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Association Between Postoperative Fever and Atelectasis in Pediatric Patients

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Abstract

Background: Postoperative fever is common after cardiac surgery. In the absence of documented infection, atelectasis is often suggested as a cause of postoperative fever. However, this link is not well supported by pathophysiologic mechanisms. The purpose of this study was to investigate whether an association exists between atelectasis and postoperative fever in pediatric patients undergoing cardiac surgery. **Methods:** A retrospective review was performed on consecutive pediatric patients who underwent cardiac surgery on cardiopulmonary bypass at a single cardiac surgery center from January 1, 2009, to December 31, 2009. Postoperative chest radiographs were evaluated and each lung was scored independently for atelectasis. Clinical parameters including the highest daily recorded temperature were noted and compared to atelectasis data. **Results:** A total of 203 patients were enrolled; 139 patients (68.5%) had fever at least once during the first 3 postoperative days. The incidence of atelectasis on each day was 41%, 57%, and 71%, respectively. There was no association between fever and atelectasis on any postoperative day ($P = .21$). Microbiological cultures were performed on 81 patients, and infection was found in 7 patients (3.5%). The frequency of either fever or atelectasis was similar between cyanotic and acyanotic patients. **Conclusions:** Postoperative fever and atelectasis are both common after pediatric cardiac surgery. In our study, there was no significant association between postoperative fever and atelectasis. In children undergoing cardiac surgery with cardiopulmonary bypass, fever in the postoperative period should not be attributed to atelectasis.

Keywords

pediatric, lung pathology, postoperative care, infection

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Introduction

Postoperative fever is common in adult patients undergoing cardiac surgery.[1] Postoperative fever is also frequently seen in pediatric patients depending on the specific type of surgery performed.[2-4] The most serious cause of fever in the postoperative period is infection; however, multiple noninfectious causes of fever in the postoperative period have also been reported.[5] Patients who undergo surgical procedures requiring intubation and general anesthesia often have postoperative atelectasis.[6] In children, atelectasis may occur when hypoventilation continues for a protracted period causing alveolar collapse. Children may also be predisposed to atelectasis because of small caliber airways and high airway resistance, which can contribute to poor clearance of airway secretions.

Fever has been frequently touted as a sign of atelectasis in postoperative patients; however, this association is not supported by known pathophysiologic mechanisms. Furthermore, data in the adult literature refute the notion that there is any association between postoperative fever and atelectasis.[1,7,8] Although there are data demonstrating the lack of association between postoperative fever and atelectasis in adult patients, there have been no published studies evaluating whether an association exists between postoperative fever

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and atelectasis in pediatric patients. The purpose of this study was to investigate whether a relationship exists between postoperative fever and atelectasis in pediatric patients undergoing cardiac surgery.

Methods

A retrospective chart review was performed on consecutive pediatric patients who underwent cardiac surgery on cardiopulmonary bypass at Children's Memorial Hospital in Chicago, Illinois, from January 1, 2009, to December 31, 2009. All pediatric patients ($\leq$18 years) undergoing cardiac surgery with cardiopulmonary bypass were eligible for inclusion. Patients were excluded if they required extracorporeal membrane oxygen support within 72 hours of surgery or had prior history of structural lung abnormality including patients with history of diaphragmatic hernia or previous pulmonary surgery with segmental resection including pneumonectomy. All patients were routinely maintained on parenteral antibiotics following cardiac surgery for at least 48 hours following surgery per usual clinical practice. The routine use of antipyretics for fever was at the discretion of the clinical team. The study was approved by the Children's Memorial Hospital Institutional Review Board.

Postoperative chest radiographs for study patients were re-evaluated by an attending radiologist. The radiologist was blinded to the patient's postoperative clinical course with respect to fever as well as intraoperative parameters or findings. Each lung was scored independently for atelectasis and graded 0 for *no atelectasis*, 1 for *diffuse atelectasis*, 2 for *focal or lobar atelectasis*, and 3 for *complete whiteout*.[1] The scores for the 2 lungs were added together to obtain the daily atelectasis score for each patient. The presence or absence of an opacity and appearance on subsequent radiographs was used to discern findings from other pulmonary infiltrative processes. Any evidence suggestive of pneumonia was also noted. Urinary bladder or surface skin temperature were monitored and recorded hourly in this patient population. Fever was defined as temperature $\geq$38°C. The highest recorded temperature on the day of surgery and on the first and second postoperative days was also noted. All available microbiological cultures were reviewed for the first 5 postoperative days. An infectious cause of fever was considered if there was a positive blood, urine, or endotracheal tube secretion culture, including viral culture or polymerase chain reaction (PCR) within 48 hours of fever. Endotracheal tube cultures were considered positive if an organism was identified with greater than 10 to 25 white blood cells per high-powered field in the sputum sample to exclude potential colonization from confounding the analysis. Patients with documented infection were not included in the analysis for association between fever and atelectasis, given the presumed alternative cause of fever. Additional patient demographics including operative data, gender, and age were collected for multivariable analysis.

The Cochran-Mantel-Haenszel test was used to assess univariate association of demographic variables with fever and atelectasis over time. Participants were stratified into groups based on demographic variables in order to increase the power to detect an association using the Cochran-Mantel-Haenszel test. We used a generalized linear model method with a cumulative logit link function to evaluate the relationship between the day of extubation and presence of atelectasis and the degree of fever and severity of atelectasis. A generalized linear model was also used to evaluate the association between fever, atelectasis score, demographic variables, and other clinical covariates. A weighted least square method was used to analyze atelectasis score changes over time. The analysis was conducted using SAS 9.2 (SAS Institute Inc, Cary, North Carolina).

Table 1. Ten Most Frequent Cardiac Diagnoses

Primary Cardiac Lesion	n (%)
VSD	36 (18)
Isolated valve abnormality	23 (12)
Tetralogy of Fallot	19 (10)
Single ventricle (not HLHS)	15 (8)
Coronary artery abnormality	15 (8)
ASD or PFO	14 (7)
Cardiac transplant	11 (6)
AV canal (AVSD)	11 (6)
Hypoplastic left heart syndrome (HLHS)	8 (4)
Conduit stenosis	8 (4)

Abbreviations: ASD, Atrial Septal Defect; VSD, Ventricular Septal Defect; PFO, Patent Foramen Ovale; AVSD, Atrioventricular Septal Defect.

Results

A total of 203 patients met the inclusion criteria. Microbiological cultures were performed on 81 patients, and presumed infection (6 positive endotracheal tube cultures and 1 positive urine culture) was found in 7 patients. There were no cases of pneumonia or bacteremia. In all, 196 patients underwent analysis for association between fever and atelectasis. Cardiac lesions and demographic data on patients included in the association analysis are presented (Tables 1 and 2). A total of 134 patients (68.4%) had fever at least once during the postoperative study period, and 155 (79.1%) patients had some degree of atelectasis. The frequency of fever and specific atelectasis scores varied by postoperative day (Table 3). There was no association between fever and presence of atelectasis on any postoperative day (Table 4). There was also no relationship between the degree of atelectasis as indicated by higher atelectasis scores and highest daily temperature ($P > .05$). In univariate analysis, cyanotic patients were less likely to have fever than acyanotic patients (odds ratio [OR] = .56, 95% confidence interval [CI]: 0.32-0.99, $P = .0448$). The frequency of atelectasis was similar between cyanotic and acyanotic patients ($P = .74$).

With respect to mechanical ventilation, 20.5% of patients were without mechanical ventilation on postoperative day 0, 56.4% were free from mechanical ventilation on postoperative day 1, and 69.2% were free from mechanical ventilation by postoperative day 2. By postoperative day 3, only 30.8% of patients continued to require mechanical ventilation. There was an increase in the number of patients with atelectasis over time

Table 2. Demographic Information on Patients Without Culture-Proven Infection (n = 196)

Variable	Temperature Analysis n (%)			Radiographic Analysis n (%)		
	Any Fever	No Fever	*P* Value	Any Atelectasis	No Atelectasis	*P* Value
Male	82 (72)	32 (28)		89 (78)	25 (22)	
Female	52 (63)	30 (37)	.2060[a]	66 (80)	16 (20)	.6814[a]
Postoperative physiology						
Cyanotic	12 (55)	10 (45)		18 (82)	4 (18)	
Acyanotic	122 (70)	52 (30)	.1390[a]	137 (79)	37 (21)	.7377[a]
Cardiopulmonary bypass time (minutes)	123.6 ± 57.0[b]	102.2 ± 48.2	.0126[c]	115.6 ± 54.8	121.4 ± 56.7	.5992
Age (months)	54.7 ± 60.6	46.1 ± 67.1	.0030	56.2 ± 63.2	35.9 ± 58.7	.0061

[a] Chi-square test.
[b] Mean ± SD.
[c] Wilcoxon rank sum test.

Table 3. Number of Patients With Fever and the Number Who Had Each Atelectasis Score (n = 196)

	Patients n (%)		
	Day 0	Day 1	Day 2
Fever ≥38.0	76 (39)	98 (50)	63 (32)
Total atelectasis score			
0	114 (58)	85 (43)	56 (29)
1	32 (16)	45 (23)	42 (21)
2	36 (19)	42 (22)	56 (29)
3	10 (5)	18 (9)	30 (15)
≥4	4 (2)	6 (3)	12 (6)

(Table 3). There was no relationship between the day of patient extubation and presence of atelectasis ($P = .6367$).

In the multivariate regression analysis, the probability of fever occurrence was significantly associated with postoperative day, age, and duration of cardiopulmonary bypass (Table 5). After adjusting other covariates, the odds of fever on postoperative day 1 was 1.69 (95% CI: 1.15-2.49) compared to fever on postoperative day 0. There was no difference in odds of fever between postoperative day 2 and postoperative day 0. Comparing the odds of fever in older patients with age greater than 24 months, neonatal patients younger than 1 month had lower risk of fever (OR = 0.18, 95% CI: 0.07-0.45, $P = .0003$); patients with age between 12 months and 48 months had higher risk of fever (OR = 2.03, 95% CI: 1.24-3.33, $P = .0049$) compared to those older than 48 months. Longer duration of cardiopulmonary bypass time was associated with higher risk of fever ($P = .002$) but not with the actual highest daily temperature ($P = .374$). Although significant in the univariate analysis, the risk of postoperative fever was not different between cyanotic and acyanotic patients ($P = .7537$) after adjusting other variables in the model.

Discussion

Postoperative fever and atelectasis are both common after pediatric cardiac surgery. However, we found no association between fever and atelectasis in the first 72 hours following surgery. This finding is consistent with adult studies that also have failed to show association between fever and atelectasis after cardiac surgery. In spite of data to the contrary, a number of recent medical textbooks continue to espouse atelectasis as a common, or even the most common cause of postoperative fever.[9-11] Given the available data, we question the practice of including atelectasis as a differential diagnosis for postoperative fever in children.

Postoperative fever after cardiopulmonary bypass is common and can be explained by known pathophysiologic mechanisms. Cardiopulmonary bypass leads to the activation of multiple inflammatory mediators through neutrophil degranulation, oxygen-free radical production, complement activation, and cytokine release.[12] Elevated concentrations of tumor necrosis factor-α (TNF-α) and interleukin 6 (IL-6) may contribute to postoperative fever in children undergoing congenital cardiac surgery.[13] The use of preoperative corticosteroids to blunt the inflammatory response has been well studied, and steroids have been shown to attenuate the release of proinflammatory cytokines in children undergoing cardiac surgery on bypass.[14]

One surprising finding in this study was that the neonatal patients in the study cohort (birth to 1 month of age) were less likely to have postoperative fever compared to those older than 4 years. This finding was unexpected, given the differences between neonates and infants with regard to the inflammatory response to cardiopulmonary bypass.[15] This finding may be a result of the relatively small number of neonates in the sample (11.3%). Also, although the univariate analysis revealed that cyanotic patients were more likely to have fever compared to acyanotic patients, this finding was not maintained when corrected for other data elements in the multivariable model.

Postoperative infection as a cause of fever appears to be a rare event. Ryan et al found that the incidence of early postoperative sepsis in adults undergoing cardiac surgery on cardiopulmonary bypass was 0.2%.[16] In our cohort, no patients were found to have positive blood cultures. Although 6 of our patients had positive endotracheal cultures, none developed radiographic evidence of pneumonia. Although we only included positive culture where sputum gram stain was positive for leukocytosis, it is unclear whether the positive endotracheal

Table 4. Association of Fever and Clinical Variables Over Time

Variable		Postoperative Day 0		Postoperative Day 1		Postoperative Day 2		*P* Value[a]
		Fever +	Fever −	Fever +	Fever −	Fever +	Fever −	
Total atelectasis score	0	45 (39)	69 (61)	37 (44)	48 (56)	15 (27)	41 (73)	.2066
	≥1	30 (37)	51 (63)	61 (55)	50 (45)	47 (34)	92 (66)	
Age group (months)	<1	4 (18)	18 (82)	2 (9)	20 (91)	1 (5)	21 (95)	<.0001
	1-12	26 (38)	42 (62)	35 (51)	34 (49)	25 (36)	44 (64)	
	12-48	23 (62)	14 (38)	26 (70)	11 (30)	12 (32)	25 (68)	
	>48	22 (32)	46 (68)	35 (51)	33 (49)	24 (36)	43 (64)	
Physiology	Cyanotic	8 (36)	14 (64)	8 (36)	14 (64)	3 (14)	19 (86)	.0448
	Acyanotic	67 (39)	106 (61)	90 (52)	84 (48)	59 (34)	114 (66)	
Gender	Male	47 (41)	67 (59)	56 (49)	58 (51)	38 (33)	76 (67)	.5000
	Female	28 (35)	53 (65)	42 (51)	40 (49)	24 (30)	57 (70)	

[a] Cochran-Mantel-Haenszel.

Table 5. Multivariate Analysis Between Fever and Other Clinical Variables Over Time

Variables	Odds Ratio	95% Confidence Interval	Chi-Square Statistic	*P* Value
Male vs female	1.13	0.75−1.71	0.34	.5599
Postop day 1 vs 0	1.69	1.15−2.49	7.04	.0080
Postop day 2 vs 0	0.73	0.47−1.13	1.97	.1605
Postop day 1 vs 2	2.31	1.63−3.28	21.90	<.0001
Age <1 vs >48 months	0.18	0.07−0.45	13.34	.0003
Age 1−12 vs >48 months	1.03	0.62−1.72	0.01	.9118
Age 12−48 vs >48 months	2.03	1.24−3.33	7.93	.0049
CPB time	1.01	1.00−1.01	9.82	.0017
Cyanotic vs acyanotic	0.88	0.40−1.92	0.10	.7537

Abbreviation: CPB, cardiopulmonary bypass.

cultures represented bacterial colonization or true tracheitis. Given the low rate of serious bacterial infection in these patients, the practice of routinely obtaining multiple bacterial cultures from blood in patients with fever in the early postoperative period may require further study.

There are a number of limitations in this study. First, this study represents a retrospective review of a limited number of consecutive cases. Also, variations in clinical care could not be controlled, given our retrospective design, and may have impacted on our findings. For example, although we do not use a specific antipyretic protocol, all postoperative patients are prescribed acetaminophen (15 mg/kg) every 4 hours as needed if febrile above 38°C. In rare cases, external cooling with ice packs or cooling blankets have been used in patients with fevers unresponsive to antipyretics or those with junctional ectopic tachycardia. We did not review the actual number of antipyretic doses given to each febrile patient and as such, this may have impacted our findings. However, given that these cardiac surgery patients were cohorted in a cardiac intensive care unit with a core group of cardiac-focused intensive care physicians and standardized admission order sets, variation in clinical practice should have been minimized. Also, although relatively small, the number of patients in our sample is nearly double those found in the studies performed in the largest adult study to date. Radiographic findings of atelectasis could be subject to interpretation by different radiologists and as a result, could have impacted our findings. Multiple reviewers with excellent interrater reliability may have increased the accuracy of identification of atelectasis. We designed our study such that a single radiologist reviewed all radiographic data in order to eliminate the risk of interrater reliability concerns and modeled the objective scoring system on previously published methodology.[1] Finally, given that the radiologist was blinded to the clinical data, there should have been no clinical bias to the radiographic findings.

Conclusions

Postoperative fever and atelectasis are both common after cardiac surgery in children. This study failed to find a significant association between fever and atelectasis during the first 72 hours following surgery with cardiopulmonary bypass.

Declaration of Conflicting Interests

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References

1. Engoren M. Lack of association between atelectasis and fever. *Chest*. 1995;107(1):81-84.
2. Yueng RSW, Buck JR, Filler RM. The significance of fever following operations in children. *J Pediatr Surg*. 1982;17(4): 347-349.
3. Fraser I, Johnstone M. Significance of early postoperative fever in children. *Br Med J*. 1981;283(6302):1299.
4. Angel JD, Blasier RD, Allison R. Postoperative fever in pediatric orthopaedic patients. *J Pediatr Orthop*. 1994;14(6): 799-801.
5. Pile JC. Evaluating postoperative fever: a focused approach. *Cleve Clin J Med*. 2006;3(1):S62-S66.
6. Duggan M, Kavanagh BP. Pulmonary atelectasis: a pathogenic perioperative entity. *Anesthesiology*. 2005;102(4):838-854.
7. Roberts J, Barnes W, Pennock M, Browne G. Diagnostic accuracy of fever as a measure of postoperative pulmonary complications. *Heart Lung*. 1988;17(2):166-170.
8. Livelli FD Jr, Johnson RA, McEnany MT, et al. Unexplained in-hospital fever following cardiac surgery: natural history, relationship to postpericardiotomy syndrome, and a prospective study of therapy with indomethacin versus placebo. *Circulation*. 1978;75(5):87-90.
9. Moosa AR, Mayer AD, Lavelle-Jones M. Surgical complications; pulmonary complications. In: Sabiston DC, ed. *Textbook of Surgery: Biological Basis of Modern Surgical Practice*. 18th ed. Philadelphia: WB Saunders Co; 2008:305-307.
10. Katz VL. Postoperative counseling and management. In Katz VL, Lentz GM, Lobo RA, Gershenson DM, ed. *Comprehensive Gynecology*, 5th ed. Philadelphia; Mosby Elsevier Inc; 2007:662-666.
11. Redelmeier D. Postoperative care and complications. In Goldman L, Ausiello D, eds. *Cecil Medicine*, 23rd ed. Saunders: Philadelphia, PA. 2008;2910.
12. Paparella D, Yau TM, Young E. Cardiopulmonary bypass induced inflammation: pathophysiology and treatment. An update. *Eur J Cardiothorac Surg*. 2002;21(2):232-244.
13. Kozik DJ, Tweddell JS. Characterizing the inflammatory response to cardiopulmonary bypass in children. *Ann Thorac Surg*. 2006;81(6):S2347-S2354.
14. Bronicki RA, Backer CL, Baden HP, Mavroudis C, Crawford SE, Green TP. Dexamethasone reduces the inflammatory response to cardiopulmonary bypass in children. *Ann Thorac Surg*. 2000; 69(5):1490-495.
15. Ashraf SS, Tian Y, Zacharrias S, Cowan D, Martin P, Watterson K. Effects of cardiopulmonary bypass on neonatal and paediatric inflammatory profiles. *Eur J Cardiothorac Surg*. 1997; 12(6):862-868.
16. Ryan T, McCarthy JF, Rady MY, et al. Early bloodstream infection after cardiopulmonary bypass: frequency rate, risk factors and implications. *Crit Care Med*. 1997;25(12):2009-2014.