immunocompromised hosts (such as preterm babies). Third, as a result of the retrospective review, the catheter-related BSI and ventilator-assisted pneumonia incidence rates were not included in the present report, even though up to 80% of the population retained vascular catheters or urinary catheters post-operation.

In accordance with previous studies in Saudi Arabia, Israel, and Italy^(8,9,11,13), causative organisms in BSI and pneumonia are predominately gram-negative bacteria, whereas the National Nosocomial Infections Surveillance (NNIS) reported that gram-positive bacteria and coagulase-negative staphylococci were the main causative organisms. Although antibiotic prophylaxis is recommended, to prevent wound infection at the surgical site, major infections still persist as postoperative problems. This has led to the widespread use of new, broad spectrum antimicrobial agents, with the resulting development of antimicrobial-resistant pathogens. Patients are thus at risk of experiencing dangerous events like fungal septicemia, prolonged ICU LOS, or death. In the present study, 4/14 mortality cases were diagnosed with major infections after cardiac surgery. Moreover, antibiotic-resistant organisms were documented in the post-mortem data: *Candida* (1), *Acinetobacter baumannii* (1), and *Pseudomonas aeruginosa* (2). The mortality rate in the major infection group was 28.5%, which was higher than that of the non-major infection group (5%). Thus, for patients who developed postoperative major infections, the increased mortality was approximately 2.6 fold higher. The mortality risk was considerably greater for BSI patients, compared to the non-BSI group (RR = 58.2, 95% CI 5.6-610), a finding that is similar to previous reports^(9,13).

The authors' multivariate analysis indicates that younger age (< 1 year-old), longer ventilator support (more than 2 days), ICU LOS > 3 days, hospital LOS > 14 days, rate of reopen procedure, and rate of postoperative extubation failure were mainly associated with the postoperative major infections. Conversely,

the more complex procedures (RACHS level > 3), high complexity in the ABC level (levels 3-4), gender, and cyanotic heart disease were not predictors of major infection. These results are similar to those reported by Grisaru-Soen et al⁽¹¹⁾. Nevertheless, other studies identified different risks, for example: length of preoperative admission > 5 days, total hospital LOS > 10 days, open chest during postoperative phase, cyanotic heart disease, central venous catheter usage > 3 days, younger age, prolonged ICU LOS, high complexity of cardiac procedures, high anesthesiologist physical status classification (ASA score), and other underlying congenital malformations^(8,9,12,21). In a one-year prospective study of BSI⁽¹³⁾, the authors found that risk increased in patients with lower weight, high complexity of cardiac procedures, longer duration central line, ICU LOS, and hospital LOS. In addition, several reports that focused on SSI^(15,16) revealed no association between the multi-severity of illness score, RACHS-1 level complexity, longer duration of postoperative antibiotic usage, and SSI risk. Recently, in a cohort multicenter study of more than 30,000 children undergoing cardiovascular surgery in the US⁽¹²⁾, the authors found an association between younger age, high complexity, previous cardiac operation, preoperative ventilatory support, preoperative LOS, and the presence of genetic syndrome with severe infections (septicemia, mediastinitis, and endocarditis). In contrast, the authors included common major infections (pneumonia, BSI, UTI, and SSI), since Siriraj Hospital is a medium-volume center in a developing country, and wanted to recognize the overall major infectious complications. The authors' main population is also classified by the RACHS-1 at less than level 4, and by the ABC level at less than level 3. Accordingly, high complexity was not deemed to be a risk factor for postoperative major infection in the present study. The preoperative classification (ASA score) was not considered, since these are likely to be higher than class 3, for our congenital cardiac patients.

To determine other etiologies of postoperative fever, all of the patients who were reported to have postoperative fever were investigated. Beyond infections, PPS is a cause that should be considered, since it can lead to serious events such as cardiac tamponade, constrictive pericarditis, and prolonged hospital LOS⁽¹⁴⁾. In the present study, major infections occurred in 13.5% of the patients, while PPS was diagnosed in 8.7%. The proportion of patients with PPS with open-heart surgery was 20/188 (10.6%). Although the sample population was small for the

comparisons, and for validating diagnostic tools, the present study implies that, beyond the first three postoperative days, an elevated level of ESR (> 23 mm/hour) was associated with the presence of major infection or PPS in children undergoing cardiac surgery who developed postoperative fever. Conversely, the pattern of fever, amount of WBC, and ANC were not shown to be useful diagnostically. Despite the lack of some CRP data in the present study, a considerable increase in CRP level in both major infections and in PPS may have clinical application for diagnosis. From anecdotal reports, the mechanism of PPS is postulated to be from an immunologic reaction, to damaged autologous tissue in the pericardial cavity and heart muscle, causing elevated levels of anti-heart antibody, ESR, CRP, and procalcitonin^(2,14). Similarly, infection may aggravate the SIR, and an immunologic reaction would give rise to mediators of the acute-phase response (e.g., IL-6, ESR, CRP, and procalcitonin)^(3,5). In any case, the issue of utility of inflammatory protein testing for diagnosing major infections in postoperative cardiac surgery is contentious. Although high CRP values were more likely in patients with co-morbidity, the plasma concentrations are more dramatically affected by cardiopulmonary bypass and the various kinetics. Some studies claim that serum CRP values are not specific and that they increase in post-cardiopulmonary bypass patients even in the absence of SIRS. High values of procalcitonin (> 2.2 ng/ml) and the activated partial thromboplastin time biphasic waveform are more probable markers for diagnosis of sepsis in pediatric patients following cardiac surgery^(3,4). Moreover, cost-effectiveness should also be considered, especially in developing countries.

Overall, a surveillance program for HAI is one of the most powerful tools for evaluating postoperative infections. The preliminary data in the present study and the analysis will be of fundamental importance for subsequent cohort studies. The present study had several limitations; for instance, the one-year, single-center experience with the retrospective observational survey. The patient population was also rather small, especially after the divisions into subgroups, which reduced the statistical power. An aggregated database over a longer period would improve the subsets for visualizing the trends.

Conclusion

Postoperative fever after cardiac surgery was found in 43% of the pediatric patients. The in-hospital major HAI patient ratio was 13.5%. Predisposing

factors of postoperative infection were: younger age (< 1 year-old), longer ventilator support (more than 2 days), ICU LOS > 3 days, hospital LOS > 14 days, rate of reopen procedure, and rate of postoperative extubation failure. ESR values have a role in the diagnosis of infection or of PPS following the congenital cardiac operation.

Acknowledgements

The authors wish to thank the faculty and staff of Pediatric Cardiology and Cardiovascular Thoracic Surgery, including Punnareuk Lekhakul MD*, Pansak Laksanabunsong MD*, Wanchai Wongkornrat MD*, and the administrators of Pediatric Cardiology and Cardiovascular Thoracic Surgery for their assistance with the database and their suggestions. The authors also thank Glen Wheeler for his proofreading and editing of the manuscript. No conflict of the interest or financial disclosure was present.

* (Division of Cardio Vascular Thoracic Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Bangkok, Thailand).

Abbreviations

ABC score	= Aristotle Basic Complexity score
ANC	= absolute neutrophil count
AoX time	= aortic clamp time
ASA	= Anesthesiologist Physical Status Classification
BSI	= blood stream infection
CBP	= cardiopulmonary bypass
CBP time	= cardiopulmonary bypass time
CI	= confidence interval
CRP	= C-reactive protein
ESR	= erythrocyte sedimentation rate
HAI	= health care associated infection
ICU	= intensive care unit
IF- γ	= interferon-gamma
IL	= interleukin
LOS	= length of stay
MRSA	= Methicillin-resistant <i>Staphylococcus aureus</i>
MSSA	= Methicillin-sensitive <i>Staphylococcus aureus</i>
NIR	= nosocomial infection rate
NNIS	= National Nosocomial Infections Surveillance
OR	= odds ratio
PPS	= postpericardiotomy syndrome
RACHS-1	= risk adjustment for congenital heart surgery-1

ROC	= receiving operated curve
SD	= standard deviation
SIR	= systemic inflammatory response
SSI	= surgical site infection
TNF- α	= tumor necrotic factor-alpha
UTI	= urinary tract infection
WBC	= white blood cell

Potential conflicts of interest

None.

References

- Garibaldi RA, Brodine S, Matsumiya S, Coleman M. Evidence for the non-infectious etiology of early postoperative fever. *Infect Control* 1985; 6: 273-7.
- Cremer J, Martin M, Redl H, Bahrami S, Abraham C, Graeter T, et al. Systemic inflammatory response syndrome after cardiac operations. *Ann Thorac Surg* 1996; 61: 1714-20.
- Seghaye MC. The clinical implications of the systemic inflammatory reaction related to cardiac operations in children. *Cardiol Young* 2003; 13: 228-39.
- Tarnok A, Schneider P. Pediatric cardiac surgery with cardiopulmonary bypass: pathways contributing to transient systemic immune suppression. *Shock* 2001; 16 (Suppl 1): 24-32.
- Pien F, Ho PW, Fergusson DJ. Fever and infection after cardiac operation. *Ann Thorac Surg* 1982; 33: 382-4.
- Pollock EM, Ford-Jones EL, Rebeyka I, Mindorff CM, Bohn DJ, Edmonds JF, et al. Early nosocomial infections in pediatric cardiovascular surgery patients. *Crit Care Med* 1990; 18: 378-84.
- Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. *Am J Infect Control* 1999; 27: 97-134.
- Valera M, Scolfaro C, Cappello N, Gramaglia E, Grassitelli S, Abbate MT, et al. Nosocomial infections in pediatric cardiac surgery, Italy. *Infect Control Hosp Epidemiol* 2001; 22: 771-5.
- Levy I, Ovadia B, Erez E, Rinat S, Ashkenazi S, Birk E, et al. Nosocomial infections after cardiac surgery in infants and children: incidence and risk factors. *J Hosp Infect* 2003; 53: 111-6.
- Tortoriello TA, Friedman JD, McKenzie ED, Fraser CD, Feltes TF, Randall J, et al. Mediastinitis after pediatric cardiac surgery: a 15-year experience at a single institution. *Ann Thorac Surg* 2003; 76: 1655-60.
- Grisaru-Soen G, Paret G, Yahav D, Boyko V, Lerner-Geva L. Nosocomial infections in pediatric cardiovascular surgery patients: a 4-year survey. *Pediatr Crit Care Med* 2009; 10: 202-6.
- Barker GM, O'Brien SM, Welke KF, Jacobs ML, Jacobs JP, Benjamin DK, Jr, et al. Major infection after pediatric cardiac surgery: a risk estimation model. *Ann Thorac Surg* 2010; 89: 843-50.
- Abou ER, Najm HK, Balkhy H, Bullard L, Kabbani MS. Impact of bloodstream infection on the outcome of children undergoing cardiac surgery. *Pediatr Cardiol* 2010; 31: 483-9.
- Engle MA, Zabriskie JB, Senterfit LB, Gay WA Jr, O'Loughlin JE Jr, Ehlers KH. Viral illness and the postpericardiotomy syndrome. A prospective study in children. *Circulation* 1980; 62: 1151-8.
- Allpress AL, Rosenthal GL, Goodrich KM, Lupinetti FM, Zerr DM. Risk factors for surgical site infections after pediatric cardiovascular surgery. *Pediatr Infect Dis J* 2004; 23: 231-4.
- Nategian A, Taylor G, Robinson JL. Risk factors for surgical site infections following open-heart surgery in a Canadian pediatric population. *Am J Infect Control* 2004; 32: 397-401.
- Jenkins KJ, Gauvreau K, Newburger JW, Spray TL, Moller JH, Iezzoni LI. Consensus-based method for risk adjustment for surgery for congenital heart disease. *J Thorac Cardiovasc Surg* 2002; 123: 110-8.
- Lacour-Gayet F, Clarke D, Jacobs J, Comas J, Daebritz S, Daenen W, et al. The Aristotle score: a complexity-adjusted method to evaluate surgical results. *Eur J Cardiothorac Surg* 2004; 25: 911-24.
- Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections 1988. *Z Arztl Fortbild (Jena)* 1991; 85: 818-27.
- Sarvikivi E, Lyytikainen O, Nieminen H, Sairanen H, Saxen H. Nosocomial infections after pediatric cardiac surgery. *Am J Infect Control* 2008; 36: 564-9.

ภาวะไข้และการติดเชื้อรุนแรงหลังการผ่าตัดหัวใจในเด็ก

ชุดชนก วิจารสรณ์, กรมิกา วินิจกุล, ดวงมณี เลาหประสีทธิพร, ปวีณา จึงสมประสงค์, ประคัลก์ จันทร์ทอง,
กฤตย์วิกรม ดุรงค์พิศิยญกุล, จาเรุพิมพ์ สูงสว่าง, อภิชาติ นานา, ดาวร ทรัพย์ทวีสิน, สมชาย ศรียศชาติ,
อุพกรรณ์ พูลເອີ່ມ

วัตถุประสงค์: เพื่อศึกษา 1) ความชุกและสาเหตุของไข้ภายหลังการผ่าตัดโรคหัวใจและหลอดเลือดในเด็ก, 2) ปัจจัยเสี่ยงในการเกิดการติดเชื้อรุนแรงหลังการผ่าตัดหัวใจและหลอดเลือดในเด็ก

วัสดุและวิธีการ: เป็นการศึกษาข้อมูล ไข้ภายหลังการผ่าตัดรักษาโรคหัวใจและหลอดเลือดในช่วงปี พ.ศ. 2548 โดยการทบทวนข้อมูลภาวะไข้และสาเหตุของไข้หลังการผ่าตัดจากแฟ้มประวัติและเวชระเบียนของโรงพยาบาลศิริราช และวิเคราะห์ผลการศึกษาโดยการพรรณนาและวิเคราะห์ปัจจัยเดี่ยงระหว่างกลุ่มที่มีภาวะแทรกซ้อนการติดเชื้อรุนแรงและกลุ่มที่ไม่มีติดเชื้อด้วยเทคนิคการลดด้อยพหุโลจิสติกส์

ผลการศึกษา: ผู้ป่วยเด็กที่ผ่าตัดรักษาโรคหัวใจและหลอดเลือดทั้งหมด 230 ราย พบรความชุกของการมีไข้หลังผ่าตัดร้อยละ 43 (จำนวนผู้ป่วย 99 ราย) พบสาเหตุไข้จากการติดเชื้อรุนแรงเท่ากับร้อยละ 13.5 (จำนวนผู้ป่วย 31 ราย) และเป็นกลุ่มอาการ postpericardiotomy ร้อยละ 8.7 (จำนวนผู้ป่วย 20 ราย) อัตราการติดเชื้อคิดเป็น 16.9 ใน 100 หัตถการ สามารถจำแนกสาเหตุการติดเชื้อตามระบบดังนี้ เป็นการติดเชื้อในปอด 29 ครั้ง การติดเชื้อในกระเพาะเลือด 6 ครั้ง จากการวิเคราะห์ด้วยเทคนิคการลดด้อยพหุโลจิสติกส์พบว่า ปัจจัยที่สัมพันธ์กับความชุกของการติดเชื้อรุนแรงหลังการผ่าตัดคือ อายุน้อยกว่า 1 ปี การใช้เครื่องช่วยหายใจมากกว่า 2 วัน การอยู่ในโรงพยาบาลนานกว่า 14 วัน การอยู่ในห้องอุปกรณานานกว่า 3 วัน การทำผ่าตัดช้า และการตัดห้องท่อช่วยหายใจไม่สำเร็จ ขณะที่ไม่พบความสัมพันธ์ระหว่างภาวะไข้และ การผ่าตัดหัวใจพิการที่มีความซับซ้อน (*high complexity operation*) กับการเกิดการติดเชื้อหลังผ่าตัด นอกจากนี้ยังพบว่า ผลบวกของอัตราการตกลงเม็ดเลือดแดง (*erythrocyte sedimentary rate*) มีความสัมพันธ์กับทั้งการติดเชื้อ และกลุ่มอาการ postpericardiotomy ($ROC = 0.72$)

สรุป: การศึกษานี้พบว่า ภาวะไข้หลังการผ่าตัดหัวใจและหลอดเลือดในเด็กยังคงเป็นปัญหาที่พบบ่อย พบรปัจจัยเสี่ยงต่อการติดเชื้อรุนแรงหลังการผ่าตัดได้แก่ อายุน้อยกว่า 1 ปี การใช้เครื่องช่วยหายใจมากกว่า 2 วัน การอยู่ในโรงพยาบาลนานกว่า 14 วัน การอยู่ในห้องอุปกรณานานกว่า 3 วัน การทำผ่าตัดช้า และการตัดห้องท่อช่วยหายใจไม่สำเร็จ
