Early and Mid-term Results of Patients Who Underwent Surgical Repair of Ventricular Septal Defect After The Infantile Period

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ABSTRACT

Introduction: The purpose of this study is to evaluate the mortality, morbidity, postoperative course, and mid-term complications of patients who underwent surgical repair of ventricular septal defect (VSD) after the infantile period.

Patients and Methods: We retrospectively reviewed 80 patients, older than 1 year, who were operated in our center between 2014 and 2018. We defined "prolonged" as the condition in which the mechanical ventilation was more than 24 hours, ICU stay was longer than 3 days, and hospital stay was longer than 7 days. We considered cardiopulmonary resuscitation, need for extracorporeal membrane oxygenator, complete atrioventricular block requiring permanent pacemaker (PM) implantation, diaphragm paralysis, neurological complications, acute renal failure, and unplanned reoperation as the major adverse events (MAE).

Results: The median age of patients was 3 (1.5-20) years. There were 31 (38.8%) female patients in our study. The median operation weight was 12.3 kg (8-60). Indications for operations were pulmonary hypertension (PH) in 30 (37.5%) patients, aortic regurgitation and aortic valve prolapse in 30 (37.5%) patients, and left ventricular (LV) dilatation in 20 (25%) patients. We did not observe mortality in any of the cases. We observed MAE only in one patient (1.3%) (PM implantation). The mean follow-up period was 2.9 ± 1.9 years. Pulmonary arterial pressure decreased significantly after surgery (20% vs. 0% of patients with severe PH, $p < 0.001$). Left ventricular end-diastolic diameters (LVEDDs) were significantly decreased after operation, and this condition persisted in the mid-term follow-ups (LVEDD: 36.9 ± 9.7 vs. 33.0 ± 6.6, $p= 0.02$).

Conclusion: Patients with VSD who are awaiting spontaneous closure after the infantile age are highly recommended to undergo rigorous follow-ups. A meticulous examination of patients with late onset VSD preoperatively with a prompt referral to surgery will maintain satisfactory outcomes in early and late mortality and morbidity rates.

Key Words: Ventricular septal defect; long term; mortality; morbidity

İnfantil Dönem Sonrası Cerrahi Tamir Yapılan Ventriküler Septal Defektli Hastaların Erken ve Orta Dönem Sonuçları

ÖZET

Giriş: Bu çalışmada infantil dönem sonrası opere edilen ventriküler septal defekt hastalarının mortalite, morbidite gelişimi, postoperatif seyir ve orta dönem komplikasyon açısından değerlendirilmesi amaçlandı.

Hastalar ve Yöntem: Merkezimizde 2014-2018 yılları arasında ventriküler septal defekt (VSD) tanısı ile opere edilmiş bir yaş üstü 80 hasta retrospektif olarak incelendi. Uzamış mekanik ventilasyon > 24 saat, uzamış yoğun bakım > 3 gün, uzamış hastane kalışı ise > 7 gün olarak kabul edildi. İstenmeyen yeniden operasyon, kalıcı bir kalp pilini gerektiren kalp bloğu, mekanik destek ihtiyacı, nörolojik defisit, diyafram paralizisi ve ani dolaşım durması majör advers olay olarak kabul edildi.

Bulgular: Ortanca yaş 3 (1.5-20) yıl idi. Hastaların 31 (%38.8)'i kız idi. Ortanca operasyon kilosu 12.3 kg (8-60) idi. Operasyon endikasyonu 30 (%37.5) hastada pulmoner hipertansiyon, 30 (%37.5) hastada aort kapak yetmezliği ve prolapsusu, 20 (%25) hastada ise sol ventrikül genişlemesi olarak saptanmıştır. Operasyona bağlı mortalite gözlenmemiştir. Majör advers olay bir hastada (pacemaker implantasyonu) (%1.3) gözlenmiştir. Hastaların ortalama takip süresi 2.9 ± 1.9 yıl saptanmıştır. Takipte pulmoner arter basınç düzeyi operasyon sonrası dönemde operasyon öncesi döneme göre anlamlı düşmüştür (ileri PHT'li hasta sayısı %20 vs. %0, $p< 0.001$). Operasyon sonrası erken dönemde sol ventrikül sonu diyastolik çaplarında belirgin azalma gözlendiği ve bu durumun orta dönemde de devam ettiği görülmüştür (36.9 ± 9.7 vs. 33.0 ± 6.6, $p= 0.02$).

Cite this article as: *Ergün S, Yıldız O, Güneş M, Kük Özalp ZG, Öztürk E, Onan İS, et al. Early and mid-term results of patients who underwent surgical repair of ventricular septal defect after the infantile period. Koşuyolu Heart J 2020;23(1):9-14.*

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Submitted: 23.10.2019
Accepted: 17.12.2019
Available Online Date: 30.04.2020

Sonuç: İnfantil dönem sonrası VSD tanılı olgularda spontan kapanmanın beklendiği hastaların takiplerinin titizlikle yapılması ve geç başvuran hastaların preoperatif ayrıntılı şekilde değerlendirilmesi ve cerrahi tamire uygun hastaların bekletilmeden opere edilmesi erken ve uzun dönem mortalite ve morbiditeye olumlu katkı sağlayacaktır.

Anahtar Kelimeler: Ventriküler septal defekt; mortalite; majör advers olay; morbidite; uzun dönem

INTRODUCTION

The surgical treatment of ventricular septal defect (VSD) is currently the standard treatment for VSD, which has a low mortality rate. Surgery is performed successfully in patients with symptoms such as congestive heart failure, growth retardation, and frequent lung infection despite medical treatment; however, the surgeries of patients with small and moderate VSDs is delayed for spontaneous closure. There are also patients who could not be operated due to delayed admission to the hospital. These patients are at a greater risk for developing complications such as aortic insufficiency (AI) and pulmonary hypertension (PH). Moreover, some publications have reported that the results of patients undergoing early and late surgeries in terms of mortality and morbidity are similar[1]. The purpose of this study is to evaluate the mortality, morbidity development, postoperative course, and mid-term complications of patients with VSD who were operated after the infantile period.

PATIENTS and METHODS

Ethics committee approval was received for this study from the Ethics Committee of the Istanbul Mehmet Akif Ersoy Training and Research Hospital (Decision Number: 140915; Decision Date: October 15, 2019).

We retrospectively analyzed patients, older than one year, with VSD who underwent surgical repair between 2014 and 2018. We included patients with VSD and concomitant atrial septal defect (ASD), patent foramen ovale, patent ductus arteriosus, aortic valve prolapse (AVP), and AI. In contrast, we excluded patients with complex pathologies, patients whose age was below one year, and patients with previous pulmonary artery banding.

We evaluated patients' preoperative demographic data, medical history, surgical data, perfusion data, clinical follow-ups, preoperative and postoperative echocardiography, and cardiac catheterization reports.

Definitions

We defined the condition as "prolonged" if the mechanical ventilation (MV) was more than 24 hours, intensive care unit (ICU) stays were longer than 3 days, and hospital stays were longer than 7 days. We determined surgical outcomes and complications such as postpericardiotomy syndrome, renal failure, chylothorax, temporary or permanent complete heart block, neurologic events, sudden circulatory collapse, diaphragmatic paralysis, postoperative support of mechanical extracorporeal membrane oxygenation (ECMO), readmission to hospital, and death according to the international standards[2]. Moreover, we considered the following conditions as major adverse events (MAE): cardiopulmonary resuscitation (CPR), need for ECMO, complete atrioventricular (AV) block requiring permanent pacemaker (PM) implantation, diaphragm paralysis, neurological complication (persistence at discharge), acute renal failure (ARF), and unplanned reoperation.

In case when the ratio of Qp and Qs was less than 1.5 and in the absence of PH, we defined VSD as small or restrictive VSD. We evaluated left ventricular (LV) internal diameter in diastole (LVIDd) and systole (LVIDs) in millimeters. Moreover, we calculated LV z-scores according to these values. We obtained pulmonary artery pressure (PAP) through echocardiography and cardiac catheterization. In case if the mean PAP was between 25 and 45 mmHg, we considered the PH as mild. Similarly, the PAP between 45 and 65 mmHg, and over 65 mmHg were considered moderate and severe PH, respectively.

According to the classification provided by the Society of Thoracic Surgeons, we classified VSD as Type 1 (subarterial), Type 2 (membranous), Type 3 (inlet), and Type 4 (muscular). Despite medical treatment, patients with heart failure and a Qp/Qs ratio greater than 1.5, and patients with AI were considered as the indications for VSD closure surgery.

Surgical Technique

All patients underwent the standardized procedure of median sternotomy. The surgeons maintained cardiopulmonary bypass (CPB) by aortic and selective caval cannulation. All VSDs were closed with native pericardial patch and running suture technique. The surgeons also performed ASD closure, PDA ligation, and valvuloplasty during the surgery in case of a simultaneous presence.

Postoperative Intensive Care Management

We routinely monitored saturation, central venous pressure, electrocardiography (ECG) findings, invasive arterial blood pressure, end-tidal carbon dioxide, and cranial near-infrared spectroscopy. We use milrinone, adrenaline, and noradrenaline as the first, second and third choices, respectively. In case of pulmonary hypertensive crisis, we used oral sildenafil, intravenous iloprost, and inhaled nitric oxide to reduce the pulmonary

vascular resistance. We evaluated patients with rhythm problems with atrial ECG and administered them with adenosine as a bolus at a dose of 100 μg/kg to reveal the diagnosis. In cases with low cardiac output syndrome, we provided inotropic support and peritoneal dialysis support to the patients. Despite medical treatment, we provided ECMO support to the patients with hemodynamic instability.

Follow-up

Patients routinely underwent preoperative transthoracic and transesophageal echocardiography at the operating room. Intraoperative epicardial echocardiography or transesophageal echocardiography were also performed. Patients were evaluated on the first postoperative day and before discharge with transthoracic echocardiography. We used echocardiographic findings of the last outpatient examination as long-term follow-up findings.

Statistical Analyses

We performed statistical analyses with the help of Statistical Package for the Social Sciences software. In the descriptive statistics, normally distributed numerical variables were expressed as mean ± SD, whereas non-normally distributed numerical variables were expressed as median (interquarters). Categorical and sequential variables were expressed in frequency (%). In the dependent group comparisons, we used Cochran's Q test for categorical variables, and Friedman test for non-normally distributed numerical variables and ordered variables. Moreover, we employed repeated measures analysis of variance for normally distributed numeric variables. A p value of less than 0.05 was considered statistically significant for this study.

RESULTS

Demography

Table 1 presents the demographic features of patients. The median age of patients was 3 (1.5-20) years. There were 31 (38.8%) female patients in our study. The median operation weight was 12.3 (8-60). The VSD subtypes were observed as membranous in 50 patients (62.5%), inlet in 23 patients (28.7%), muscular in 5 patients (6.3%), and subarterial in 1 (2.5%) patient. The indications for surgery were PH in 30 (37.5%) patients, AI and AVP in 30 (37.5%) patients, and LV enlargement in 20 (25%) patients. Genetic anomalies were present in five (6.3%) patients (Table 1).

Table 1. Demography

Variables	
Age (years), mean ± SD	3 (1.5-20)
Weight (kg) , mean ± SD	12.3 (8-60)
Body surface area (m^2), mean ± SD	0.6 (0.4-1.68)
Female, n (%)	31 (38.8)
VSD subtypes, n (%)	
Membranous	50 (62.5)
Inlet	23 (28.7)
Muscular	5 (6.3)
Subarterial	2 (2.5)
Indication, n (%)	
PH	30 (37.5)
AI	30 (37.5)
LV enlargement	18 (22.5)
Others	2 (2.5)
Concomitant defects, n (%)	
ASD	
PDA	
ASD + PDA	
Patent foramen ovale	
MI	
AVP	3 (3.8)
Genetic syndrome, n (%)	
Down	5 (6.3)
Aristotle basic score, mean ± SD	6 (6-6)/6.2 ± 0.5
Aristotle comprehensive score, mean ± SD	6 (6-6.1)/6.3 ± 0.7

VSD: Ventricular septal defect, AI: Aortic valve insufficiency, LV: Left ventricle, ASD: Atrial septal defect, PDA: Patent ductus arteriosus, MI: Mitral valve insufficiency, AVP: Aortic valve prolapse.

Preoperative Echocardiography Data

AVP was detected in 3 (3.8%) patients, whereas AI was detected in 27 (33.7%) patients. AI was mild in 25 (31.2%) patients and moderate in 1 (2.5%) patient. Subarterial VSD and moderate AI were detected in only 2 (2.5%) patients. Muscular VSD was detected in 5 (6.3%) patients; however, AI was not detected in any of these patients. PH was detected in 30 (37.5%) patients, and PH was severe in 16 (20%) of these patients. PH was moderate in 8 (10%) patients and mild in 6 (7.5%) patients. The mean LVIDd was 36.9 ± 9.7 mm. The mean z-score was -2 (0 - (-3.2)). The mean LVIDs was 23.2 ± 7.1 mm, and the z-score was -1.9 (0 - (-2.7)).

Preoperative Catheter Data

Catheter angiography was performed in only 8 (10%) patients. The median systolic PAP was 45 (37-78) mmHg, median diastolic PAP was 18 (10-30) mmHg, mean PAP median value was 34.5 (26-52) mmHg, the median pulmonary vascular resistance was 3.05 (1.8-5.9) Wood units, and the median Qp/Qs was 3.25 (5.9-1.8).

Operative Data

The examination of the operative data of the patients revealed that the mean CPB time was 83.2 ± 28.7 minutes. Additionally, The mean aortic cross clamp (ACC) time was 59.0 ± 25.7 minutes (Table 2).

Postoperative Results

The most common complications were arrhythmia. Arrhythmia was observed in 6 (7.5%) patients. Temporary AV block was observed in 2 (2.5%) of these patients, and junctional ectopic tachycardia was observed in other 4 (5%) patients. Permanent complete AV block requiring PM implantation was observed in 1 (1.3%) patient. Pulmonary complications (atelectasis) were observed in 5 (6.3%) patients. In these 5 (6.3%) patients, a temporary decrease in cardiac systolic functions (shortening fraction of less than 28% was measured on echocardiography) was observed postoperatively. Moreover, these patients had improved LV functions after medical treatment. We did not observe any neurological complications, infectious complications, and wound problems. There was no need for early or long-term medical treatment for PH. We also did not observe mortality in any of the cases. The MAE was observed only in 1 (1.3%) patient (Table 3).

The mean ventilation time was 7.7 ± 8.1 hours. Prolonged MV was observed in only 2 (2.5%) patients. The mean ICU stay time was 1.9 ± 1.4 days. The prolonged ICU time was observed in 10 (12.5%) patients. The mean length of hospital stay was 6.9 ± 3.4 days. The prolonged hospital stay was observed in 15 (18.8%) patients (Table 4).

Table 2. Operative variables

Variables	
Hypothermia (°C), mean ± SD	34 (31.5-34)/32.7 ± 2.2
CPB time (min), mean ± SD	77 (64.6-94.3)/83.2 ± 28.7
ACC time (min), mean ± SD	54 (42.8-65.5)/59.0 ± 25.7

CPB: Cardiopulmonary bypass, ACC: Aortic cross clamp.

Table 3. Postoperative variables

Variables	
Pulmonary complications, n (%)	5 (6.3)
Arrythmia, n (%)	6 (7.5)
Junctional ectopic tachycardia	4
Temporary complete AV block	2
Impairment of cardiac function n (%)	5 (6.3)
PM implantation n (%)	1 (1.3)
Major adverse event n (%)	1 (1.3)

CPR: Cardiopulmonary resuscitation, ECMO: Extracorporeal membrane oxygenator, PM: Pacemaker, AV: Atrioventricular.

Table 4. Mechanical ventilation, intensive care unit and hospital stay durations

Ventilation time (hours), median (min-max)	**5.5 (2-9.5)/7.7 ± 8.1**
≤ 24 hours, n (%)	78 (97.5)
> 24 hours, n (%)	2 (2.5)
ICU duration (days), median (min-max)	**1 (1-2)/1.9 ± 1.4**
≤ 3, n (%)	70 (87.5)
> 3, n (%)	10 (12.5)
Hospital stay duration (days), mean ± SD	**6 (5-7)/6.9 ± 3.4**
≤ 7, n (%)	65 (81.3)
> 7, n (%)	15 (18.8)

ICU: Intensive care unit.

Echocardiography Findings from the Postoperative 1st Day

AVP was detected in 1 (1.3%) patient, whereas AI was detected in 29 (36.3%) patients. AI was mild in 27 (33.8%) patients and moderate in 2 (2.5%) patients. PH was detected in 11 (13.7%) patients, and PH was severe in 2 (2.5%) of these patients. PH was moderate in 1 (1.3%) patient and mild in 8 (10%) patients. The mean LVIDd was 33.0 ± 6.6 mm, whereas the mean LVIDs was 21.5 ± 5.5 mm.

Echocardiography Findings from the Long-term Follow-up

The mean follow-up period of the patients was 2.9 ± 1.9 years. AI was observed in 23 (28.8%) patients. AI was mild in 22 (27.5%) patients and moderate in 1 (1.3%) patient. We did not observe AVP in any of the cases. PH was observed in 7 (8.8%) patients. Gladly, there was no case of severe PH. PH was moderate in 1 (1.3%) patient and mild in 6 (7.5%) patients. The mean LVIDd was 33.0 ± 6.6 mm, whereas the mean LVIDs was 21.5 ± 5.5 mm. There was a reduction in PH after the operation. In terms of PH, the difference between the patients' findings before and after the operation was statistically significant (< 0.001). Although there was a decrease in the number of patients with AVP and AI, the difference between the findings before and after the operation was not statistically significant (p= 0.10 and p= 0.15, respectively). There was a decrease in LV volume load after the operation. After the operation, the decrease in the LVIDd was also statistically significant (p= 0.02). However, the difference between the LVIDs was not statistically significant (p= 0.75) (Table 5).

Table 5. Echocardiographic findings

	Preoperative	Postoperative 1. day	Long term	p
AVP (%)	3 (3.8)	1 (1.3)	0	0.10
AI (%)				0.15
Mild	25 (31.2)	27 (33.8)	22 (27.5)	
Moderate	2 (2.5)	2 (2.5)	1 (1.3)	
Severe	0	0	0	
LV enlargement diastolic	2 (0-3.2)/1.8 ± 1.6	-	-	
LV enlargement systolic	1.9 (0-2.7)/1.4 ± 1.5	-	-	
LVIDd	36.9 ± 9.7	33.0 ± 6.6	34.3 ± 7.2	0.02
LVIDs	23 (18.5-26)/23.2 ± 7.1	21 (17.3-25)/21.5 ± 5.5	21.5 (20-25)/21.9 ± 3.7	0.75
PH				< 0.001
Mild	6 (7.5)	8 (10.0)	6 (7.5)	
Moderate	8 (10.0)	1 (1.3)	1 (1.3)	
Severe	16 (20.0)	2 (2.5)	0	

AVP: Aortic valve prolapse, AI: Aortic valve insufficiency, LV: Left ventricle, LVIDd: Left ventricular internal diameter in diastole, LVIDs: Left ventricular internal diameter in systole, PH: Pulmonary hypertension, VSD: Ventricular septal defect.

DISCUSSION

In our study, we aimed to evaluate the early and mid-term results of patients who underwent VSD surgery after the age of one year. We did not observe mortality in any of cases, and observed MAE in only one patient. We observed that the incidence of AI decreased after the operation, and there was a decrease in LV diameters along with an immediate reduction of PH after the operation.

Although VSD surgery is performed with low mortality, there are still reports of complicated postoperative courses[1,3-5]. Studies have reported that morbidity is higher especially in low weight and young age patients[3,6]. A study reported a mortality rate of 1.5%[3]. No mortality was observed in the patient series of Kogon et al.[5]. Scully et al. reported a mortality rate of 1.4%[4]. However, not all these patient groups were focused on the patient population after the age of one year. We did not observe mortality in our study. Various morbidity rates were reported in the literature. Anderson et al. reported that the incidence of MAE was 5.3% and Schipper et al. reported the incidence of MAE was 2.9% in their respective studies[1,3]. Our study focused on the population under the age of one year and found that the incidence of MAE was 5.4%[7]. However, we observed that the incidence of MAO was quite low in the patient population after the age of one year. Only 1 (1.4%) patient needed PM implantation. We did not observe any death, CPR, need for mechanical support, neurological deficits, renal failure, and diaphragm paralysis in our study cohort. In our study, only 2 (2.5%) patients had prolonged MV duration, 10 (12.5%) patients had prolonged ICU duration, and 15 (18.8%) patients had a prolonged hospital stay.

AI is a serious complication in patients without surgical repair, especially in patients with subarterial VSD. Complications such as venturi effect, leaflet structural deficiency, and commissural suspension anomalies play a role in the development of AI[8]. The incidence of AI is reported between 69 and 83% in patients with subarterial VSD[9,10]. A study that (only two patients with subarterial VSD) included 231 patients with restrictive VSD reported the incidence of AI at 26%[11]. In our study, we examined patients with restrictive VSD and patients with non-restrictive VSD who were not operated because of delayed admission. In total, 27 (33.7%) patients had AI, and 25 (31.2%) patients had moderate AI. Severe AI was not observed in any of the patient. Studies have reported that the there was an early decrease in AI after the operation[12,13]. We found that the difference between the groups was not statistically significant in terms of the incidence of AI before and after the operation in the early period. However, there was a decrease in the incidence of AI in the long-term follow-up.

Another complication of unrepaired VSD is PH. Increased pulmonary flow and pressure lead to the remodeling of pulmonary arteries, thereby increasing the PVR. Patients with large VSD develop the symptoms of increased pulmonary flow in the early period. In our clinic, patients with large VSD are operated on the first year of life. However, with the effect of the increasing refugee population, there is an increase in the number of late admissions to the hospital. These patients require a detailed evalu-

ation before the operation. In case of suspected persistent PH, it is necessary to evaluate the same with catheter angiography. In our study, the mean age was 3 (1.5-60) years, and 16 of our patients (20%) were patients with nonrestrictive VSD were admitted later. Catheter angiography was performed in eight of these patients. None of these patients required an early PH treatment. PH decreased in the early postoperative period in all the patients (p= 0.001). During the long-term follow-up, only 1 (1.3%) patient had moderate PH and 6 (7.5%) patients had mild PH.

Another complication of the long-term VSD is LV enlargement. Even in restrictive VSD patients, LV enlargement can be observed due to volume load. Some studies have reported that complication rates increase in patients with enlarged left ventricular end-diastolic diameter[14,15]. Klitsie et al. reported that there was a decrease in right and left ventricular functions in the early postoperative period. Although the LV functions improved within one year, there was a continued decrease in right ventricular functions[16]. Some research publications reported that LV enlargement decreases after operation[17]. In our study, cardiac dysfunctions were observed in 5 (6.3%) patients at the early postoperative period. It was observed that cardiac functions improved after medical treatment in all these patients. In addition, we observed that LV dilation decreased especially after surgery and reduction in LVIDd (p= 0.02).

Complications such as AI, persistent PH, LV volume loading, and cardiac dysfunctions are the risks faced by patients who are admitted late. However, early and mid-term results in these patients are extremely satisfying.

Limitations

This study had a retrospective design and was conducted at a single center. These factors serve as the major limitations of this study.

CONCLUSION

It is extremely important to have a careful follow-up of patients who are expected to have spontaneous closure. Preoperative detailed evaluation along with an immediate surgical repair of late-admitted patients will contribute in favorable early and long-term mortalisy and morbidity rates.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of the Istanbul Mehmet Akif Ersoy Training and Research Hospital (Decision Number: 140915; Decision Date: October 15, 2019).

Informed Consent: This study is retrospective. Not required in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - SE; Analysis/Interpretation – SE, OY; Data Collection – SE, MG; Writing – SE, ZGKÖ; Critical Revision – SH, AG; Final Approval – SH, SO; Statistical Analysis – SE, EÖ; Obtained Funding – SE; Overall Responsibility - SE

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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