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ORIGINAL ARTICLE

Preoperative Factors as a Predictor for Early Postoperative Outcomes After Repair of Congenital Transposition of the Great Arteries

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Abstract Transposition of the great arteries (TGA) requires early surgical repair during the neonatal period. Several preoperative factors have been identified for the postoperative poor outcome after arterial switch operation (ASO). However, the data remain uncertain an association. Therefore, we investigated the preoperative factors which affect the early postoperative outcomes. Between March 2005 and May 2012, a retrospective study was performed which included 126 infants with an ASO for TGA. Preoperative data included the vasoactive inotropic score (VIS) and baseline hemodynamics. Early postoperative outcomes included the duration of mechanical ventilation, the length of stay in the intensive care unit and hospital, and early mortality. Multivariate linear regression and receiver operating characteristics analysis were performed. The duration of mechanical ventilation was significantly correlated with the preoperative mechanical ventilator support and VIS, and CPB time. On multivariate linear regression analysis, a higher preoperative VIS, preoperative B-type natriuretic peptide (BNP) level, and the CPB time were identified as independent risk factors for delayed mechanical ventilation. Preoperative VIS (OR 1.154, 95 % CI 1.024–1.300) and the CPB time (OR 1.034, 95 % CI 1.009–1.060) were independent parameters predicting early mortality. A preoperative VIS of 12.5 had the best combined sensitivity (83.3 %) and specificity (85.3 %) and an AUC of 0.852 (95 % CI 0.642–1.061) predicted early mortality. Our results suggest that preoperative VIS and BNP can predict the need for prolonged postoperative mechanical ventilation. Moreover, preoperative VIS may be used as a simple and feasible indicator for predicting early mortality.

Keywords Arterial switch operation · Early mortality · Mechanical ventilation · Transposition of the great arteries · Vasoactive inotropic score

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Introduction

Transposition of the great arteries (TGA) is a ventriculoarterial discordant lesion in which the aorta arises from the right ventricle and the pulmonary artery from the left ventricle. TGA accounts for almost 20 % of all cyanotic congenital heart disease [7], and requires early surgical repair during the neonatal period. Delaying the surgery allows the left ventricle to pump against the lower resistance pulmonary circulation, which may result in myocardial deconditioning [6]. In such patients, postoperative exposure of the left ventricle to an acute pressure load associated with systemic vascular resistance can cause acute ventricular failure, which results in poor outcomes. Ma et al. [19] reported that most of death after congenital heart surgery occurred in infants and less than 1 year of age, especially in the newborn period of 30 days or less. In these patients, the most common cause of death after congenital heart surgery was reported to be low cardiac output syndrome [19], because of immature neonatal myocardium [1].

It has been known that risk factors for mortality after the arterial switch operation (ASO) have identified as prematurity, the presence of other congenital heart defects; such as hypoplasia of the right ventricle or aortic arch, pulmonary stenosis and an abnormal coronary artery pattern, longer cardiopulmonary bypass (CPB) time, postoperative serum lactate level, and the need for postoperative inotropic support [2, 11, 22]. Gottlieb et al. [11] concluded that even with a technically satisfactory operation, these anatomic factors remain to be associated with mortality after ASO. The association of prematurity and a poor outcome for infants with congenital heart disease, in particular ASO, has been found in many other studies [5, 16], the risks associated with preterm birth, such as necrotizing enterocolitis and acute and chronic respiratory insufficiency [23]. However, the data remain uncertain an association with preoperative factors related to the patient's clinical status and early postoperative outcomes after ASO.

Therefore, we investigated which preoperative factors can affect the early postoperative outcomes after surgery for TGA. The aim of this study is to investigate the preoperative factors affecting the early postoperative outcomes in infants undergoing surgery for TGA.

Methods

Patients

Between March 2005 and May 2012, we evaluated 126 patients (range 1–90 days) who had undergone ASO for TGA at Asan Medical center, Seoul, Korea. During the time period of our study, the same two surgeons performed 126 ASO. Patients were excluded if they had a concomitant congenital heart defect, such as hypoplasia of the right ventricle, aortic arch obstruction (hypoplasia, coarctation, and interruption), or pulmonary stenosis or if they were less than 37 weeks of gestational age. The dextro type of TGA was included and the congenitally corrected TGA was excluded. All patients were diagnosed using fetal ultrasonography and were confirmed after birth by echocardiography or cardiac computed tomography. We retrospectively collected all perioperative variables from medical records. The study was approved by our institutional review broad.

Perioperative Variables

Patient demographics included age and weight at the time of surgery, and associated anatomic variables as follows: such as the presence or absence of a ventricular septal defect or an atrial septal defect. Preoperative data included the need for balloon atrial septostomy or mechanical ventilator support, arterial oxygen saturation at ward, mean blood pressure, heart rate, and vasoactive inotropic score (VIS). In addition, the preoperative hemoglobin and B-type natriuretic peptide (BNP) were analyzed the day before surgery. Intraoperative data included the duration of CPB and the fluids administered during surgery. Postoperatively, we also investigated the need for cardiac pacing, extracorporeal membrane oxygenation (ECMO) and peritoneal dialysis, serum lactate level within 1 h after admission to the intensive care units (ICU), and postoperative VIS during the first 48 h after surgery. The inotropic score was first described in the Boston Circulatory Arrest Study performed to quantify the amount of pharmacologic cardiovascular support required after ASO [25]. Gaies et al. [8] proposed expanding the inotropic score to include other commonly used vasoactive medications, such as milrinone, vasopressin, and norepinephrine, and termed it a VIS as follows; (dopamine [μg/kg/min]) + (dobutamine [μg/kg/min]) + (10,000 × vasopressin [U/kg/min]) + (10 × milrinone [μg/kg/min]) + (100 × epinephrine [μg/kg/min]) + (100 × norepinephrine [μg/kg/min]) [8].

Early Postoperative Outcomes

We were primarily interested in whether preoperative clinical variables were associated with the early postoperative outcomes. Early postoperative outcomes included the duration of mechanical ventilation, the length of stay in the ICU and hospital, and early mortality. Early mortality was defined as death before hospital discharge or within 30 days of ASO. If a patient failed extubation, they were excluded from the statistical analysis for the duration of mechanical ventilation and early mortality.

Statistical Analysis

The parametric and nonparametric statistical tests were used. Data were described as frequencies, median with ranges or interquartile range (IQR). We chose to analyze appropriate factors that associated with early postoperative outcomes. Univariate analysis was performed to determine which factors were associated with prolonged duration of mechanical ventilation using linear or logistic regression analyses. Logistic regression analyses were also performed in order to identify the factors associated with early mortality. All factors associated with early postoperative outcomes, as identified on univariate analysis with p value less than or equal to 0.1 were subsequently included in a multivariate linear and logistic regression analysis. Receiver operating characteristics (ROC) analyses were used to determine any significant relationship between preoperative factors and worse early postoperative outcomes, and we also calculated the area under the curve (AUC). The

Table 1 Demographic data, perioperative risk factors and postoperative outcomes ($n = 115$)

Variable	Value
Preoperative factors	
Age (days)	6 (1–90)
Weight (kg)	3.2 (2.0–5.3)
Sex (M/F)	80/35 (69.6/30.4 %)
ASD (no/yes)	92/23 (80.0/20.0 %)
VSD (no/yes)	81/34 (70.4/29.6 %)
BAS (no/yes)	78/37 (67.8/32.2 %)
Mechanical ventilation (no/yes)	69/46 (60.0/40.0 %)
SaO2 (%)	89 (60–98)
MBP (mmHg)	45 (32–70)
HR (beats/min)	158 (108–181)
VIS	6 (0–45)
Hb (g/l)	13.5 (6.0–19.5)
BNP (pg/ml)	2,025.0 (25–10,276)
Serum lactate (mmol/l)	1.9 (0.5–7.8)
Creatinine	0.6 (0.1–1.1)
Intraoperative factors	
CPB time (min)	130 (92–19,509)
Crystalloid (ml)	45 (0–210)
Postoperative factors	
Serum lactate (mmol/l)	2.5 (0.8–12.3)
VIS	15 (0–64)
Postoperative outcomes	
Mechanical ventilation (hours)	65 (23–521)
Length of stay in the ICU (days)	5 (2–75)
Length of stay in the hospital (days)	9 (6–105)
Early mortality	6 (5.2 %)

Values are the median (range) or the number of patients (%)

ASD atrial septal defect, *VSD* ventricular septal defect, *BAS* balloon atrial septostomy, *SaO2* arterial oxygen saturation, *MBP* mean blood pressure, *HR* heart rate, *VIS* vasoactive inotropic score, *Hb* hemoglobin, *BNP* B-type natriuretic peptide, *CPB* cardiopulmonary bypass, *ICU* intensive care unit

significant variable was categorized into two groups according to the cutoff value, which was defined in this study. We then compared two groups using the *t* test or the Chi-squared test. A value less than or equal to 0.05 was considered significant. Analyses were performed using SPSS version 18.0 software (SPSS Inc., Chicago, IL, USA).

Results

Of 126 patients, 11 were excluded, because seven had aortic arch obstruction and four had pulmonary stenosis. Therefore, we analyzed the data of 115 patients. The demographic characteristics and perioperative variables were shown in Table 1. The median preoperative VIS was 6.0 [IQR 0–7], and 67 (58.3 %) patients did not require preoperative inotropic support. The median period of CPB was 130 [IQR 110–153] minutes.

Table 2 Preoperative risk factors associated with increased duration of mechanical ventilation and early mortality

Variable	Duration of mechanical ventilation		Early mortality	
	Beta	*p* value	Beta	*p* value
Age (days)	−0.096	0.323	0.134	0.316
Weight (kg)	−0.071	0.463	2.457	0.025
ASD	−0.001	0.854	−0.235	0.834
VSD	0.000	0.932	−0.775	0.487
BAS	−0.003	0.367	0.791	0.348
Mechanical ventilation	0.230	0.016	2.115	0.057
SaO2 (%)	−0.027	0.801	−0.009	0.888
MBP (mmHg)	0.144	0.184	0.005	0.993
HR (beats/min)	0.068	0.511	−0.040	0.400
VIS	0.385	0.000	−0.117	0.000
Hb (g/l)	−0.041	0.670	−0.158	0.460
BNP (pg/ml)	0.169	0.092	0.000	0.520
Serum lactate (mmol/l)	0.329	0.008	−0.479	0.52

ASD atrial septal defect, *VSD* ventricular septal defect, *BAS* balloon atrial septostomy, *SaO2* arterial oxygen saturation, *MBP* mean blood pressure, *HR* heart rate, *VIS* vasoactive inotropic score, *Hb* hemoglobin, *BNP* B-type natriuretic peptide

The median duration of mechanical ventilation postoperatively was 65 [IQR 45–96] hours (Table 1). Initial tracheal extubation failed in one infant, who required an additional 11 days of mechanical ventilation. The duration of mechanical ventilation was significantly correlated with preoperative need for mechanical ventilator support ($p = 0.016$), VIS ($p < 0.001$) and BNP ($p = 0.092$), and lactate ($p = 0.008$) (Table 2). The preoperative mean blood pressure ($p = 0.184$) and heart rate ($p = 0.511$) were not associated with prolonged duration of mechanical ventilation. Especially, preoperative VIS was associated with a higher postoperative serum lactate level ($p = 0.002$) and VIS ($p = 0.002$), which were significant associated with delayed mechanical ventilation ($p = 0.014$ and $p = 0.001$, respectively). Postoperative temporary pacing was needed for 3 (2.4 %) patients, and ECMO and peritoneal dialysis were required for 6 (4.8 %) and 51 (40.5 %) patients, respectively. However, there was no statistically significant difference.

Of the patients, six patients (5.2 %) died before hospital discharge (Table 1). We were unable to wean two infants from CPB. They were placed on mechanical cardiac support in the ICU, and died on postoperative days one and three, respectively. On logistic regression, a higher preoperative VIS ($p < 0.001$) and the need for mechanical ventilator support ($p = 0.057$) and less body weight ($p = 0.025$) were associated with early mortality (Table 2).

Table 3 Multivariate analysis of factors independently predicting delayed mechanical ventilation and early mortality after ASO

Variable	Duration of mechanical ventilation		Early mortality	
	Beta	*p* value	OR	*p* value
Preoperative VIS	0.635	<0.001	1.154	<0.001
Preoperative BNP (pg/ml)	0.323	0.005		

VIS vasoactive inotropic score, *BNP* B-type natriuretic peptide, *OR* odd ratio

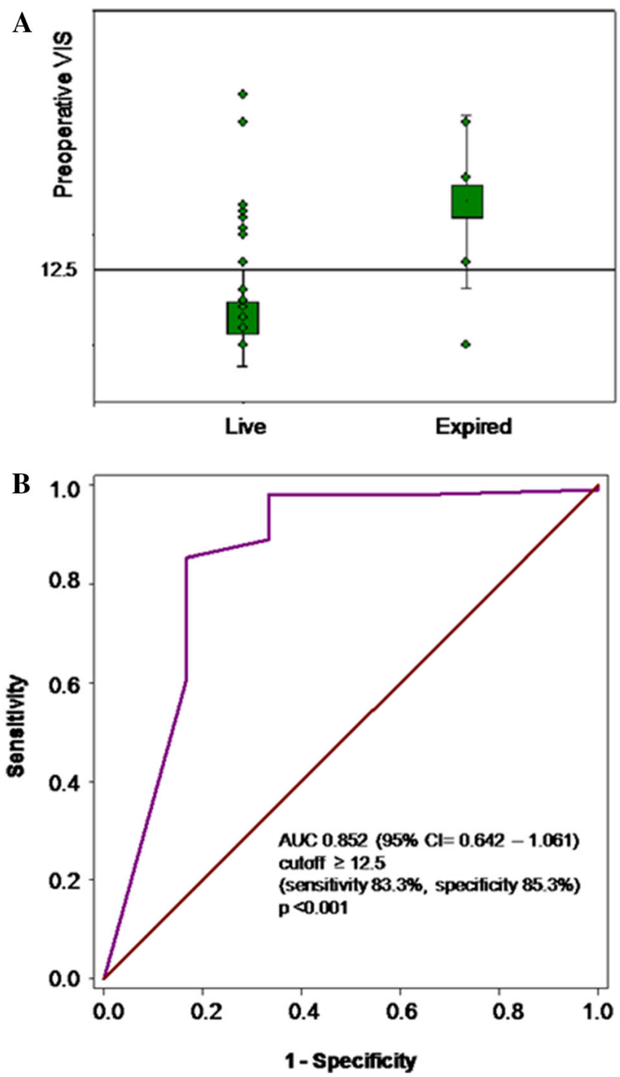

Fig. 1 Interactive *dot* diagram showing the individual values of preoperative VIS (4.9 vs 25.8) in patients (**a**). Based on ROC curve analysis, it was observed that a preoperative VIS higher than 12.5 predicted early postoperative mortality (**b**)

On multivariate linear regression analysis, higher preoperative VIS (95 % CI 3.604–7.885) and high preoperative BNP level (95 % CI 0.004–0.020) were identified independent preoperative risk factors for delayed mechanical ventilation (Table 3). On stepwise multivariate logistic regression analysis, only a higher preoperative VIS (OR 1.154, 95 % CI 1.024–1.300) was an independent risk factor for early mortality (Table 3).

A ROC curve analysis was performed to identify the preoperative VIS that best predicted early mortality. A preoperative VIS of 12.5 had the best combined sensitivity (83.3 %) and specificity (85.3 %), and the AUC was 0.852 (95 % CI 0.642–1.061) (Fig. 1). Patients with a higher preoperative VIS (>12.5) had a lower arterial oxygen saturation at ward (87.2 vs 83.5 %, $p = 0.050$), required balloon atrial septostomy (27.6 vs 52.3 %, $p = 0.032$) or preoperative mechanical ventilator support (28.7 vs 90.4 %, $p < 0.001$) (Table 4).

Table 4 Preoperative factors associated with preoperative VIS

Variable	VIS ≤ 12.5 (*n* = 94)	VIS > 12.5 (*n* = 21)	*p* value
Sex (M/F)	66 (82.5)/28 (80.0)	14 (17.5)/7 (20.0)	0.750
Age (days)	6.5 (1–90)	4 (1–17)	0.067
Body weight (kg)	3.2 (2.1–5.3)	3.1 (2.0–4.1)	0.257
ASD (*n*)	22 (23.4 %)	1 (4.7 %)	0.086
VSD (*n*)	31 (32.9 %)	3 (14.2 %)	0.101
BAS (*n*)	26 (27.6 %)	11 (52.3 %)	0.032
SaO_2 (%)	89 (69–98)	85 (60–95)	0.050
Mechanical ventilation	27 (28.7 %)	19 (90.4 %)	<0.001

Values are median (range) or number of patients (percentage)

ASD atrial septal defect, *VSD* ventricular septal defect, *BAS* balloon atrial septostomy, SaO_2 arterial oxygen saturation

Discussion

These results suggest that higher preoperative VIS and BNP may be associated with prolonged duration of mechanical ventilation. In addition, higher preoperative VIS may be independently associated with early mortality.

In congenital heart surgery patients, a substantial number of infants and children who died from a low cardiac output state had ventricular failure [20]. Poor right ventricular failure was strongly associated with late death [9], and congestive heart failure was the most common cause of death in adults with TGA [4]. Therefore, the ventricular function has been considered to be very important in predicting the patient outcome after cardiac surgery [4, 12].

In the present study, we found that preoperative VIS was associated with postoperative serum lactate level and postoperative VIS. Xi Wang et al. [18] recently reported that low body weight at the time of surgery, a longer CPB time, a high postoperative serum lactate level, a higher postoperative inotropic score, and hematocrit on postoperative 1 day were associated with prolonged recovery among infants undergoing ASO. Similarly, we found that a higher postoperative serum lactate level and VIS were associated with prolonged recovery, especially a prolonged duration of mechanical ventilation. Nonetheless, there is limited information about the preoperative clinical risk factors affecting early outcomes after ASO. The importance of our study is that we have found that preoperative VIS was an independent risk factor associated with the prolonged duration of mechanical ventilation as well as early mortality. The VIS was to quantify the amount of cardiovascular support [8], with a higher VIS considered to indicate poor ventricular function. Butts et al. [3] reported that postoperative maximum VIS, although superior to low cardiac output syndrome, has only a modest correlation with the length of postoperative mechanical ventilation, the postoperative ICU stay, and the total hospital charges. Collectively, our study suggests that preoperative VIS, which is able to quantify preoperative ventricular dysfunction, may be a simple and feasible indicator predicting early postoperative outcomes.

We found some evidence that the preoperative VIS was associated with preoperative ventricular function and a patient's critical condition. Based on ROC curve analysis, we observed that a preoperative VIS higher than 12.5 predicted early mortality. A higher preoperative VIS may be associated with a greater need for preoperative mechanical ventilator support, balloon atrial septostomy, and low arterial oxygen saturation. Neonates with TGA were provided adequate initial treatment which is stabilized cardiac and pulmonary function and maintained adequate systemic oxygenation. Because infants with TGA have limited mixing of oxygenated and deoxygenated blood [21], they needed mechanical ventilator support and balloon atrial septostomy in order to maintain adequate systemic oxygenation, and inotropic support was required to augment cardiac output and maintain adequate systemic blood pressure. The preoperative hemodynamic condition, rather than preoperative noncardiac condition, was more important for the early outcomes of congenital heart surgery [24]. This result emphasizes that the preoperative hemodynamic condition is more important for the early outcomes of ASO.

We found that preoperative BNP was associated with the duration of mechanical ventilation, although it was not associated with early mortality. In general, plasma BNP concentration was increasingly used to aid the diagnosis and to assess the prognosis in adults with congestive heart failure [13]. However, some data dealing with BNP in neonates and children suggested that BNP is also useful in pediatric patients [14]. Koch A and Singer H [15] reported that the plasma BNP concentrations in newborns and infants were relatively high, vary greatly, and decreased rapidly during the first weeks of life. They speculated that perinatal circulatory changes lead to an increase in left ventricular volume and pressure load, it may stimulate BNP synthesis and secretion. In addition, they found that BNP was associated with age, sex, renin concentration, plasma renin activity, concentration of aldosterone, and other steroids [10, 15, 17]. Accordingly, elevated BNP may be limited reflecting the degree of ventricular dysfunction and for predicting early postoperative outcomes in neonates.

This study has some limitations. First, this is a single-center study and the surgery was performed by only two pediatric cardiac surgeons who were very skillful. Second, the data were retrospectively reviewed, and the ventricular function and ventricular mass on echocardiography were not measured. In addition, the preoperative clinical risk factors were only compared with two early outcome measures. In previous studies, it was found that preoperative anatomic risk factors, such as aortic arch obstruction, hypoplastic right ventricle, and ventricular septal defect were associated with mortality after ASO [11, 22, 23]. The abnormal coronary pattern still remains controversial [11, 23]. In our study, however, anatomic risk factors were excluded except for ventricular septal defect, which was not associated with early mortality. Their relationship to other early and late outcomes warrants further investigation. Finally, as none of our patients underwent cardiac catheterization, therefore we could not directly measure the cardiac output. Further studies with a prospective design should be performed to assess directly the cardiac output and be evaluated association between preoperative VIS and cardiac output.

Conclusion

Our results suggest that preoperative VIS and BNP can predict prolonged postoperative mechanical ventilation. Moreover, preoperative VIS may be used as a simple and feasible indicator to predict early mortality.

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