Outcome of pediatric cardiac surgery and predictors of major complication in a developing country

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ABSTRACT

Background : **Evaluating outcome and identifying predictors of major complications among children undergoing cardiac surgery are essential to improve care. We evaluated short-term outcomes of postcardiac surgery and predictors of major complications in a national referral hospital in Indonesia.**

Methods : **A prospective cohort study was conducted from April 2014 to March 2015 on all children undergoing cardiac surgery. Participants were followed up from the time of surgery until hospital discharge and 30-day mortality. We performed univariate and multivariate logistic regression using STATA 12.1 to identify predictors of postsurgical major complications.**

Results : **A total of 257 patients (median age: 36 months) were recruited; 217 (84.1%) had complications, including low cardiac output syndrome (19.8%), arrhythmia (18.6%), sepsis (17.4%), and pleural effusion (14.8%). Forty-nine (19%) patients had major complications, including cardiac arrest (5%), need for emergency chest opening (3.9%), and multiple organ failure (7.4%). 12.8% died during hospital stay, and 30-day mortality was 13.6%. Predictors of major complications were cyanotic congenital heart disease (odds ratio [OR]: 4.6, 95% confidence interval [CI]: 1.5–14.2), longer duration of cardiopulmonary bypass (CPB, OR: 4.4, 95% CI: 1.5–13.4), high inotropes (OR: 13.1, 95% CI: 3.2–54.2), and increase in lactate >0.75 mmol/L/h or more in the first 24 h (OR: 37.1, 95% CI: 10.1–136.3).**

Conclusion : **One-fifth of children undergoing cardiac surgery experienced major complications with around 13% mortality. Cyanotic congenital heart disease, longer duration of CPB, high inotropes on leaving operating theater, and increase in blood lactate are associated with major complications in children after cardiac surgery.**

Keywords : Cardiac surgery, children, complication, mortality, outcome, predictor

INTRODUCTION

The performance of pediatric cardiac surgery programs should be continually evaluated to improve the quality of patient care.[1] Outcomes of pediatric cardiac surgery are well described in high-income countries; however, data from low-to-middle-income countries have been limited. Mortality has been used as a robust indicator to evaluate

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the quality of pediatric cardiac surgery care.[2] However, morbidities or complications after cardiac surgery may serve an additional indicator to determine the quality of cardiac surgical services.[2]

In low-to-middle-income countries, limitations of human resources and facilities for cardiac surgery and postoperative management may adversely affect the outcomes of the pediatric cardiac surgery. Major complications are often preceded by a period of inadequate oxygen balance, and identifying the oxygen imbalance is challenging in children after cardiac surgery.[3,4] Therefore, knowing the predictors for major complication is important to formulate a preventive strategy for major complications after cardiac surgery and to improve care. Given limited data, studies are needed to identify predictors for adverse outcomes of pediatric cardiac surgery performed. This study aimed to evaluate the outcomes and predictors for major complications in children undergoing cardiac surgery as initial problems at a national referral hospital of cardiac service in Indonesia.

METHODS

Study design and population

A prospective cohort study was conducted in cardiac intensive care unit (CICU), Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia, between April 2014 and March 2015. Dr. Cipto Mangunkusumo National General Hospital is the national referral hospital in Indonesia. The CICU is an 8-bed unit providing postoperative care for both adult and pediatric patients and is managed by intensivist and pediatric cardiac intensivist. There are two pediatric cardiac surgeons in this hospital. The hospital started working on pediatric cardiac care in 2002. This study had been approved by the Ethics Committee of the University of Indonesia, Jakarta, Indonesia. The ethics committees did not require individual patient consent, but all parents of children in the ward were informed of the study.

We consecutively enrolled pediatric patients admitted to CICU after cardiac surgery for both congenital and acquired heart diseases. All participating children were monitored daily from the time of surgery performed until they were discharged or died to identify the presence of complication after cardiac surgery. Complications were defined based on the multisocietal database committee for pediatric and congenital heart disease criteria.[5] Factors associated with the development of major complications were identified.

Data collection

We collected data using a standardized form to record major complications, which included death, multiorgan dysfunction, cardiac arrest, and need for emergency chest opening. We also recorded baseline characteristics of patients, clinical signs or symptoms, the outcomes of cardiac surgery, and potential predictors of major complications after surgery. Risk Adjustment for Congenital Heart Surgery-1 (RACHS-1) category was used to compare outcome data for children undergoing cardiac surgery.

Five potential predictors were included as follow: preoperative congestive heart failure, cyanotic congenital heart disease, longer duration of cardiopulmonary bypass (CPB) (>120 min), high inotropic drug requirement on discharge from operating room, and increase in blood lactate level (>0.75 mmol/L/h or more in the first 24 h after cardiac surgery).[3,6] High inotropic drug requirement was defined as the use of at least two types of drugs with high doses (≥10 mcg/kg/min of dopamine or dobutamine, or epinephrine or norepinephrine at least 0.1 mcg/kg/min, or milrinone at least 0.5 mcg/kg/min).

Outcome measures

We set inhospital mortality, 30-day mortality, and the incidence of complications including major complications after cardiac surgery as the primary outcomes. A 30-day mortality was defined when death occurred outside of the hospital but within 30 days after cardiac surgery performed. Complication was defined as a deviation from the expected outcome of cardiac surgery.[7] In addition, we secondarily looked at factors to predict the development of major complications after pediatric cardiac surgery in children in Indonesia.

Data analysis

We first described baseline data and outcomes using mean, median, or proportions as appropriate. We first performed univariate analysis using the Chi-square test to determine the association between each predictor and the occurrence of major complications. We further conducted a multivariate logistic regression to determine predictors which were independently associated with major complications after cardiac surgery. All potential predictors, including all variables found to be statistically significant on the univariable analysis, were included in the multivariable model. Findings are presented as odds ratios with corresponding 95% confidence intervals (CIs) and *P* values. The Hosmer–Lemeshow test was used to check for goodness of fit for logistic regression model.

Data analysis was performed using STATA version 12.1, StataCorp LP, College Station, Texas, USA. $P < 0.05$ or a CI not including 1 was considered as statistically significant.

RESULTS

Two hundred and fifty-seven patients were enrolled. Their baseline characteristics are described in Table 1. Most patients were undernourished and about half had

failure to thrive. The most common congenital heart operation performed was ventricular septal defect (VSD) repair (28.7%), and the most common cyanotic congenital heart disease surgery was for tetralogy of Fallot (TOF) repair, which comprised 24.4% of the total procedures. The majority of patients who underwent definitive cardiac surgery were included in the RACHS-1 category 2 (84.4%). Approximately more than 10% of children had long duration of mechanical ventilation (>7 days) and hospital stay (>14 days) [Table 2].

Most patients (84.1%) experienced some postoperative complications. The most common complication was hypocalcemia (63%), hyperglycemia (61.5%), low cardiac output syndrome (LCOS) (19.8%), arrhythmia (18.6%), nosocomial bloodstream infections or sepsis (17.4%), and pleural effusion (14.8%) [Table 3]. Around 13% of all blood cultures obtained were positive and the causes of nosocomial bloodstream infections were mostly Gram-negative bacteria including *Acinetobacter baumannii, Escherichia coli,* and *Klebsiella pneumoniae.* The incidences of postoperative arrhythmia and total atrioventricular (AV) block in our cohort were 18.6 and 5.8%, respectively.

About one-fifth (19%) developed at least one major complication after cardiac surgery during the follow-up. In-hospital mortality occurred in 33 (12.8%) and a 30-day mortality in 35 (13.6%) children after cardiac surgery [Table 4]. Two patients died within 30 days after cardiac surgery outside the hospital, including a patient with congenitally corrected transposition of the great arteries (TGAs) undergoing bidirectional cavopulmonary shunt (BCPS), and one patient following repair of complete atrio ventricular septal defect (CAVSD). The possible causes of death were recurrent massive pleural effusion in the patient after BCPS procedure and total AV block in the patient with CAVSD repair.

We evaluated five potential predictors to predict major complications after cardiac surgery among these children. The univariate analysis identified that all predictors were significantly associated with the development of major complications. In the multivariate logistic regression analysis, cyanotic congenital heart disease, longer duration of CPB, high inotropic drugs on leaving operating room, and increased blood lactate level were independently associated with the development of major complications after cardiac surgery. Cyanotic congenital heart disease and longer duration of CPB were associated with around 4-fold higher risk in the probability of developing major complications, while high inotropic drugs on discharge from operating theater and increased blood lactate level were independently associated with around 13- and 30-fold increased risk, respectively [Table 5].

Table 1: Baseline characteristics

Characteristics	*n*=257
Sex, *n* (%)	
Female	134 (52.1)
Age, median in months (minimal-maximal)	36 (0.5-211)
Nutritional state, *n* (%)	
Undernourished	149 (58)
Normal	98 (38.1)
Overweight	10 (3.9)
Failure to thrive, *n* (%)	68 (26.5)
Syndrome, *n* (%)	20 (7.8)
Diagnosis, *n* (%)	
Ventricular septal defect	74 (28.7)
Tetralogy of Fallot	63 (24.5)
Atrial septal defect	23 (8.9)
Mitral stenosis or regurgitation	17 (6.6)
DORV	16 (6.2)
Single ventricle	12 (4.7)
Atrioventricular septal defect	9 (3.5)
PA-VSD	8 (3.1)
PA-IVS	6 (2.3)
Patent ductus arteriosus	5 (1.9)
TGA-VSD	4 (1.6)
TGA-IVS	4 (1.6)
TAPVD or PAPVD	4 (1.6)
Tricuspid atresia	3 (1.2)
Ebstein's anomaly	3 (1.2)
Mitral atresia	2 (0.8)
Truncus arteriosus	1 (0.4)
Others	3 (1.2)
Definitive operation, *n* (%)	200 (77.5)
RACHS-1, *n* (%)	
Category 1	24 (9.4)
Category 2	217 (84.4)
Category 3	5 (1.9)
Category 4	9 (3.5)
Category 5	2 (0.8)

SD: Standard deviation, CI: Confidence interval, PA-VSD: Pulmonary atresia with ventricular septal defect, PA-IVS: Pulmonary atresia with intact ventricular septum, DORV: Double outlet right ventricular, TGA-VSD: Transposition of the great arteries with ventricular septal defect, TGA-IVS: Transposition of the great arteries with intact ventricular septum, TAPVD: Total anamolous pulmonary venous drainage, PAPVD: Partial anamolous pulmonary venous drainage, RACHS-1: Risk Adjustment for Congenital Heart Surgery-1

Table 2: Outcomes of pediatric cardiac surgery

Outcomes	*n*=257
Use of CPB, *n* (%)	204 (79.4)
CPB time, median (min), minimal-maximal	75 (17-313)
Aortic clamp time, median (min), minimal-maximal	35 (6-239)
ICU stay, median (h), minimal-maximal	24 (5-960)
Duration of mechanical ventilation, median (h), minimal-maximal	18 (2-912)
Use of ventilator >7 days, *n* (%)	27 (10.5)
Hospital stay, median (days), minimal-maximal	6 (1-120)
Hospital stay ≥14 days, *n* (%)	40 (15.5)

CPB: Cardiopulmonary bypass, ICU: Intensive care unit

DISCUSSIONS

As far as we are aware, this study was the first study in Indonesia evaluating the outcomes of children after cardiac surgery, demonstrating an inhospital mortality of 12.8%. Mortality rates after surgery differ markedly depending on the complexity and severity of cases attempted, comorbidities (such as malnutrition and

Table 3: Proportion of complications after pediatric cardiac surgery

Type of complications	*n*=257
Readmission, *n* (%)	9 (3.5)
Multiple organ dysfunctions, *n* (%)	19 (7.4)
Shock, *n* (%)	4 (1.6)
Cardiac complications, *n* (%)	85 (33.1)
Low cardiac output syndrome	51 (19.8)
Metabolic acidosis	65 (25.3)
Pericardial effusion	2 (0.8)
Pulmonary hypertension	19 (7.4)
Pulmonary hypertension crisis	8 (3.1)
Cardiac tamponade	2 (0.8)
Procedure complications, *n* (%)	36 (14)
Bleeding	28 (10.9)
Need for emergency chest reopening	10 (3.9)
Arrhythmia, *n* (%)	48 (18.6)
Lung complications, *n* (%)	78 (30.4)
Acute respiratory distress syndrome	11 (4.3)
Atelectasis	16 (6.2)
Chylothorax	5 (1.9)
Diaphragm paralysis	4 (1.6)
Pleural effusion	38 (14.8)
Pneumonia	15 (5.8)
Pneumothorax	2 (0.8)
Reintubation	7 (2.7)
Pulmonary edema	2 (0.8)
Vocal cord dysfunction	8 (3.1)
Renal complications, *n* (%)	68 (26.4)
Renal dysfunction	36 (14)
Acute renal failure	32 (12.4)
Infections, *n* (%)	45 (17.5)
Sepsis	45 (17.5)
Wound infection	6 (2.3)
Systemic inflammatory response syndrome, *n* (%)	50 (19.5)
Neurological complications, *n* (%)	20 (7.8)
Encephalopathy	7 (2.7)
Neurological deficit	9 (3.5)
Seizure	10 (3.9)
Gastrointestinal complications, *n* (%)	9 (3.5)
Ascites	1 (0.4)
Gastrointestinal bleeding	7 (2.7)
Necrotic enterocolitis	1 (0.4)
Endocrine complications, *n* (%)	205 (79.8)
Hypocalcemia	162 (63)
Hypoglycemia	35 (13.6)
Hyperglycemia	158 (61.5)
Vascular complications, *n* (%)	2 (0.8)
Superior vena cava syndrome	2 (0.8)

chronic infections), as well as the quality of surgery and postoperative care.[8]

A study in other developing countries found mortality of similar or lower levels to us: Iran (12.4%),[9] Guatemala (10.7%),[10] India (7.9%),[11] and China (5.5%).[12] In large pediatric cardiac services in high-income countries, mortality after cardiac surgery in children has been reported to be <5%.[13] There is an inverse relationship between volume of cardiac surgery performed and mortality. Compared with units that perform more than 300 operations annually, units with around 101 cases/year were associated with increased mortality of 3-fold, whereas those with <10 cardiac surgery cases per year were associated with an 8-fold increased mortality.[14] In addition, the surgeons should recognize a learning curve when undertaking new surgical procedure. Introduction of a new procedure using training courses and expert assistance might reduce the learning curve.[15]

The 30-day mortality rate in our study was 13.6%. The highest mortality among our patients occurred in those undergoing an arterial switch operation for TGA with VSD and TGA with intact ventricular septum. In our study, the most common cause for mortality was pulmonary hypertension, which often resulted from delayed timing of surgery associated with late presentations of children with congenital heart diseases. Most patients who died after arterial switch operation mostly suffered from pulmonary hypertensive crisis, which is challenging to deal with in setting with limited resources.

The incidence of complications in our patients was as high as 81%, which was relatively high compared to previously published studies. This may be caused by different definitions of complications, in which we included endocrine complications after cardiac surgery, such as hypocalcemia, hyperglycemia, and hypoglycemia, which were rarely accounted in previous studies as such complications could physiologically occur after cardiac surgery using CPB. Hyperglycemia and hypocalcemia occurred in >60% patients after cardiac surgery in our study. This was similar to findings reported by other studies in developing countries.[16,17] When we excluded the endocrine complication, the incidence of complication after cardiac surgery in our patients decreased to 44%. The most complications occurring after cardiac surgery were LCOS, arrhythmia, nosocomial sepsis, and pleural effusion.

Finding from this study shows that the incidence of LCOS was similar to other studies, which was 25%–32% in patients after cardiac surgery.[18] The management of children after cardiac surgery includes avoiding factors contributed to the development of LCOS. These include maintaining adequate preload, using vasoactive drugs to improve contractility, and maintaining systemic and pulmonary vascular resistance.[7,18] In our hospital, when managing LCOS, we used inotropic and inodilator drugs simultaneously including dopamine, epinephrine, norepinephrine, and milrinone.

Total AV block occurred in 5.8% patients after TOF correction, CAVSD repair, and VSD closure. This is in accordance with a previous study that total AV block commonly occurred in patients with TOF, CAVSD, and VSD as the conduction system located along those defects, which had injured.[19]

Another frequent postoperative complication is nosocomial bloodstream infections or sepsis, which occurred in 17.4% children after cardiac surgery. This incidence is much higher compared to a previous

study, which only found 8.6% patients suffered from nosocomial sepsis.[20] Gram-negative sepsis is prevalent in children with postoperative bloodstream infections in low-to-middle-income countries and is associated with significant morbidity, higher mortality, and development of antibiotic resistance. Practical steps can be taken to make surgery safer since good nutrition, early corrective surgery, and measures to reduce nosocomial infection are likely to play a role.[21]

We identified factors predicting the development of major complications after cardiac surgery to guide further preventative strategies. Predictors for developing major complications in our study were cyanotic congenital heart disease, longer duration of CPB, high inotropic drugs on leaving operating theater, and increase in blood lactate.

In patients with cyanotic congenital heart disease, especially those suffering from complex heart lesions usually need longer surgery and CPB time because of higher surgical complexity. They might suffer from severe metabolic acidosis and tissue hypoxemia, which is likely to predispose them for mortality.[9] The presence of cyanotic congenital heart disease is an intrinsic factor that cannot be controlled in increasing the risk of developing major complications after cardiac surgery, but it can raise awareness to mitigate harmful outcomes.

The use of high inotropes on leaving operating room was associated with mortality and cardiac arrest in children after cardiac surgery. The more severe the hemodynamic state, the lower the cardiac index, and therefore, higher inotropic support was needed.[22]

Increase in blood lactate could reflect the presence of anaerobic metabolism, which is caused by inadequate oxygenation, reduced oxygen delivery, or cellular hypoxia. Increase in blood lactate >0.75 mmol/L can predict early outcome of neonates after cardiac surgery with high specificity[6] but low sensitivity since this might physiologically reflect hyperlactatemia after CPB and impaired lactate clearance.[4]

This finding highlights the need for comprehensive interventions to improve the quality of pediatric cardiac surgery services and reduce mortality and other major complications among children after cardiac surgery by preventing the occurrence of clinical conditions that required longer CPB, high inotropes, and caused increase in blood lactate after cardiac surgery.

Some facts in developing world related to cardiac surgery program include competing priorities, poor structural organizations, lack of financial resources, lack of trained human resources, and absence of stable training and education infrastructure.[13] These require an effective policy response to make efforts for improving quality of cardiac surgery program in such low-to-middle-income countries. Attempts should be conducted earlier before the actual implementation of the cardiac surgery and critical care program. These include training in pediatric cardiac surgery and critical care in low-and-middle-income countries from well-established pediatric cardiac center program in high-income countries. In addition, a model of mentoring physicians

Table 4: Proportion of major complications after pediatric cardiac surgery

Major complication	*n*=257
Major complications, *n* (%)	49 (19)
Death	35 (13.6)
Cardiac arrest	13 (5)
Re-operation	10 (3.9)
Multiple organ dysfunction	19 (7.4)
Mortality based on diagnosis, *n* (%)	
TGA-VSD	2/4 (50)
TGA-IVS	2/4 (50)
Mitral atresia	1/2 (50)
Single ventricular	5/12 (41.7)
Ebstein's anomaly	1/3 (33.3)
Tricuspid atresia	1/3 (33.3)
Atrioventricular septal defect	3/9 (33.3)
PA-VSD	2/8 (25)
TAPVD	1/4 (25)
Double outlet right ventricular	3/16 (18.8)
PA-IVS	1/6 (16.7)
Tetralogy of Fallot	8/63 (11)
Mitral stenosis or regurgitation	2/18 (11)
Truncus arteriosus	0/1 (0)
Ventricular septal defect	0/74 (0)
Atrial septal defect/patent ductus arteriosus	0/28 (0)

PA-VSD: Pulmonary atresia with ventricular septal defect, PA-IVS: Pulmonary atresia with intact ventricular septum, DORV: Double outlet right ventricular, TGA-VSD: Transposition of the great arteries with ventricular septal defect, TGA-IVS: Transposition of the great arteries with intact ventricular septum, TAPVD: Total anomaly pulmonary venous drainage

Table 5: Predictors of major complications after pediatric cardiac surgery

Predictors	Major complication (*n*=49)	Without major complication (*n*=208)	Unadjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Preoperative, *n* (%)						
Congestive heart failure	6 (12.2)	16 (7.6)	1.6 (0.6-4.5)	0.31		
Cyanotic CHD	40 (81.6)	81 (31.5)	7 (3.2-15.1)	<0.0001	4.6 (1.5-14.2)	0.007
Intra-operative, *n* (%)						
Duration of CPB >120 min	24 (50)	28 (13.5)	6.2 (3.1-12.3)	<0.0001	4.4 (1.5-13.4)	0.008
High inotropic support	25 (51)	4 (2)	53.1 (17.1-165.6)	<0.0001	13.1 (3.2-54.2)	<0.001
Postoperative, *n* (%)						
Increase in lactate in 1 h	46 (93.9)	32 (15.3)	84.3 (24.7-287.7)	<0.0001	37.1 (10.1-136.3)	<0.0001

CHD: Congenital heart disease, CPB: Cardiopulmonary bypass, OR: Odds ratio, CI: Confidence interval

and other staff from well-established centers to establish high-quality referral and cardiac training centers in low-to-middle-income countries is needed. Furthermore, a member of subspecialties from low-and-middle-income countries should visit a well-established cardiac center to observe the unit or participate in overseas training or education programs.[23-26]

Limitation of this study is that this study was performed in a single national referral hospital and therefore may not represent the status of other hospitals in Indonesia. Howeverare it is likely that practices in Jakarta are not so different from other referral hospitals which provide pediatric cardiac surgery services. To be generalizable, this study should be reproduced in other tertiary referral hospitals in Indonesia and other low-to-middle-income countries. Other limitations are lactate clearance time, and venous oxygen saturation (SvO_2) was not measured routinely in conjunction with blood lactate examination after cardiac surgery. A SvO_2 may suggest different pathophysiology of tissue hypoxia compared to lactate.[4] An abnormality in SvO_2 could be present without an abnormality in blood lactate and therefore might explain small changes in lactate and improve the accuracy of blood lactate in predicting major complications after cardiac surgery.[4]

CONCLUSION

Approximately one-fifth of children undergoing cardiac surgery at a national referral hospital in Indonesia had major adverse events and around 13% died. Cyanotic congenital heart disease, longer duration of CPB, high inotropes on leaving operating room, and increase in blood lactate were associated with increased risk of mortality and developing other major complications in children after cardiac surgery.

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Conflicts of interest

There are no conflicts of interest.

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