Evaluation of risk factors affecting morbidity in patients who underwent surgical closure of ventricular septal defect

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Abstract

Objective: Surgical closure of ventricular septal defect is still the most common pediatric cardiac surgical procedure. The aim of this study was to define the risk factors of the complications of ventricular septal defect surgery. Methods: We evaluated the preoperative, perioperative, and postoperative data from echocardiography reports, perfusion reports, and clinical, inpatient, and operative notes of all the patients. The following were the outcome variables for this study: in-hospital death; duration of mechanical ventilation in hours; duration of pediatric intensive care unit stay in days; and duration of hospital stay in days. Herein, we report our single pediatric cardiac center experience between October 2015 and October 2018. Results: A total of 108 patients underwent surgical ventricular septal defect closure during the study period. Prolonged pediatric intensive care unit stay, hospital stay and mechanical ventilation time was associated with younger age and low weight. The patients with genetic syndromes had statistically longer mechanical ventilation time ($p < 0.001$), pediatric intensive care unit stay ($p < 0.001$), and hospital stay ($p = 0.002$). Conclusion: Although genetic syndromes did not affect the complication rates, it affected the lengths of hospital and pediatric intensive care unit stays and mechanical ventilation duration. Young age and lower body weight was a risk factor of prolonged hospitalization, prolonged pediatric intensive care unit stay and prolonged mechanical ventilation. Therefore, these situations should be considered in the postoperative follow-up of patients with ventricular septal defect.

Introduction

Ventricular septal defect is the most common cardiac defect and accounts for 25% of all congenital heart diseases. Large ventricular septal defects with excessive pulmonary blood flow are responsible for dyspnea, feeding difficulties, poor growth, recurrent pulmonary infections, and cardiac failure in early infancy. For these reasons, large ventricular septal defects cause significant morbidity and mortality in infants [1]. Surgical closure of ventricular septal defect is still the most common pediatric cardiac surgical procedure. Recent advances in surgical techniques and postoperative patient care have led to a reduction in mortality and morbidity [2]. However, complications still occur, and the risk factors associated with these complications must be identified [3]. Some studies have found that low birth weight and young age (<6 months) at the time of the operation are related to morbidity [2]. However, this finding conradicts those reported in some studies [4]. The aim of this study was to evaluate the outcomes of ventricular septal defect surgery in our center and to define the risk factors of the complications of ventricular septal defect surgery.

Methods

We reviewed a series of patients who underwent surgical ventricular septal defect closure between October 1, 2015, and October 1, 2018. Patients with a concomitant atrial septal defect, patent ductus arteriosus, patent foramen ovale, and stenotic/regurgitate semilunar valves were included. Patients with all other complex cardiac anomalies were excluded. Patients who received prior pulmonary artery banding were included in this study.

One hundred eight patients met the inclusion criteria. We evaluated the preoperative, perioperative, and postoperative data from the echocardiography reports, perfusion reports, and clinical, inpatient, and operative notes of all the patients.

The patients' preoperative characteristics, including sex, cardiac and non-cardiac comorbidities, age at operation, body weight at operation, type of ventricular septal defect, and underlying genetic condition, were examined. The ventricular septal defect types were subdivided into three groups based on transthoracic echocardiography findings of perimembranous, muscular, and infundibular defects. The outcome variables in this study were as follows: in-hospital death, mechanical ventilation (MV) duration in hours, pediatric intensive care unit (PICU) stay duration in days, hospital stay duration in days, pediatric index of mortality 2 (PIM-2), and pediatric risk of mortality 3 (PRISM-3). The postoperative complications included acute kidney injury, pleural effusion requiring chest tube placement, atelectasis, junctional ectopic tachycardia, complete atrioventricular block, and major adverse events. The significant major adverse events included unplanned reoperation, complete heart block requiring implantation of a permanent pacemaker, sudden cardiac arrest, and death. Acute kidney injury is defined in accordance with the pRIFLE (pediatric risk, injury, failure, loss, end-stage renal disease) criteria [5]. The MV duration was considered to be prolonged if it lasted >6 hours, and an extended PICU or hospital stay lasted >3 and 7 days, respectively [3, 6].

The mediastinum was accessed through a median sternotomy in all the operations. The operation was performed under a moderate hypothermic cardiopulmonary bypass with aortic and bicaval cannulations and antegrade blood cardioplegia. All the operations were performed by the same two surgeons. All ventricular septal defect closures were accomplished with a polytetrafluoroethylene patch using the interrupted suture technique. The surgical approach to the ventricular septal defect was through the right atrium in 104 patients, pulmonary arteriotomy in 2, and aortotomy in 2. Transesophageal echocardiography was routinely used except in the patients with contraindications such as patient size or esophageal stenosis. Concomitant atrial septal defect repair, patent foramen ovale closure, patent ductus arteriosus ligation and/or division, valvuloplasty, and vascular ring repair were performed when indicated.

Statistical analyses were performed using the Statistical Package for the Social Sciences version 24.0 software (Armonk, NY: IBM Corp). The normal distribution of the variables was evaluated using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov and Shapiro-Wilk test). A descriptive analysis was performed using frequency tables for the categorical variables, while means and standard deviations were used to describe the normally distributed variables. Medians and ranges were used to describe the variables with a non-normal distribution. The effects of genetic syndrome on outcome variables were assessed with the Mann-Whitney U test. Receiver-operating characteristic (ROC) analysis was performed to determine the effects of age and weight, and the cutoff values for the development of complications. The risk factors that affected the patients' outcomes were examined with a logistic regression analysis.

Results

A total of 108 patients underwent surgical ventricular septal defect closure during the study period. Their demographic characteristics are presented in Table 1. Their median age at operation was 11.5 months (range, 1.5–156 months). Of the patients, 61 (56.5%) were male and 47 (43.5%) were female. The median body weight of the patients was 7 kg (range, 3.2–60 kg) at the time of operation. The most common defect was perimembranous ventricular septal defect (n = 90, 83.3%), followed by infundibular ventricular septal defect (n = 16, 14.9%) and muscular ventricular septal defect (n = 2, 1.9%). The most frequent concomitant cardiac defects were patent ductus arteriosus (n = 42, 38.9%) and atrial septal defect (n = 31, 28.7%). Genetic anomalies were present in 17 patients (15.7%); the most common genetic anomaly was Down syndrome (n

= 11, 10.2%). Of all the patients, 13.9% (n = 15) had undergone pulmonary artery banding prior to the ventricular septal defect repair. The mean cardiopulmonary bypass time was 61 ± 17 minutes (range, 20–109 minutes). The mean aortic cross-clamp time was 46 ± 15 minutes (range, 16–87 minutes).

Table 2 summarizes the examined complications and outcomes. The median (range) MV duration, PICU stay, and hospital stay of the patients were 2 hours (1–56 hours), 3 days (1–34 days), and 5 days (2–66 days), respectively. Prolonged MV occurred in 11 patients (10.2%); prolonged PICU stay, in 65 patients (60.2%); and delayed discharge, in 37 patients (34.3%). Pulmonary complications such as atelectasis and pleural effusion requiring chest tube placement were the most frequent (n = 8, 7.4%), followed by acute kidney injury (n = 6, 5.6%) and heart rhythm problems (n = 4, 3.7%) such as transient atrioventricular block and junctional ectopic tachycardia. In the patients with pleural effusion, the fluid was serous. None of the patients died, had a significant residual defect, and had a persistent heart block requiring placement of a permanent pacemaker. One patient experienced a major adverse event (sudden cardiac arrest). The patient with genetic syndromes had a significant congestive heart failure preoperatively. In addition, the body weight during the operation was 3,400 g.

The effects of genetic syndrome are presented in Table 3. The patients with genetic syndromes had statistically longer MV times ($p < 0.001$), PICU stay ($p < 0.001$), and hospital stay ($p = 0.002$).

The univariate analysis results are shown in Table 3. In the analysis, while the PICU hospitalization stay, hospitalization duration, and MV duration were longer in the patients with complications, their ages and weights were lower and initiation times of nutritional therapy were later. The patients with prolonged PICU stay, hospital stay, and MV duration had similar chacteristics to those with complications but had lower ages and weights and later initiation times of nutritional therapy. In the patients with prolonged hospitalization, the PIM-2 score, PRISM score, and MV duration were also longer. In addition, the PRISM score was higher in the patients who needed prolonged MV. The results of the ROC analysis performed to determine the effects of age and weight, and the cutoff values for the development of complications are shown in Figure 1. The area under the curve was 0.76 for age and 0.76 for body weight. The cutoff age of 5 months had 76% sensitivity and 71% specificity, and the cutoff weight of 5.8 kg had 74% sensitivity and 71% specificity.

A multivariable model was used to assess the association between a patient's characteristics and prolonged MV time, or prolonged PICU or hospital stay (Table 4). Prolonged PICU stay was associated with MV time of patients (odds ratio [OR], 0.9; 95% confidence interval [CI], -1.22–3.03; $p < 0.001$), and nutritional therapy time (OR, 0.05; 95% CI, 0.01–0.1; $p = 0.044$). Prolonged hospital stay was associated with MV time of patients (OR, 0.6; 95% CI, 0.44–0.74; $p < 0.001$). Prolonged MV time was associated with nutritional therapy time (OR, 0.25; 95% CI, 0.13–0.35; $p < 0.001$) and, PRISM score (OR, 0.43; 95% CI, 0.16–0.7; $p = 0.002$).

Discussion

Many factors affect the morbidity and mortality in surgical ventricular septal defect closure. In most patients, surgeon experience and the anatomical location of the ventricular septal defect are as important as the patient's clinical state in deciding whether to perform an early surgical ventricular septal defect closure. Owing to the heterogeneous patient distribution that occurs with the combination of these factors that affect surgical outcomes, questions are raised in surgical planning. Despite the multifactorial features of patients and the improvements in the surgical and perfusion approaches, outcomes in terms of mortality and morbidity have been improving. Although total correction of ventricular septal defect in patients with a younger age and lower body weight sometimes seem to be ambiguous and risky for cardiac surgeons and cardiologists, it is the first-choice approach with the advances in congenital heart surgery. Palliative pulmonary artery banding has lost importance together with complete repair in children with symptomatic ventricular septal defect and pulmonary overcirculation. It is no longer the preferred palliative surgical approach because of complete repair can now be performed safely at a younger age and in patients with lower body weights. In the decision making on the surgical timing during the follow-up period, the first factor should be the clinical condition of the patient with ventricular septal defect. By contrast, given the improvements of the results of neonatal total corrective surgery, the pediatric cardiologist challenges the surgeon to proceed with surgical closure of symptomatic ventricular septal defects in ever smaller patients [4]. Although surgical ventricular septal defect closure in patients low body weights and ages (<6 months) can be safely performed with a low incidence of complications, no clear consensus has been reached on the timing of surgical ventricular septal defect closure.

Currently, surgical ventricular septal defect closure seems to be a reasonably safe procedure, with near-zero hospital mortality and low complication rates. However, mortality and prolonged PICU or hospital stay due to complications have still been reported. According to previous studies, the mortality rate ranges from 0% to 2.8%, reoperation rates due to residual defects range from 0% to 4.9%, pacemaker implantation rates range from 0% to 5.6%, and major adverse event rates range from 2.9% to 5.9% [2–4, 6–8]. In this study, none of the patients died, had a residual defect requiring reoperation, and needed a permanent pacemaker, and the incidence of major adverse event was 0.9%. In fact, on postoperative echocardiography, none of the patients had a residual ventricular septal defect of [?]2 mm in size.

Schipper et al. found that genetic syndrome was associated with MV and PICU hospitalization times [3]. Similarly, Anderson et al. reported a strong relationship between genetic syndromes and prolonged hospitalization in their study [2]. In this study, we found that patients with genetic syndromes had longer hospitalization ($p = 0.002$), PICU hospitalization ($p < 0.001$), and MV durations ($p < 0.001$).

In the study of Anderson et al., patients who received delayed postoperative nutrition had longer postoperative hospitalization and MV durations [9]. Sahu et al. found that early nutritional therapy was associated with decreased ventilation duration, infection rate, length of hospital stay, lenght of ICU stay, and mortality [10]. Similarly, in our study, prolonged PICU stay, hospital stay, and MV duration, as well as the occurrence of complications, were associated with the initiation time of nutritional therapy.

Despite the development of surgical techniques and perfusion technology, some studies have shown that morbidity was higher in infants with lower body weights and ages < 6 months. In their study, Anderson et al. found that those who were aged >6 months had less hospitalizations and lower risk of temporary or permanent heart block. In addition, higher body weight during operation was associated with a significant decrease in the incidence of postoperative bleeding. Again, in the group aged <6 months, the ICU hospitalization duration decreased by 2.3 days in every kilogram increase in body weight, and the complication rate increased 1.8 times in every kilogram loss of body weight [2]. In the study of Schipper et al., patients who weighed <6 kg had longer postoperative ICU hospitalization and MV durations [3]. In a study conducted by Kogon et al., body weight did not affect the operation, aortic cross-clamp, bypass, and MV times, and complication rate [4]. Aydemir et al. showed no significant difference between age groups in terms of morbidity [7]. Ergun et al. showed that the increase in body weight was associated with the decrease in the risk of major adverse events and shortened ICU and hospital stays. In the study, <4-kg body weight was a risk factor of prolonged MV time [6]. Vaidyanathan et al. found that younger age was associated with longer ICU and hospital stays. In this study, no effects of body weight and height Z scores were demonstrated [11].

In our study, the univariate analysis revealed lower age and weight in the patients with complications and prolonged ICU and hospitalization stays, and MV duration. In terms of the presence of complications, the cutoff age and weight were 5 months and 5.8 kg, respectively, similar to those in other studies.

In the study of Mildh et al., in a population-based group of patients who underwent pediatric open-heart surgery, PRISM proved to be a poor tool for risk stratification owing to its low discrimination and calibration values [12]. The PIM-2 measures demonstrated good performance regarding the capacity to discriminate between survivors and non-survivors in a population of patients with postoperative congenital heart disease in the study of Rezende et al [13]. These studies only provided information about the effects of the PIM and PRISM score systems on mortality. We evaluated the effects of these scoring systems on morbidity. In our study, prolonged hospitalization was associated with higher PIM-2 and PRISM scores. In addition, the PRISM score was found to be higher in the patients who needed prolonged MV.

In the multivariable analysis of our study, prolonged PICU stay was associated with MV time of patients (odds ratio [OR], 0.9; 95% confidence interval [CI], -1.22–3.03; $p < 0.001$), and nutritional therapy time (OR, 0.05; 95% CI, 0.01–0.1; $p = 0.044$). Prolonged hospital stay was associated with MV time of patients (OR, 0.6; 95% CI, 0.44–0.74; $p < 0.001$). Prolonged MV time was associated with nutritional therapy time (OR, 0.25; 95% CI, 0.13–0.35; $p < 0.001$) and, PRISM score (OR, 0.43; 95% CI, 0.16–0.7; $p = 0.002$). In this respect, multicenter studies may provide more-precise results.

The limitations of our study are that it had a retrospective design and was conducted in a single center. The other limitations of the study are the absence of long-term follow-up, small number of patients with major adverse events, and absence of mortality cases.

Conclusion

As shown earlier, ventricular septal defect closure operations are safe surgical procedures with low mortality and morbidity rates. Although the presence of genetic syndrome did not affect the complication rates, it affected the length of hospital and PICU stays and MV duration. Young age and lower body weight was a risk factor of prolonged hospitalization, prolonged pediatric intensive care unit stay and prolonged mechanical ventilation.

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Ethical Standards: This retrospective study was approved by our institutional ethics committee (file reference:32/6/2016) and conducted in accordance with the principles of the Declaration of Helsinki.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from

the corresponding author upon reasonable request.

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Tables and Figures

Table 1. Patients' demographic characteristics and operative variables

Variable	**Variable**	**Patients (n = 108)**
Age (months), median (range)	Age (months), median (range)	11,5 (1,5–156)
Weight (kg), median (range)	Weight (kg), median (range)	7 (3,2–60)
Female, n (%)	Female, n (%)	47 (43,5)
Type of ventricular septal defect, n (%)	Perimembranous	90 (83,3)
	Infundibular	16 (14,9)
	Muscular	2 (1,9)
Genetic syndrome, n (%)	Down syndrome	11 (10,2)
	Others	6 (5,5)
Pulmonary artery banding before surgery, n (%)	Pulmonary artery banding before surgery, n (%)	15 (13,9)
Bypass time (min), mean ± SD	Bypass time (min), mean ± SD	61 ± 17
Aortic cross-clamp time (min), mean ± SD	Aortic cross-clamp time (min), mean ± SD	46 ± 15

SD, standard deviation.

Table 2. Postoperative outcomes and complications

Outcomes	**Outcomes**	**Patients**
MV time (hours), median (range)	MV time (hours), median (range)	2 (1–56)
PICU hospitalization duration (days), median (range)	PICU hospitalization duration (days), median (range)	3 (1–34)
Total hospitalization duration (days), median (range)	Total hospitalization duration (days), median (range)	5 (2–66)
Total complications, n (%)	Total complications, n (%)	18 (16,6)
Death, n (%)	Death, n (%)	-

Outcomes	Outcomes	Patients
Complications	**Complications**	**Patients**
Respiratory event, n (%)	Pulmonary atelectasis	4 (3,7)
	Pleural effusion required chest tube	3 (2,8)
Acute kidney injury, n (%)	Acute kidney injury, n (%)	5 (4,6)
Arrhythmia, n (%)	Junctional ectopic tachycardia	1 (0,9)
	Transient complete AV block	3 (2,8)
	Permanent complete AV block	-
Need for treatment of pulmonary hypertension, n (%)	Need for treatment of pulmonary hypertension, n (%)	1 (0,9)
Major adverse event, n (%)	Major adverse event, n (%)	1 (0,9)
Reoperation for residual VSD, n (%)	Reoperation for residual VSD, n (%)	-

AV, atrioventricular; MV, mechanical ventilation; PICU, pediatric intensive care unit; VSD, ventricular septal defect.

Table 3. Univariate analysis of complications and prolonged ventilation time, intensive care unit (ICU) stay, and hospital stay

Complication	p Value
MV time (hours)	<0.001
PICU hospitalization duration (days)	0.033
Total hospitalization duration (days)	0.007
Age (months)	0.003
Weight (kg)	0.003
PRISM score	0.039
Nutritional therapy time (hours)	0.007
Genetic syndrome	
MV time (hours)	<0.001
PICU hospitalization duration (days)	<0.001
Total hospitalization duration (days)	0.002
Prolonged hospital stay	
Age (months)	0.001
Weight (kg)	0.009
Nutritional therapy time (hours)	0.028
Prolonged PICU stay	
Age (months)	<0.001
PIM-2 score	0.033
PRISM score	0.015
Weight (kg)	<0.001
MV time (hours)	0.004
Nutritional therapy time (hours)	0.002
Prolonged MV	
Age (months)	0.036
PRISM score	0.001
Weight (kg)	0.006
Nutritional therapy time (hours)	0.002

MV, mechanical ventilation; PICU, pediatric intensive care unit; PIM, pediatric index of mortality; PRISM, pediatric risk of mortality

Table 4. Multivariate analysis to determine the independent predictive factors of pediatric intensive care unit and hospital stay times

Dependent variable and predictive factor	Dependent variable and predictive factor	Odds ratio (95% CI)
Length of PICU stay	MV time (per hour)	0,9 (-1,22–3,03)
	Nutritional therapy time (per hour)	0,05 (0,01–0,10)
Length of hospital stay	MV time (per hour)	0,6 (0,44–0,74)
MV time	Nutritional therapy time (per hour)	0,25 (0,13–0,35)
	PRISM (per unit)	0,43 (0,16–0,7)

CI, confidence interval; MV, mechanical ventilation; PICU, pediatric intensive care unit; PRISM, pediatric risk of mortality.

Figure 1. Receiver-operating characteristic (ROC) analysis of the effects of age and weight and the cutoff values for the development of complications.