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Early Pleural Effusions Related to the Myocardial Injury after Open-heart Surgery for Congenital Heart Disease

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Abstract

Objectives—The degree of effusion immediately after cardiopulmonary bypass (CPB) can vary and may reflect several factors including the degree of myocardial injury. We compared the degree of pleural effusions after CPB to the overall myocardial injury as determined by serum cardiac troponin I (cTnI) levels after elective repair of a variety of congenital heart defects, including univentricular surgeries via cavopulmonary shunts.

Methods—Serum was collected pre-CPB, post-CPB, and daily after that and cTnI level measured. The postoperative pleural effusion was measured each day until the chest tube was removed.

Results—The 21 study patients were of average age of 5.5 years (± 5.6). The duration of chest-tube drainage after open-heart surgery was 4.3 days (± 3.5) and the amount was 2.4 mL/kg/hour (± 2.9). For the biventricular repairs, cTnI levels on the postoperative day (POD) 1 best correlated with amount of effusion ($n = 16$, $r = 0.5$, $P = 0.02$) and the average (POD 0–3) cTnI levels with the total duration ($n = 16$, $r = 0.4$, $P = 0.01$) and also the amount ($n = 16$, $r = 0.5$, $P = 0.02$) of effusions. For the cavopulmonary shunts, the post-CPB cTnI level best correlated with the duration ($n = 5$, $r = 0.8$, $P = 0.02$) and amount ($n = 5$, $r = 0.9$, $P = 0.02$) of effusions. A cTnI level on the first postoperative day ≥ 15 $\mu\text{g/L}$ was associated with effusions >2 days (sensitivity of 81% and specificity of 80%).

Conclusion—We found that higher the cTnI released, especially ≥ 15 $\mu\text{g/L}$, longer the duration and greater the amount of early pleural effusions for a variety of congenital heart surgeries including cavopulmonary shunts. A number of factors may lead to excessive pleural effusions and the degree of myocardial injury may be one of them.

Keywords

Cardiac Troponin I; Cardiopulmonary Bypass; Cavopulmonary Shunts; Fontan Surgery; Glenn Surgery; Congenital Cardiac Malformation

Introduction

After cardiopulmonary bypass (CPB), some children have a longer period of postoperative effusions than others, leading to prolonged hospitalization^{1,2} and thereby increasing the risk for infections, other morbidities, and mortality, and thus leading to higher resource utilization. The etiology of these effusions is thought to be multi-factorial, including persistent slow bleeding that may cause gradual accumulation of blood in the pericardial space,^{3–5} warfarin use,³ hemodynamics after the surgery (low blood pressure,⁶ increased central venous pressure^{1,7}), longer CPB time,^{8–10} systemic inflammation⁹ with increased vascular permeability¹¹ leading to overall capillary leak and edema, postpericardiotomy syndrome,³ immune mediation,^{11,12} and postoperative infections.^{1,8}

The ability to predict duration and amount of effusions and to determine the causative factors can improve long-term outcomes. We have previously demonstrated that for all types of surgeries in children, the best independent predictor for postoperative effusion was CPB time when compared with the central venous pressure and systemic inflammation.⁹ Furthermore, for cavopulmonary shunts for a univentricular heart, such as Fontan and Glenn surgeries, where elevated central venous pressure^{1,7} has been associated with effusions; a longer CPB time,^{9,10} lower pulmonary vascular compliance,¹⁰ and low blood pressure requiring fluid resuscitation on first postoperative night⁶ were found to be an independent risk factors for prolonged effusions. For the cavopulmonary shunts, the preoperative pulmonary artery pressure and resistance, thought to be important hemodynamic factors, were not found to predict the effusions postoperatively.¹ Various scoring systems using clinical and laboratory data have been used to predict cardiac patients outcome.^{11,13} However, to our knowledge, there are very few studies in literature regarding the etiology and the ability to predict the amount^{7,9} and duration⁹ of these effusions after CPB for congenital heart defects.

We hypothesized that the length of CPB and the degree of low cardiac output states may be related to the degree of myocardial injury and ischemia as measured by cardiac troponin I (cTnI),¹⁴ and be reflected by the degree of early postoperative effusions for all types of surgeries, including cavopulmonary shunts for univentricular hearts.

Patients and Methods

Study Design

The study was prospective and observational involving pediatric patients who underwent open-heart surgeries at the New York Presbyterian Hospital. The protocol was approved by the Institutional Review Board. Informed written consent from parents was required for enrolling. We carefully maintained full patient confidentiality, safeguarded the rights and welfare of human subjects, and informed subjects confidentially of the results obtained from the study.

Study Population

Children who underwent consecutive and elective open-heart surgery under CPB were recruited prospectively. The inclusion criteria included body weight 5 kg or greater (because of daily blood collection for the study). The exclusion criteria were any emergent surgery and presence of other systemic disease, such as diabetes or systemic lupus erythematosus or recent infections. The following data were collected: demographic data, cardiac diagnoses, types of surgery performed, CPB time, cross clamp time, postoperative parameters including

blood pressure, central venous pressure, use of anticoagulant and inotropes, and occurrence of pericardial effusion.

Surgery

All operations were performed under general anesthesia, via a median sternotomy and CPB. The cardiopulmonary bypass unit included the membrane oxygenator (Terumo, Somerset, NJ, USA), roller pump (Cobe, Arvada, CO, USA), non-heparin coated polyvinyl chloride circuit tubing (Cobe), with an arterial filter (Cobe), and hemoconcentrator (Minntech HP 400, Minneapolis, MN, USA). The cardiopulmonary bypass unit was primed with an electrolyte solution with albumin, mannitol, and heparin and with donor blood as needed. The flow rate was maintained at 2.2 L/min/m² and the hematocrit was maintained at 25%. Myocardial protection was achieved with 15 mL/kg at 4°C of cardioplegia solution containing 5% dextrose water 500 cc with 15 mEq of sodium bicarbonate, 25 cc of 25% mannitol, and 15 mEq of potassium chloride. Hypothermia (19.9–35.7°C) was maintained in every patient. All patients underwent modified ultrafiltration after cardiopulmonary bypass.

Sample Collection

Blood samples were collected using sterile technique from each patient before CPB, within 2 hours after chest closure and early morning of each subsequent day hospitalized in the intensive care unit. The blood was centrifuged for 20 minutes and the serum separated and frozen at –70°C. Serum levels of cTnI were measured in a single batch by microparticle enzyme immunoassay with Abbott AxSYM system, (Abbott Laboratories, Abbott Park, IL, USA).

Postoperative Hemodynamic Monitoring

All patients received routine postoperative care in the intensive care unit. The postoperative days were defined as follows: postoperative day 0 was the day of surgery; postoperative day (POD) 1 was 1 day after the surgery and so forth. The following parameters were followed and recorded: pressor support, number of blood transfusions, urine output, central venous pressure, number of days of intubation, chest tube drainage, number of days of fever, and the laboratory data. Patients were examined further for clinical signs and symptoms of infection and postpericardiotomy syndrome which is characterized by malaise, fever, pericardial effusion, leukocytosis, electrocardiographic abnormalities, and pericardial friction rub after cardiac surgery.

Pleural Effusion

The primary outcomes of interest were duration and volume of effusions after the surgery. The output from the chest and mediastinal drains was selected as surrogate measure of early pleural effusions. In the immediate postoperative period in the intensive care unit, each tube was connected to a disposable water seal drainage system with 20 cm H₂O suction. Chest tubes were frequently milked and stripped in the early postoperative period to ensure tube patency. Patients' chest drainage amounts and the macroscopic appearances of the drainage fluid were noted hourly. The drains were removed when the drainage fluid turned to serosanguineous macroscopically and with significant decrease in output (<2 mL/kg/day) for each tube along with a chest roentgenogram (CXR) that did not show significant residual pleural effusion. The duration of drain output was measured in days from the date of the operation to the final removal of the drains. The volume was measured as the average amount of output expressed in milliliters per kilogram per hour. Patients were evaluated for significant pleural effusions by CXR on the day of drain removal, following day, day of discharge and on return visit to the clinic in 2–4 weeks.

Statistical Analysis

The Spearman's rank correlations were calculated to demonstrate associations between numeric variables between subjects and within subjects. The Mann–Whitney test was carried out to compare all continuous variables. The Fisher's Exact test was carried out to determine association between categorical variables. A *P* value <0.05 was considered significant. The results were expressed as mean values $\pm$ one standard deviation.

Results

The 21 patients (Table 1) were of age 5.5 years (± 5.6 , range 3.5–19). The elective surgeries were (A) biventricular repairs including atrial septal defect repairs (4), ventricular septal defect repairs (4), atrioventricular septal defect repairs (3), supramitral stenosing ring resection (1), tricuspid valve repair (1), tetralogy of Fallot repair (3); and (B) cavopulmonary shunts for univentricular hearts including modified lateral tunnel Fontan procedures without fenestration (4) and the bidirectional Glenn procedure (1). There were no deaths and all patients remained enrolled until the end of the study. All patients enrolled completed the study, none had postoperative renal failure, and there were no deaths. All had normal ventricular systolic function prior to surgery and upon discharge per echocardiogram. The cTnI values in mg/L were as follows: preoperative (*n* = 21, 0.18 ± 0.19 , 0–0.6), post CPB (*n* = 21, 50.5 ± 62.5 , 4.2–222.3), POD 1 (*n* = 16, 28.7 ± 32 , 2.3–105.1), POD 2 (*n* = 15, 22.2 ± 20.2 , 0.6–56.7), POD 3 (*n* = 5, 10.7 ± 11.7 , 1.4–26.7), and POD 4 (*n* = 3, 5.1 ± 3.3 , 0.7–17.1). The CPB time and cross-clamp time did not correlate with post-CPB or postoperative or average cTnI level. There was no significant difference (*P* = 0.2) in cTnI levels between preoperative cyanotic (*n* = 7) and non-cyanotic children (*n* = 14). The length of stay correlated with the number of days of effusions (*n* = 21, *r* = 0.5, *P* = 0.01).

The average duration of pleural effusion after open-heart surgery was 4.3 days (± 3.5 , 1–16, *n* = 21). The average amount of pleural effusion was 2.4 mL/kg/hour (± 2.9 , 0.2–13.6, *n* = 21). All patients with cavopulmonary shunts and two patients with tetralogy of Fallot repair had additional thoracocentesis postoperatively but none required re-exploration for bleeding after surgery. None had chylothorax or exudative effusion, or a hemodynamically significant effusion for greater than 1 month duration. The serum cTnI levels on the POD 1 correlated with other markers of cell injury on the POD 1, aspartate aminotransferase (*n* = 14, *r* = 0.9, *P* = 0.001), lactate dehydrogenase (*n* = 10, *r* = 0.6, *P* = 0.01), a creatine kinase (*n* = 13, *r* = 0.8, *P* = 0.01), and with the amount of effusions (Figure 1) for the biventricular repairs (*n* = 16, *r* = 0.5, *P* = 0.02). For the biventricular repairs the average (POD 0–3) cTnI levels best correlated with the total duration (*n* = 16, *r* = 0.4, *P* = 0.01) and amount (*n* = 16, *r* = 0.5, *P* = 0.02) of effusions (Figure 2). For the cavopulmonary shunts (Figure 3), the post-CPB cTnI level correlated best with the duration (*n* = 5, *r* = 0.8, *P* = 0.02) and amount (*n* = 5, *r* = 0.9, *P* = 0.02) of effusions.

When compared with biventricular repairs, patients with cavopulmonary shunts had significantly higher number of days of inotropic support and blood transfusions, and higher central venous pressure and duration of pleural effusions, although the CPB time, cross-clamp time and cTnI levels after CPB and on the first postoperative day and the number of days of fever did not differ significantly between the two groups (Table 1).

Discussion

In our present study a variety of congenital heart defects with various complexities and different hemodynamic status were evaluated and the degrees of pleural effusions postoperatively were seen to correlate to the cTnI levels. Cardiac troponin I is a specific and sensitive marker for myocardial ischemia and injury.¹⁴ Postoperative cTnI elevation has

been found to reflect intraoperative myocardial acidosis and damage in one study and the investigators found a strong relationship between cTnI, adverse events, and cost after cardiac surgery in adults.¹⁵ Another combined study of 1356 adult and pediatric cardiac surgery patients found cTnI levels at 24 hours as independent predictor of short, medium, and long-term outcomes.¹⁶ Postoperative elevation in serum cTnI levels may be because of several and combined factors including myocardial ischemia-reperfusion injury, systemic inflammatory response, mechanical cardiac trauma, and retransfusion of shed mediastinal blood rich in troponin, during or after the procedure. Myocardial ischemic injury can occur not only from the time spent on CPB, but also to cross clamping the aorta thus reducing the perfusion of the myocardium via the coronary arteries.¹⁷ Thus cTnI level may serve as a better predictor than CPB time alone. Measurement of serum cTnI is preferable over cardiac troponin T because it has the advantage of being uninfluenced by renal failure.^{18,19} The myocardial injury sustained intraoperatively as measured by cardiac troponin is also a major determinant of the postoperative outcomes in children^{18,20–25} including duration of stay at the intensive care unit and length of intubation, as shown in our study and by other investigators. In the present study, the higher the cTnI released, especially 15 µg/L, the longer the duration and greater the amount of postoperative pleural effusions for a variety of congenital heart surgeries including cavopulmonary connections. A cTnI level on the first postoperative day 15 µg/L, could serve as a simple prognostic indicator for of effusions >2 days (sensitivity of 81% and specificity of 80%). The present study is limited by the small number of patients after open-heart surgery for congenital heart defects and the findings need to be confirmed with a larger study population. In conclusion, a number of factors may lead to excessive pleural effusions and the degree of myocardial injury may be one of them.

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Figure 1. Serum cardiac troponin I level ($\mu\text{g/L}$) on first postoperative day and total amount of effusion (mL/kg/hour) for biventricular corrections.

Figure 2. Serum cardiac troponin I level averaged over first 3 postoperative days and total amount of effusion for biventricular corrections.

Figure 3. Serum cardiac troponin I level ($\mu\text{g/L}$) post cardiopulmonary bypass and total amount of effusion (mL/kg/hour) in univentricular corrections with cavopulmonary shunts.

Table 1

Clinical, Operative, and Laboratory Data

Characteristics	All Patients	Biventricular Repair	Cavopulmonary Shunts	P value
N	21	17	5	
Age, years	5.5 (5.6)	5.6 (6)	5.3 (3.8)	0.9
Males, %	52	53	50	0.8
CPB temperature, °C	30.2 (3.8)	31 (3)	27 (4.8)	0.2
CPB time, min	103 (63)	83 (50)	171 (62)	0.3
Cross-clamp time, min	53 (46)	47 (40)	76 (59)	0.4
Aspartate aminotransferase, units/L	153 (401)	67 (40)	395 (787)	0.4
Lactate dehydrogenase, units/L	274 (90)	282 (97)	252 (75)	0.6
Creatine kinase, units/L	593 (460)	669 (505)	347 (40)	0.04
Cardiac troponin I post-CPB, µg/L	50.5 (62.5)	57.5 (70)	28 (23)	0.2
Cardiac troponin I POD 1, µg/L	28.3 (31)	30.8 (36)	20.4 (3.8)	0.3
Cardiac troponin I peak, µg/L	61.2 (32.6)	72.2 (60)	30 (21.8)	0.04
Number of days intubated	1.1 (0.6)	1.1 (0.6)	1.2 (0.4)	0.7
Number of days of inotropic support	1.2 (1.4)	0.9 (1.6)	2 (0)	0.01
Number of days of fever	2 (3)	1.5 (1.8)	3.8 (5.4)	0.4
Number of days of urinary catheter	3.4 (2.9)	2.6 (1.2)	6 (5.1)	0.2
Number of days of pleural effusion	4.3 (3.5)	2.9 (1.7)	9.2 (4.3)	0.03
Amount of pleural effusion (mL/kg/h)	2.3 (2.9)	1.2 (0.8)	5.9 (4.4)	0.07
Blood transfusion, n (%)	17 (77)	12 (71)	5 (100)	0.02
CVP POD 1, mm Hg	12 (5.7)	10 (4.8)	18 (3.5)	0.003
CVP peak, mm Hg	13 (5.4)	11 (4.6)	18.6 (2.8)	<0.001

All values are in mean (standard deviation) unless specified.

P value between biventricular repair and cavopulmonary shunts.

CPB, cardiopulmonary bypass; CVP, central venous pressure; ICU, intensive care unit; POD, postoperative day.