Bloodstream infections after median sternotomy at a children's hospital

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Objectives: Postoperative bloodstream infections are a major source of morbidity and increased health care costs. In adults, mediastinitis has been described as a risk factor for bloodstream infections. The objectives of this retrospective cohort study were to determine the incidence and to identify risk factors for postoperative bloodstream infections among children after median sternotomy in an urban tertiary care children's hospital.

Methods: For this study, 192 patients were randomly selected from among all patients undergoing median sternotomy between January 1, 1995, and December 31, 2003.

Results: Ninety-eight (51%) of the 192 eligible patients were male. The median patient age was 5.4 months (interquartile range: 1 day–41.5 years). Bloodstream infections occurred in 12 (6.3%; 95% confidence interval [CI]: 3.3%–10.7%) patients within the first 30 days after median sternotomy. Bloodstream infections developed a median of 11 days (range: 3–29 days) after median sternotomy. Gram-negative bacilli caused 6 (50%) of the 12 bloodstream infections. Specific causes of bloodstream infections included *Pseudomonas aeruginosa* (n = 3), coagulase-negative staphylococci (n = 3), *Pseudomonas fluorescens-putida* (n = 2), *Staphylococcus aureus* (n = 2), *Serratia marcescens* (n = 1), and *Candida albicans* (n = 1). Multivariable analysis revealed that the development of mediastinitis (odds ratio [OR], 28.16; 95% CI, 3.37–235.22) and the requirement for postoperative extracorporeal membrane oxygenation (OR, 12.52; 95% CI, 2.99–52.41) were associated with bloodstream infections after median sternotomy.

Conclusions: Postoperative bloodstream infections occurred in 6.3% of children undergoing median sternotomy. Postoperative mediastinitis and the requirement for extracorporeal membrane oxygenation were risk factors for bloodstream infections after median sternotomy. These findings warrant exploration in a larger, multicenter study.

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Postoperative bloodstream infections (BSIs) are a major source of morbidity and increased health care costs. Few studies report the incidence or describe the epidemiology of BSI in children undergoing cardiac surgery.^{1,2} A high prevalence of concurrent BSI has been described in children with postoperative mediastinitis.^{3,4} We⁵ previously found that mediastinitis caused by *Staphylococcus aureus* (*S. aureus*) had a higher risk of being complicated by BSI than mediastinitis caused by other pathogens. In adults, mediastinitis has been described as a risk factor for postoperative BSI.⁶⁻⁸

The objectives of this study were to determine the incidence of and to identify risk factors for postoperative BSI among children after median sternotomy. We hypothesized that mediastinitis would be associated with an increased risk for BSI after median sternotomy.

Materials and Methods

Study Design and Setting

This was a retrospective cohort study conducted at The Children's Hospital of Philadelphia, an urban tertiary care children's hospital. The institutional review board of the Children's Hospital of Philadelphia approved this study.

Participants. Patients who had a median sternotomy performed between January 1, 1995, and December 31, 2003, were eligible for inclusion.

Study definitions. BSIs were defined by the following criteria: (1) the patient had a recognized pathogen from one or more blood cultures or (2) the patient had signs or symptoms of systemic infection and a common skin contaminant (eg, diphtheroids, *Bacillus* spp, *Propionibacterium* spp, coagulase-negative staphylococci, or micrococci) isolated from two or more blood cultures obtained on separate occasions or from separate sites. We chose this more stringent definition for BSI because the definition for laboratory-confirmed BSIs used by the National Nosocomial Infection Surveillance System overestimates the true incidence of BSI. *Sternal wound infections* were defined according to the guidelines of the Centers for Disease Control and Prevention.⁹ Superficial *surgical site infections* (SSIs) involved only skin or subcutaneous tissues, *deep SSIs* involved deep soft tissues (fascial and muscular layers), and *organ/space SSIs* involved tissues other than the incision. *Mediastinitis* was defined as a wound infection involving the mediastinum or sternum that met the Centers for Disease Control and Prevention criteria for organ/space SSI.⁹ In addition, patients must have had either purulent discharge in the mediastinum requiring surgical debridement or positive mediastinal cultures. *Endocarditis* was classified as definite or possible according to the modified Duke criteria.¹⁰ Postoperative *antibiotic use* was classified as receipt of vancomycin, aminoglycosides (eg, amikacin, gentamicin, tobramycin), third-generation cephalosporins, and antianaerobic agents (eg, clindamycin, carbapenems, beta-lactam/beta-lactamase inhibitor combinations). *Duration of bacteremia* was defined as the time in days between the first positive and the first negative blood culture. During the study period, patients received cefazolin intravenously for perioperative

Abbreviations and Acronyms

BSI = bloodstream infection
CI = confidence interval
OR = odds ratio
SSI = surgical site infection

prophylaxis. Patients with a severe penicillin or cephalosporin allergy received vancomycin.

Study protocol, data collection, and statistical analysis. Patients undergoing median sternotomy during the study period were identified by the cardiac surgical database. Data were collected as part of an ongoing study of risk factors for SSI.^{3,5} The medical records of each potential study patient were reviewed to verify that a median sternotomy procedure had been performed. The following information was collected through review of inpatient medical records: sex, patient age at operation, underlying cardiac defect, associated chromosomal abnormalities, and antibiotic use from hospitalization until operation. *Intraoperative variables* collected included the type of surgical procedure, requirement for deep hypothermic circulatory arrest, and duration of circulatory arrest, cardiopulmonary bypass, and operation. *Postoperative variables* collected included time to onset of BSI after surgery, blood culture results, requirement for extracorporeal membrane oxygenation, duration of hospitalization, duration of intensive care unit stay, requirement for delayed sternal closure or postoperative sternal re-exploration, and the presence of thoracostomy tubes, endotracheal tubes, intracardiac catheters, and central venous catheters. Antibiotic prophylaxis could not be assessed as a potential risk factor because all patients had appropriate timing of antibiotic prophylaxis documented in the medical record.

Data were analyzed by STATA version 9.0 (Stata Corp, College Station, Tex). Bivariable analyses were conducted to determine the association between potential risk factors and BSI. We were primarily interested in the association between mediastinitis and BSI. Categorical variables were compared via either the χ^2 test or the Fisher exact test. An odds ratio (OR) and 95% confidence interval (CI) were calculated to evaluate the strength of any association, as well as the precision of the estimate of the effect. ORs were calculated instead of relative risks in this cohort study to facilitate comparison of unadjusted and adjusted ORs in the multivariable model. Continuous variables were compared with the Wilcoxon rank-sum test. Stratified analyses were then performed to help identify where data were sparse and to elucidate where confounding and effect modification were likely to exist in multivariable analysis. Adjusted ORs were calculated by multiple logistic regression analysis with BSI as the dependent outcome. The model for BSI began with inclusion of the primary risk factor of interest (ie, mediastinitis), which was based on our a priori hypothesis of an association between mediastinitis and BSI. Other variables were considered for inclusion in a multivariable model if they were found to be associated with BSI on bivariable analysis ($P \leq .20$) or if they were involved in confounding on stratified analysis.¹¹ These variables remained in the final multivariable model if their inclusion in the model resulted in a 15% change or

TABLE 1. Characteristics of median sternotomy patients with and without BSIs

Variable	BSI (n = 12)	No BSI (n = 180)	OR (95% CI)	P value
Median age	17.5d (4 d–8.7 y)	164.5d (31.5 d–2.2 y)	—	.521
Male sex	5 (41.7%)	93 (51.7%)	0.67 (0.16–2.56)	.502
Operative class				.365
Two ventricle repair; no arch obstruction	4 (33.3%)	99 (55.0%)	—	
Two ventricle repair; arch obstruction	1 (8.3%)	9 (5.0%)	—	
Single ventricle repair; no arch obstruction	0 (0%)	8 (4.4%)	—	
Single ventricle repair; arch obstruction	3 (25.0%)	43 (23.9%)	—	
Other cardiac surgical procedure	1 (8.3%)	7 (3.9%)	—	
Heart or lung transplantation	2 (16.7%)	11 (6.1%)	—	
No structural heart disease	1 (8.3%)	3 (1.7%)	—	
Prematurity	3 (25.0%)	26 (14.4%)	1.97 (0.32–8.59)	.323
Median birth weight (kg)*	2.8 (2.2–3.4)	3.2 (2.75–3.72)	...	.127
Genetic syndrome or chromosomal abnormality	3 (25.0%)	30 (16.7%)	1.67 (0.27–7.19)	.459

The odds ratio (OR) represents the risk of bloodstream infection (BSI) in the presence of the specified variable. Values are listed as median (interquartile range) or number (percent). CI, Confidence interval. *Calculated if patient was less than 90 days of age.

greater in the effect size of the primary association of interest (ie, the association between mediastinitis and BSI); otherwise, these variables were excluded from the final multivariable model.¹² For variables with a prevalence of 30% or more, the inclusion of 192 patients would allow us to detect an OR of 2.5 or greater with 80% statistical power (α -level = .05) if BSI occurred in more than 6% of the study patients. Subjects were randomly selected for inclusion from among all 4853 children undergoing median sternotomy during the study period. Each of these patients was assigned a unique study number on the basis of the medical record number and selected through the use of a computer-generated random-number table.

Results

A total of 220 patients were considered for study inclusion. Four (1.8%) of the 220 patients were excluded because a thoracotomy rather than median sternotomy had been performed. Complete medical records were available for 192 (89%) of the 216 eligible subjects. Ninety-eight (51%) of the 192 patients were male. The racial distribution included patients who were classified as African American (18.2%), white (62.5%), or other (19.3%) race. The median patient age was 5.4 months (range: 1 day–41.5 years). Premature birth (gestational age < 37 weeks) occurred in 29 (15.1%) patients. A known genetic syndrome or chromosomal abnormality was present in 33 (17.2%) patients; trisomy 21 (n = 14) and chromosome 22q deletions (n = 6) were the most commonly identified syndromes or chromosomal abnormalities.

BSI occurred in 12 (6.3%; 95% CI, 3.3%–10.7%) patients within the first 30 days after median sternotomy. The characteristics of patients with and without BSI are shown in Table 1. BSI developed a median of 11 days (range: 3–29 days) after median sternotomy. The median duration of

bacteremia was 1 day (range: 1–9 days); for all patients in whom a BSI was diagnosed, blood cultures had been obtained daily until resolution of the bacteremia. Gram-negative bacilli caused 6 (50%) of the 12 BSIs. Specific causes of BSI included *Pseudomonas aeruginosa* (n = 3), coagulase-negative staphylococci (n = 3), *Pseudomonas fluorescens-putida* (n = 2), *S. aureus* (n = 2), *Serratia marcescens* (n = 1), and *Candida albicans* (n = 1). There were no polymicrobial episodes of BSI. SSIs occurred in 7 (3.7%) patients and were classified as deep SSI (n = 3) or mediastinitis (n = 4). No patients with deep SSI but 2 patients with mediastinitis had BSI. *S. aureus* was the causative organism in both cases of BSI associated with mediastinitis. Other foci of infection were not identified. Neither definite nor possible endocarditis was diagnosed in any patient.

The type of surgical repair was not significantly different for patients with and without BSI. Results of the bivariable analyses to detect preoperative, intraoperative, and postoperative risk factors are shown (Table 2). The duration of preoperative hospitalization was not significantly different for patients with BSI (median, 2.5 days) compared with patients without BSI (median, 1 day; $P = .13$). The variable any SSI, which encompassed superficial SSI, deep SSI, and mediastinitis, was not associated with an increased risk of BSI (OR, 7.00; 95% CI, 0.58–48.96; $P = .063$). However, inasmuch as BSI did not develop in any patients with a deep SSI but did develop in 2 (50%) of the 4 patients with mediastinitis, only the variable mediastinitis was included as a risk factor in the multivariable model. Multivariable analysis revealed that the development of mediastinitis and the postoperative requirement for extracorporeal membrane ox-

TABLE 2. Results of the bivariable analysis to detect preoperative, intraoperative, and postoperative risk factors for BSI among children after median sternotomy

Exposure	BSI (n = 12)	No BSI (n = 180)	OR (95% CI)	P value
Preoperative/intraoperative				
Prostaglandin infusion	5 (41.7%)	39 (21.7%)	2.50 (0.59–9.67)	.124
Highest preoperative creatinine (mg/dL)	0.8 (0.6–1.0)	0.5 (0.4–0.8)	—	.005
Duration of operation (min)	163 (135–278)	161 (134–226)	—	.815
Duration of cardiopulmonary bypass (min)	79 (68–116)	77 (59–106)	—	.348
Deep hypothermic circulatory arrest	6 (50.0%)	108 (60.0%)	0.67 (0.17–2.61)	.495
Minimum intraoperative temperature (°C)	18 (16.8–27.6)	18 (17–26)	—	.951
Preoperative third-generation cephalosporin use	0 (0%)	8 (4.4%)	0 (0–7.33)	.456
Preoperative aminoglycoside use	2 (16.7%)	20 (11.1%)	1.60 (0.16–8.32)	.558
Preoperative vancomycin use	2 (16.7%)	9 (5.0%)	3.80 (0.35–22.12)	.092
Postoperative				
Delayed sternal closure	2 (16.7%)	13 (7.2%)	2.57 (0.25–14.02)	.238
Initial postoperative pH	7.48 (7.45–7.53)	7.53 (7.46–7.58)	—	.133
Initial postoperative Po ₂ (mm Hg)	155 (31–372)	146 (47–372)	—	.399
Initial postoperative Pco ₂ (mm Hg)	33 (32–37)	34 (28–40)	—	.792
Surgical re-exploration required	5 (41.7%)	31 (17.2%)	3.43 (0.80–13.42)	.051
Mediastinitis	2 (16.7%)	2 (1.1%)	17.80 (1.13–258.19)	.02
Duration of postoperative chest tube (d)	4 (2–6)	1 (1–2)	—	.008
Pleural effusion	1 (8.3%)	44 (24.4%)	0.27 (0.01–1.98)	.190
Extracorporeal membrane oxygenation	4 (33.3%)	9 (5.0%)	9.50 (1.72–43.73)	<.001
Cardiac arrest	2 (16.7%)	6 (3.3%)	5.80 (0.50–37.78)	.081
Duration of intracardiac pacing wires (d)	5 (5–9)	3 (1–6)	—	.108
Duration of intracardiac catheter (d)	5 (3–12)	2 (1–5)	—	.024
Duration of arterial catheter (d)	10 (4–18)	2 (1–4)	—	.001

The odds ratio (OR) estimates the risk of bloodstream infection (BSI) in the presence of the specified exposure. Values listed as median (interquartile range) or number (percent). CI, Confidence interval; Po₂, oxygen tension; Pco₂, carbon dioxide tension.

ygenation were independently associated with BSI after median sternotomy (Table 3).

The median duration of intensive care unit stay was longer for those who had BSIs (32 days; interquartile range, 10–47 days) than for those who did not have BSIs (4 days; interquartile range, 2–11 days; $P < .001$). The mortality rate for those with BSIs (16.7%) was not significantly higher than for those without BSIs (4.4%; OR, 4.3; 95% CI, 0.4–25.7).

Discussion

The incidence of postoperative BSI in patients undergoing median sternotomy was 6.3%. We also identified postoperative mediastinitis and the requirement for postoperative extracorporeal membrane oxygenation as risk factors for BSI after median sternotomy.

Several prior studies reported the incidence of BSI in children after cardiac surgery. Pollock and associates¹ reported BSIs in 21 (6.8%) of 310 children after cardiac surgery; however, the causative organisms were not identified. Bacteremia complicated 18 (7.0%) of 256 cardiac surgical procedures examined by Mehta and colleagues.² Although *S. aureus* was the predominant organism, Gram-negative bacteria accounted for 5 (42%) of 12 cases of BSI

occurring in the absence of concurrent SSI.² The rate of postoperative BSI in our study was similar to those in these earlier studies; gram-negative organisms accounted for one half of all cases of BSI and for 6 of the 10 cases not associated with SSI. Colonization and subsequent infection with flora endemic in the intensive care unit setting was the likely mechanism of infection, because BSI developed after the first week following surgery in most patients. We could not retrospectively determine whether the BSIs were primary or attributable to the presence of indwelling devices.

Previous studies in children did not attempt to identify risk factors for postoperative BSI in children undergoing median sternotomy. Among children with mediastinitis at our institution, we⁵ previously identified *S. aureus* wound infection as an independent risk factor for BSI (OR, 6.4; 95% CI, 1.4–29.3). In adults, postoperative mediastinitis is associated with BSI caused by *S. aureus* but not with BSI caused by other pathogens.^{6,7} San Juan and coworkers⁸ studied 266 adult patients evaluated for fever developing within 60 days after a median sternotomy procedure; *S. aureus* BSI had a sensitivity of 68% and a positive predictive value of 87% for diagnosing concurrent mediastinitis. Among adults undergoing coronary artery bypass grafting, mediastinitis was associated with BSI caused by

TABLE 3. Results of a multivariable and adjusted analysis performed to identify variables independently associated with BSI after median sternotomy

Variable	Adjusted OR (95% CI)	P value
Multivariable model		
Mediastinitis	28.16 (3.37–235.22)	.002
Extracorporeal membrane oxygenation	12.52 (2.99–52.41)	.001
Adjusted analysis*		
Birth weight	0.53 (0.14–1.93)	.33
Prostaglandin infusion	1.22 (0.70–2.14)	.48
Highest preoperative creatinine	2.34 (0.60–9.22)	.22
Preoperative vancomycin use	2.46 (0.36–16.74)	.36
Initial postoperative pH	0.12 (0–55.69)	.49
Surgical re-exploration required	1.02 (0.15–6.88)	.98
Duration of postoperative chest tube	1.11 (0.89–1.38)	.33
Pleural effusion	0.31 (0.04–2.72)	.29
Cardiac arrest	1.12 (0.12–10.56)	.92
Duration of intracardiac pacing wires	1.12 (0.90–1.40)	.30
Duration of intracardiac catheter	1.03 (0.93–1.15)	.59
Duration of arterial catheter	1.08 (0.96–1.22)	.20

BSI, Bloodstream infection; OR, odds ratio; CI, confidence interval. *Variables adjusted for the occurrence of mediastinitis and the requirement for extracorporeal membrane oxygenation postoperatively. Only values with a P value $\leq .2$ were considered in the adjusted analysis.

S. aureus (OR, 52.98; 95% CI, 26.46–106.08) and, to a lesser extent, BSI caused by other organisms (OR, 2.05; 95% CI, 1.08–3.91).⁷ In the current study, we identified mediastinitis as a risk factor for BSI after median sternotomy in children; *S. aureus* was responsible for both cases of BSI associated with mediastinitis. Additionally, children with BSI required a significantly longer period of intensive care unit hospitalization but did not have a higher mortality rate than patients without BSI. Our data suggest that although mediastinitis is an infrequent complication of median sternotomy procedures, interventions to prevent mediastinitis may decrease the rate of postoperative BSI. In a study of adult surgical patients, while mupirocin prophylaxis did not reduce the overall rate of SSIs caused by *S. aureus*, it did significantly reduce the overall rate of nosocomial *S. aureus* infections, including BSI.¹³

Conclusions

This study had several limitations. The incidence of detectable BSI depends in part on the timing of antibiotic administration relative to the timing of blood sampling for culture. If antibiotics were frequently administered before the performance of blood culture, we may have underestimated the true incidence of BSI in this population. Additionally, we presumed that mediastinitis was the source of BSI. It is possible that mediastinitis in some patients develops as a consequence of hematogenous dissemination after primary

BSI. Retrospectively, we cannot determine whether a patient's initial symptoms were attributable to BSI or mediastinitis. The timing of blood and mediastinal cultures may not accurately reflect the underlying pathogenesis of BSI because blood cultures are relatively easy to obtain while the timing of mediastinal cultures depends on many factors, including patient stability. As with any study based on retrospective review of medical records, we were limited to data contained in the inpatient hospital records. Although the potential data deficiency from missing or incomplete records was of concern, it likely resulted in nondifferential bias given that the information regarding exposures was documented by the treating physicians before the occurrence of the outcome. Inasmuch as some patients undergoing cardiac surgery are referred from great distances, it is possible that not all children in whom mediastinitis developed after discharge returned to our institution for treatment. We expect that misclassification of the exposure in this manner would bias our results toward the null since BSIs occur in approximately 50% of patients with mediastinitis.^{3,4}

Although we present the first study of risk factors for BSI in children undergoing median sternotomy, the relatively small sample size is an important limitation. Our primary findings of the association between mediastinitis, postoperative extracorporeal membrane oxygenation requirement, and BSI warrant exploration in a larger, prospective study. Additionally, our study was inadequately powered to detect relatively small differences between the two groups in the association of variables, such as the duration that the intravascular catheters were in place, that have contributed to the development of BSIs in other settings. This important issue should be addressed in future studies of BSI in children undergoing cardiac surgery.

In summary, BSI complicated the postoperative course of 6.3% of children undergoing median sternotomy. Mediastinitis and the postoperative requirement for extracorporeal membrane oxygenation were risk factors for BSI. BSI was significantly associated with prolonged intensive care unit hospitalization.

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