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Risk Factors for Adverse Postoperative Outcomes in Children Presenting for Cardiac Surgery with Upper Respiratory Tract Infections

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Background: **Otherwise healthy children who present for elective surgery with an upper respiratory infection (URI) may be at risk for perioperative respiratory complications. This risk may be increased in children with congenital heart disease who undergo cardiac surgery while harboring a URI because of their compromised cardiopulmonary status. Therefore, this study was designed to determine the incidence of peri- and postoperative complications in children undergoing cardiac surgery while harboring a URI.**

Methods: **The study population consisted of 713 children scheduled to undergo cardiac surgery. Of these, 96 had symptoms of URI, and 617 were asymptomatic. Children were followed prospectively from induction of anesthesia to discharge from the hospital to determine the incidence of postoperative respiratory, cardiovascular, neurologic, and surgical adverse events. Duration of postoperative ventilation, time in the intensive care unit (ICU), and length of hospital stay were also recorded.**

Results: **Children with URIs had a significantly higher incidence of respiratory and multiple postoperative complications than children with no URIs (29.2 *vs.* 17.3% and 25 *vs.* 10.3%, respectively; $P < 0.01$) and a higher incidence of postoperative bacterial infections (5.2 *vs.* 1.0%; $P = 0.01$). Furthermore, logistic regression indicated that the presence of a URI was an independent risk factor for multiple postoperative complications and postoperative infections in children undergoing open heart surgery. Children with URIs also stayed longer in the intensive care unit than children with no URIs (75.9 ± 89.8 h *vs.* 57.7 ± 63.8, respectively; $P < 0.01$). However, the overall length of hospital stay was not significantly different (8.4 *vs.* 7.8 days, URI *vs.* non-URI groups; $P > 0.05$).**

Conclusions: **The presence of a URI was predictive of postoperative infection and multiple complications in children presenting for cardiac surgery. Despite this, the presence of a URI does not appear to affect the patient's overall length of hospital stay nor the development of long-term sequelae.**

THE issue of whether to cancel surgery for the child who presents with an upper respiratory infection (URI) remains contentious. Although previous studies have found that children who present for surgery with a URI are at increased risk of perioperative respiratory complications,[1–3] these complications are generally easily managed and result in minimal morbidity.[1,4,5] Therefore, decisions to cancel elective surgery for the child with a URI must be made on a case-by-case basis taking into careful consideration any risk and benefit of proceeding with anesthesia.

Typically, the decision to postpone elective surgery for otherwise healthy children with URIs has minimal impact on the child's condition. However, for children requiring cardiac surgery, the benefits of expedient surgery may outweigh the potential risks associated with the presence of a URI. On the other hand, children with congenital cardiac anomalies may have concomitant cardiac and respiratory compromise that may be exacerbated by the presence of a URI.[6] Unfortunately, little is known regarding the impact of a URI on postoperative outcome for children undergoing cardiac surgery. In a recent study from our institution,[7] children with URIs undergoing cardiac surgery had an increased overall incidence of postoperative complications compared with children with no URIs; however, the presence of symptoms had no effect on hours of ventilation, duration of intensive care unit (ICU) stay, and overall duration of hospitalization.

However, our previous study was retrospective in nature and may have suffered some of the biases inherent in this type of study design. With this in mind, we designed a prospective study to examine the relationship between the presence of URI symptoms and postoperative complications in children undergoing cardiac surgery. The hypothesis to be tested was that children who present for cardiac surgery with URIs have an increased risk of postoperative respiratory complications compared with children with no URIs.

Materials and Methods

The University of Michigan's Institutional Review Board (Ann Arbor, Michigan) approved this prospective, observational cohort study, and informed consent was obtained from the parents or legal guardians. The study sample consisted of 713 children aged 1 month to 16 yr who underwent nonemergent open heart surgery during a 4-yr period from 1996 to 1999 at a large tertiary care pediatric hospital. A trained research assistant interviewed preoperatively the parents of all children pre-

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senting for open heart surgery regarding the presence of URI symptoms. Diagnosis of an active URI required that the child present with a minimum of two URI symptoms (rhinorrhea, sore or scratchy throat, sneezing, nasal congestion, malaise, cough, or fever > 38°C)[8] together with confirmation by a parent.[9] Based on these criteria, children were classified into one of two groups (active URI *vs.* non-URI) before surgery by one of the investigators. Children were excluded if they had evidence of lower respiratory involvement (*i.e.*, those with abnormal findings on chest auscultation or radiograph), complex cyanotic heart disease, presence of a tracheostomy, or required ventilatory support preoperatively. Participation in the study did not alter the decision of whether to proceed with surgery, which was made by the faculty anesthesiologist in each case, nor did it alter the perioperative care of the child.

Demographic information was recorded including age, gender, height, weight, American Society of Anesthesiologists (ASA) physical status, and surgical procedure. Data related to premedications and agents used for induction and maintenance of anesthesia were noted. Any respiratory complications during the perioperative period, including laryngospasm (defined as a partial or complete closure of the vocal cords that required positive pressure or administration of a muscle relaxant), bronchospasm, breath holding for 15 s or more, and persistent cough, were identified by the faculty anesthesiologist and documented by a research assistant. In addition, the baseline oxygen saturation and the lowest saturation on induction and emergence were recorded for each patient. The duration of anesthesia and surgery, and aortic cross-clamp, circulatory arrest, and cardiopulmonary bypass (CPB) times were documented. At the end of each procedure, the anesthesiologist was questioned whether the presence of an URI had altered his or her management, and specific interventions were recorded. Postoperatively, information was obtained regarding the duration of ventilatory support together with the times spent in the ICU and in the hospital overall. Maximum temperatures for each child on each postoperative day were recorded. Furthermore, all postoperative respiratory, cardiovascular, surgical, multiple (more than one type), and neurologic complications and deaths were recorded daily on standard data collection sheets by trained research assistants. Radiographic and laboratory data, including blood gas, sputum cultures, and leukocyte counts, were also collected with details of the ventilator settings in the ICU.

Statistical Analysis

Statistical analysis was performed using SPSS® statistical software (SPSS Inc., Chicago, IL). Sample size determination was based on our previous retrospective study using overall postoperative complications as the outcome measure. Based on the clinically important difference in incidence of this outcome between children with URIs and those without URIs (*i.e.*, 42 *vs.* 23%), we calculated that we would need 94 subjects per group to detect a statistically significant difference at least that large ($\alpha = 0.05$ and $\beta = 20\%$, two tailed).

Parametric data were analyzed using unpaired *t* tests. Nonparametric data were analyzed by chi-square and Fisher exact test as appropriate. Relative risks (RR) were calculated using the formula RR = incidence of outcome in URI group/incidence of outcome in non-URI group. Independent variables that were found to be significantly associated with outcome by univariate analysis were further analyzed by logistic or multiple linear regression. Data are expressed as mean ± SD and percentages. *P* values of less than 0.05 were considered statistically significant.

Table 1. Demographics

	Active URI (n = 96)	Non-URI (n = 617)
Age, yr (mean ± SD)	2.2 ± .2.7*	3.4 ± 4.1
Gender, male/female %	61.5/38.5	56.4/43.6
Preoperative weight, kg	11.4 ± 7.9*	15.6 ± 15.0
ASA status, II/III/IV%	17/73/11	18/74/8
Baseline Spo_2, %	89.1 ± 10.1	91.1 ± 8.8
Surgical procedures	—	—
Septal defects/repairs	31 (33.3)	215 (36.1)
Valve replacement/repair	13 (14.0)	72 (12.1)
Fontan	14 (15.1)	93 (15.6)
Hemi-Fontan	15 (16.1)	69 (11.6)
Tetralogy of Fallot	5 (5.4)	51 (8.6)
Other	15 (16.1)	95 (16.0)
Surgery time, min	213 ± 69	214 ± 66
CPB time, min	94.4 ± 48.4	89.2 ± 50.9
Aortic cross-clamp time, min	48.3 ± 27.9	49.2 ± 32.3
Circulatory arrest time, min	22.7 ± 11.9	25.4 ± 12.4

ASA, American Society of Anesthesiologists; CPB, cardiopulmonary bypass; Spo_2, oxygen saturation; URI, upper respiratory infection.
* $P < 0.05$ *vs.* non-URI.

Results

Data were obtained for 713 children, of whom 96 comprised the URI group and 617, the non-URI group. The demographics of the study population are described in table 1. The children with URIs were significantly younger and weighed less than those without. Patients in the URI group presented with the following symptoms: cough (65.6%), rhinorrhea (59.4%), nasal congestion (59.4%), sneezing (39.6%), malaise and decreased activity (11.5%), sore throat (3.1%), and low-grade fever (1.0%). There were no differences between groups with respect to history of underlying respiratory disease, *e.g.*, asthma, bronchitis, croup, hay fever, pneumonia, respiratory failure, or bronchopulmonary dysplasia. In addition, there were no differences in the durations of surgery, anesthesia, aortic cross-clamp, CPB, and circulatory arrest between the two groups.

Table 2. Postoperative Complications

Complication	Active URI, n (%)	Non-URI, n (%)	RR (95% CI), n (%)
Overall*	42 (43.8)	220 (35.7)	1.2 (0.9, 1.6)
Respiratory‡	28 (29.2)†	108 (17.5)	1.7 (1.2, 2.4)
Cardiovascular§	3 (3.1)	16 (2.6)	1.6 (0.5, 4.7)
Surgical‖	10 (10.4)	41 (6.6)	1.5 (0.8, 2.9)
Seizures	4 (4.2)	15 (2.4)	1.7 (0.6, 5.1)
Infection#	5 (5.2)†	6 (1.0)	5.2 (1.7, 17.2)
Mortality	4 (4.2)	10 (1.6)	2.6 (0.8, 8.0)
Multiple	24 (25.0)†	65 (10.5)	2.4 (1.6, 3.6)
Duration of mechanical ventilation, hr (median)	40.3 ± 57.3 (21.5)	30.8 ± 57.4 (19.0)	—
ICU LOS, hr (median)	76.4 ± 89.5† (48.2)	57.7 ± 63.8 (45.0)	—
Hospital LOS, days (median)	8.4 ± 5.1 (7.0)	7.8 ± 5.4 (6.0)	—

* At least one complication. † $P < 0.01$ *vs.* non-URI group. ‡ Nebulized bronchodilators (n = 82), escalation of care including reintubation (53), pneumonia (1 non-URI). § Ventricular dysfunction (18), pulmonary hypertension (2). ‖ Bleeding (11), pericardial effusion (9), diaphragm paresis (9), residual defect (7), multiple surgical (3), other (12). # Urinary tract infection (1), surgical wound infection (10).

CI, confidence interval; ICU, intensive care unit; LOS, length of stay; URI, upper respiratory infection; RR, relative risk.

Per routine practice at our institution, pediatric anesthesiology fellows who were closely supervised by one of six pediatric cardiac anesthesiologists anesthetized all children. Nineteen children (19.8%) in the URI group and 126 (20.4%) in the non-URI group received midazolam as a premedicant (P = NS). Fifty-nine children (61.5%) in the URI group and 426 (69.5%) in the non-URI group underwent anesthetic induction *via* inhalation of a volatile agent (P = NS), and 27 (28.1%) and 92 (15%), respectively, received intramuscular ketamine as an induction agent (P = NS). The remaining children received intravenous ketamine, fentanyl, or propofol for induction of anesthesia with no intergroup differences in induction techniques. All children received 40 mg/kg cefazolin or, if allergic to cephalosporins, 20 mg/kg vancomycin after induction of anesthesia for prevention of subacute bacterial endocarditis. Anesthesia was maintained with a combination of volatile anesthetic (either sevoflurane or isoflurane) with an opioid (either fentanyl or morphine sulfate) in 422 children (68.4%) in the non-URI group and in 68 (70.8%) in the URI group (P = NS). The remaining children in each group received a combination of opioids and a benzodiazepine for maintenance of anesthesia. There were no intergroup differences in the choice of volatile anesthetic, opioid, or benzodiazepine. A humidified circuit was used for all patients as per routine practice. In six patients in the URI group, the anesthesiologist believed that the URI had altered the treatment of the patient. Of these, four children required more frequent suctioning of the endotracheal tube, one child could not be extubated early as planned, and one child experienced laryngospasm on induction of anesthesia.

The overall incidence of airway complications (laryngospasm, bronchospasm, breath holding, and so on) at induction of anesthesia was significantly higher in the URI group compared with the non-URI group (4.2 *vs.* 1.0%; $P = 0.04$). Although children in the URI group experienced a greater decrease in oxygen saturation than those in the non-URI group (87.5 *vs.* 90.3% of baseline, respectively; $P = 0.02$), the number of children who experienced a decrease in oxygen saturation to less than 90% of baseline was not significantly different between groups (50 *vs.* 39%, URI *vs.* non-URI groups; $P = 0.07$). All events were easily managed and resulted in no long-term adverse sequelae. The postoperative care of all children, including extubation and airway and ventilator management, was at the discretion of a pediatric cardiology fellow supervised by a pediatric cardiologist. The cardiologists were not specifically informed regarding the presence or absence of an URI but could have elicited this history from the patient's family or the presurgical evaluations. No specific maneuvers were instituted in the URI group unless indicated by the clinical picture. There were no differences between groups in terms of initial ventilator settings (inspired oxygen concentration, tidal volume, backup rate, or positive end-expiratory pressure) and those 6 h after ICU admission.

The incidences of adverse postoperative outcomes are described in table 2. There were no differences between groups with respect to overall postoperative complications; however, children in the URI group had higher incidences of respiratory complications, multiple complications, and postoperative infections than those in the non-URI group. Overall, 136 (19.1%) children experienced respiratory complications. Of these, 82 (60.3%) required nebulized metered treatments (NMT) for minor wheezing or stridor (42.9 URI *vs.* 64.8% non-URI; $P = 0.057$). Fifty-three (39%) children required reintubation or other escalation of care (57 URI *vs.* 34.3% non-URI; $P = 0.046$). One patient in the non-URI group developed pneumonia. There were no differences in the radiographic evidence for pulmonary opacities between the two groups. On postoperative day (POD) 2, however, there was a significantly higher incidence of pulmonary atelectasis in the URI group compared with the non-URI group (67.9 *vs.* 45.3%; $P = 0.002$). This difference resolved by POD 3. There were no differences between

Table 3. Risk Factors for Postoperative Complications

Complication	Risk Factors	B	Significance
Respiratory Cx	Age	−0.21	0.0000
Infection	Surgical time	0.0002	0.0015
—	URI	1.86	0.0066
—	Age	−1.43	0.0054
Multiple Cx	Surgical time	0.0001	0.0000
—	Weight	−0.79	0.0015
—	URI	0.823	0.0077
—	Baseline Spo_2	−0.033	0.0194
ICU LOS (days)	Hours of ventilation	1.03	0.0001
—	Baseline Spo_2	−0.22	0.022
—	CPB time	0.042	0.033

B, coefficient; CPB, cardiopulmonary bypass; Cx, complications; ICU, intensive care unit; LOS, length of stay; URI, upper respiratory infection; Spo_2, oxygen saturation.

groups in the incidence of positive blood or sputum cultures; however, children in the URI group had a significantly higher incidence of infection (5.2 *vs.* 1.0%; $P < 0.01$). Of the 11 patients who experienced postoperative infections, 10 developed surgical wound infections, and 1 developed a urinary tract infection. In the ICU, there were no differences in patient temperatures between the two groups on the day of surgery and on PODs 1 and 2. There were no significant differences between groups with respect to the time to extubation and overall hospital stay; however, children in the URI group spent significantly longer time in the ICU (table 2).

The outcomes associated with the presence of a URI, *i.e.*, respiratory and multiple complications, infection, and ICU length of stay, were further analyzed to determine the contribution of other factors. The variables examined included ASA status, age, weight, gender, history of respiratory disease, anesthetic agent, type of surgery, CPB times, aortic cross-clamp times, duration of surgery, and baseline oxygen saturation measured by pulse oximetry (Spo_2) values. Variables that were found to be significantly ($P < 0.05$) associated with these outcomes were subsequently analyzed by logistic regression for dichotomous outcomes or by multivariate linear regression for continuous outcomes. The results of these analyses are described in table 3. Multivariate analysis of factors predictive of duration of ventilation revealed young age ($P < 0.0001$), CPB time ($P < 0.0001$), and ASA physical status more than II ($P = 0.035$).

Discussion

Children with congenital heart defects who present for open heart surgery while harboring a URI pose a perplexing clinical dilemma for the surgical team. Although decreased cardiac and respiratory reserve in this population may place these children at increased risk for postoperative complications, the need for surgical expedience may outweigh these risks. Furthermore, it is frequently difficult to distinguish true URI symptoms from those of congestive heart failure, and for some patients it may be prudent to proceed with surgery to prevent further progression of heart failure. Therefore, it is important to identify the potential impact of URI symptoms on postoperative outcomes in this population. Although several studies have addressed this issue in otherwise healthy children, only one previous retrospective study has evaluated the risk of proceeding with surgery in children with URIs undergoing open heart surgery.[7]

Viral respiratory infections have been shown to promote several morphologic and physiologic changes. Although these changes may be of little clinical consequence for the otherwise healthy patient, they may have a profound effect on patients with congenital cardiac anomalies and compromised respiratory and cardiovascular systems. Viral infections have also been shown to increase airway hyperreactivity for 6–8 weeks after infection and may result in increased ventilation–perfusion mismatching, increased closing volumes, and compromised diffusion capacity.[10–13] Together, these effects may exacerbate the adverse pulmonary effects of anesthesia and have important implications for the patient with decreased cardiopulmonary reserve.

Results of this study demonstrated an increase in the incidence of perioperative respiratory complications in children with URIs. However, despite this, all acute events were managed without long-term adverse sequelae. These findings are consistent with several studies that show an increase in the incidence of respiratory events in children with URIs, including laryngospasm, bronchospasm, and oxygen desaturation.[1–3,9,14,15] Children with URIs also had a higher incidence of postoperative respiratory and multiple complications, and infections. The reason for this latter observation is unclear because all postoperative infections were bacterial. However, the children with URIs may have exhibited some degree of immunocompromise that placed them at risk for bacterial infection. This finding is important and may have implications for decisions made regarding choice of pharmaceutical prophylaxis for children with URIs. There was a significantly greater incidence of atelectasis on POD 2 in the URI group compared with the non-URI group. Although this had resolved by POD 3, there is concern that atelectasis may result in increased intrapulmonary shunting and worsening of existing ventilation–perfusion mismatching and hypoxemia in children with congenital heart defects. Furthermore, areas of collapse may serve as a nidus for secondary bacterial infection. In 1979, McGill[16] reported a case series of 11 pediatric patients who suffered intraoperative atelectasis and increased alveolar–arterial oxygen gradients. All but 1 of these patients had a history of URI within 1 month before surgery. Although a cause–effect relationship could not be established, this was thought to have occurred as a result of viral-induced changes in airway secretions.[17]

In a previous retrospective study from our institution, the presence of a URI was found to be a risk factor for overall postoperative complications in children undergoing open heart surgery; however, like the present study, children with URIs had no significant increase in serious morbidity or mortality.[7] One could argue that a 2.5-fold increase in mortality for children with URIs, as we found, is clinically, if not statistically, significant; however, logistic regression using mortality as an endpoint showed no predictive value of a URI. Furthermore, it would take approximately 387 patients per group (80% power) to detect a difference at least as large as that shown in this study.

Although the prospective design of this study reduces the potential biases inherent in our earlier retrospective study, there are, nevertheless, limitations that need to be considered. Specifically, this study was nonrandomized, and observers were not always blinded to the patients' URI status. Although we are sensitive to the potential for selection and observer bias, we believe that any effect would be minimal given the relatively large sample size and the carefully defined and objective endpoints selected.

The criteria used for diagnosis of a URI have been described elsewhere;[8] however, for the purposes of this study, diagnosis of a URI also required confirmation by a parent. This additional requirement was based on the findings of a study by Schreiner *et al.*,[9] indicating that parental confirmation of a URI was a better predictor of laryngospasm than the use of symptom criteria alone.

This study has identified several predictors of postoperative complications in children undergoing open heart surgery for correction of congenital cardiac defects. The presence of a URI was associated with an increased incidence of respiratory complications and an extended stay in the ICU, and was a predictor of postoperative infection and multiple complications. However, all these complications were easily managed and resulted in no long-term sequelae. Given the nature of the underlying heart disease, the need for expedience, and the fact that existing heart failure may confound the diagnosis of a URI, each child should be carefully evaluated on a case-by-case basis, bearing in mind all the risk factors for adverse postoperative outcomes, including the child's age and weight, presence of a URI, baseline arterial saturation, and anticipated durations of surgery and CPB.

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