Surgical Repair for Acute Myocardial Infarction Induced Ventricular Septal Defect: Does Time Matter?

Tzuhsuan Chan,[1,3] Yunxing Xue,[2,3] Hoshun Chong,[3] Qing Zhou,[3] Dongjin Wang[1,2,3]

[1]Department of Thoracic and Cardiovascular Surgery, The Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, 210008, China; [2]Nanjing Medical University Drum Tower Clinical Medical College; [3]Department of Thoracic and Cardiovascular Surgery, The Affiliated Drum Tower Hospital of Nanjing University Medical School

ABSTRACT

Objective: Ventricular septal defect (VSD) induced by acute myocardial infarction (AMI) is rare but lethal, with high mortality even after surgical repair. Our aim was to assess the association between the time interval and surgical repair effects in patients with VSD following AMI.

Methods: From January 2003 to December 2017, 14 patients with VSD induced by AMI received surgical therapy in our department. We retrospectively reviewed the patients' clinical manifestations, surgical methods, and outcomes. According to the time interval from AMI onset and surgery, we divided the patients into two groups: Group 1 ($N = 9$), more than one week, and Group 2 ($N = 5$), less than one week. A comparison study was performed, and differences were analyzed.

Results: The mean age of the entire group was 65.5±3.3 years, with 78.6% males (11/14). VSDs were anterior apical in 10 (71.4%) and posterior inferior in 4 (28.6%) patients. The average size of the VSD was 15.8±5.8 mm. Compared with Group 1, Group 2 had poorer left ventricular function (LVEF 40.8±10.3% vs. 30.4±2.3%, $P = 0.035$) and a higher rate of urgent procedures (11.1% vs. 100.0%, $P = 0.003$). The mortality rate was 14.3% (2/14). Mechanical support was more common in Group 2 than Group 1. No resistant shunt or death was found during follow up.

Conclusions: VSD following AMI is safer for more than one week, but surgical treatment is also acceptable for patients requiring urgent surgery due to hemodynamic instability. Mechanical assistive devices can improve the perioperative success rate.

INTRODUCTION

VSD induced by AMI is rare, with a prevalence of 0.17-0.31% [Moreyra 2010]. As the age of patients receiving myocardial revascularization through cardiovascular intervention increases, the incidence rate may be lower than reported.

However, the natural history of VSD induced by AMI is catastrophic, and medical therapy has no effect, with a mortality rate of nearly 100% [Coskun 2009]. Surgical therapy can save patients, even with a mortality rate of 13.3-65% [David 1995; Arnaoutakis 2012; Cinq-Mars 2016]. Risk factors have been analyzed based on the national database or single-center experiences. The time interval is thought to be the main factor influencing mortality and morbidity. A recent STS database reviewed 2876 patients with VSD following AMI, and total mortality was 42.9% and 54.1% at less than 7 days and 18.4% at more than 7 days, respectively [Arnaoutakis 2012]. The other item thought to be an influencing factor is the surgical method. The infarct exclusion method introduced by David is widely used because of its acceptable mortality and uncomplicated surgical manipulation [David 1995]. However, resistant VSD postoperation still is a problem, even with complex surgical operations.

Our aim was to investigate the relationship between the time interval and surgical mortality, the surgical method, and the resistant VSD rate based on experiences at a single center.

METHODS

Patients: Fourteen patients were treated for VSD post AMI in our center from 2003-2017, and clinical data were collected and retrospectively reviewed. The patients all were first diagnosed and medically treated in the cardiology department at the same hospital and transferred to the cardiac intensive care unit (CICU) in the cardiothoracic surgery department after being diagnosed with VSD. There were 11 male patients and 3 female patients, with a mean age of 65.5±3.3 years. According to the study's aim, we divided the patients into two groups, according to the time duration from AMI onset to surgical correction. The confirmed diagnosis of AMI was inferred by cardiologists through clinical manifestations, ECG, and biomarkers. The confirmed diagnosis of VSD was inferred through transthoracic echocardiography (TTE). The intercept time point from AMI onset to surgical correction was 7 days. Nine patients in Group 1 underwent surgical treatment after more than 7 days of AMI onset, whereas the other five patients in Group 2 were treated in 7 or fewer days of AMI onset.

More details and comparisons between Group 1 and Group 2 are listed in Table 1. (Table 1) The locations and sizes of VSD

Table 1. Baseline characteristics of patients with VSD following AMI

Category	Total	Group 1 (9)	Group 2 (5)	P-value
Gender, male (%)	11/78.6%	7/77.8%	4/80.0%	1.000
Age, years	65.5±3.3	64.8±5.6	66.2±4.2	0.631
BMI, kg/m2	25.6±1.9	26.1±2.0	24.7±1.5	0.217
Hypertension, N/%	8/57.1%	4/44.4%	4/80.0%	0.301
Diabetes, N/%	6/42.9%	5/55.6%	1/20.0%	0.301
Smoke, N/%	7/50%	5/55.6%	2/40.0%	1.000
Chronic lung disease, N/%	3/21.4%	2/22.2%	1/20.0%	1.000
Myocardial infarction in ECG, N/%	8/57.1%	4 (50.0%)	4 (80.0%)	0.565
Three coronary vessels disease	9/64.3%	7/87.5%	2/40.0%	0.217

Table 2. Characteristics of VSD and associated hemodynamics

Category	Total	Group 1 (9)	Group 2 (5)	P-value
VSD location, N/%	-	-	-	0.790
Anterior apical	10/71.4%	7/70.0%	3/75.0%	
Posterior inferior	4/28.6%	3/30.0%	1/25.0%	
Size of VSD, mm	15.8±5.8	15.7±6.7	16.0±4.2	0.922
LVEF, %	37.0±10.0%	40.8±10.3%	30.4±2.3%	0.035
Left ventricular aneurysm, N/%	8/57.1%	6/66.7%	2/40.0%	0.580
Mitral valve insufficiency	-	-	-	0.427
Mild	6/42.9%	3/33.3%	3/60.0%	
Moderate	4/28.6%	3/33.3%	1/20.0%	
Moderate-severe	3/21.4%	2/22.2%	1/20.0%	
Severe	1/7.1%	1/11.1%	0	
Creatinine, umol/L	120.7±41.7	114.8±48.8	131.4±26.0	0.184
Preoperative pulmonary edema, N/%	3/21.4%	1/11.1%	2/40.0%	0.505
Preoperative cardiac shock, N/%	8/57.1%	3/33.3%	5/100.0%	0.031
Preoperative IABP support, N/%	6/42.9%	2/22.2%	4/80.0%	0.091
Preoperative ECMO support, N/%	1/7.1%	0	1/20.0%	0.357
Urgent procedure	6/42.9%	1/11.1%	5/100.0%	0.003

were determined from TTE. Detailed data associated with mitral valve regurgitation, left ventricular EF, and left ventricular aneurysm also were determined from TTE. We defined cardiac shock as unstable hemodynamics that required an inotropic medication or mechanical support (intra-aortic balloon pump, IABP or extracorporeal membrane oxygenation, ECMO). The urgent procedure involves surgical treatment 24 hours after transfer to the cardiology department. (Table 2)

Surgical treatment: Media sternotomy was chosen, and regular cardiopulmonary bypass (CPB) was performed through the ascending aorta, superior vena cava, and inferior vena cava. Root delivery of cardioplegia with a combination of cold crystalloids and blood was applied for cardiac arrest, and retrograde perfusion from the coronary sinus was applied at the same time. In the case of coronary artery graft bypass (CABG), a graft perfusion with cardioplegia was started after distal anastomosis was performed. If the VSD was located in the anterior apical, the incision was opened on the apical side of the left ventricle 10 mm away from and parallel to the anterior descending artery. After the incision, we were able to identify the VSD and the boundary between the normal myocardium and infarcted myocardium. The infarct exclusion method introduced by David was performed using a Dacron patch. Four patients whose VSD was located in the posterior inferior region were treated with the two-patch method involving our proposed technique. One incision was made from the infarcted ventricle 10 mm away from and parallel to the posterior descending artery, and the other incision was made from

the right ventricle through the tricuspid valve. Two patients required the tricuspid valve to be cut and reconstructed after VSD repair. Two Dacron patches were cut to a suitable size, according to the two sides of the VSD. One patch was sewn continuously from the outer incision, and the other was sewn through the right ventricle. A single interrupted suture was implanted if the angle of the VSD was difficult to observe.

Three patients underwent mitral valve repair, two patients required tricuspid valve repair, and all patients required CABG for complete revascularization during the same procedure. If the patients had difficulty with CPB after surgical correction, even with a high dose of inotropic medicines, then we used IABP and ECMO for support.

Follow up: As of June 2018, all 12 surviving patients were followed up, with a mean follow-up time of 53.6 months. TTE was performed to detect leak post-VSD repair, heart function and valve condition.

Statistical analysis: We used the t test for continuous variables, which are presented as mean values with the SD. Two tests for categorical variables with Fisher's exact probability test when necessary were performed and are presented as numbers with percentages. The Wilcoxon rank-sum test was used for continuous nonparametric variables, and the data are presented as mean values with the median. A 2-tailed $P < 0.05$ was considered statistically significant.

RESULTS

Baseline characteristics: No significant differences were found regarding gender, age, or BMI. Histories of hypertension, diabetes, smoking, and chronic lung disease all were insignificant. More patients had a prior obvious ST segment elevation in the ECG in Group 2 than in Group 1, but the difference was not significant, whereas patients in Group 1 had a greater proportion of three coronary artery diseases from cardiac angiography than those in Group 2 (Table 1).

Characteristics of VSD and associated hemodynamics: Regarding the location of VSD, 71.4% (10/14) were in the anterior apical region and 28.6% (4/14) were in the posterior inferior region. The average VSD size was 15.8±5.8 mm, and no difference was found between the two groups (Group 1 vs. Group 2, 15.7±6.7 vs 16.0±4.2 mm, $P = 0.922$). A severely reduced left ventricular EF was observed in Group 2 (Group 1 vs. Group 2, 40.8±10.3% vs. 30.4±2.3%, $P = 0.035$). Eight patients (57.1%) were treated for cardiac shock, and all the patients in Group 2 had preoperative shock, a significantly greater number than in Group 1 (Group 1 vs. Group 2, 33.3% vs. 100%, $P = 0.031$). Six patients required IABP support, which was more common in Group 2 than Group 1 but not significantly different (Group 1 vs. Group 2, 22.2% vs. 80.0%, $P = 0.091$). Only one patient required ECMO support on the basis of IABP being unable to provide effective support in Group 2. All five patients in Group 2 underwent an urgent procedure followed by transfer from the cardiology department, while one patient in Group 1 underwent an urgent procedure because of a rapid change in hemodynamic condition (Table 2).

Operative data: The average times of CPB and aortic clamp was 203.9±52.3 and 152.4±44.8 minutes, respectively. Two patients were hard to wean from CPB, and they were supported by ECMO and IABP. One patient received IABP during surgery after CPB. (Table 3)

Mortality and morbidity: All-cause mortality in the hospital or at 30 days was 14.3% (2/14). One patient died in each group (Group 1 vs. Group 2, 11.1% hours vs. 20.0%, $P = 1.000$). The ICU stay was 11.3±9.5 days. Group 2 showed a longer time of mechanical ventilation than Group 1, but the difference was not significant (Group 1 vs. Group 2, 37.2±44.2 hours vs. 74.5±31.6 hours, $P = 0.069$). No patient required re-exploration. Two patients in Group required CRRT during CICU. The rate of pulmonary infection was nearly the same in the two groups (Group 1 vs. Group 2, 37.5% hours vs. 60.0%, $P = 1.000$) (Table 3).

Follow up: During the mean follow-up time of 53.6±65.5 (6-179) months, 12 patients survived. No complications were reported. According to the ultrasound results, no leak was found, and no patient had more than moderate mitral valve regurgitation (Table 3).

DISCUSSION

Time interval: High surgical mortality has motivated surgeons to determine the main risk factors influencing the treatment of VSD following AMI. Recently, Arnaoutakis summarized data from the STS database, and 2876 patients with VSD from 1999-2010 were included in the analysis. There were 1990 patients who received surgery within 7 days of VSD confirmation, with a mortality rate of 54.1%. The other 856 patients underwent surgery after more than 7 days of VSD confirmation, with a mortality rate of 18.4% [Arnaoutakis 2012]. The significant differences indicated that the time interval was the key factor. Seven days post-VSD confirmation is a time point that may be supported by studies stating it was the median interval time. Multivariate analysis performed in a previous study identified time (7 days) as an independent predictor of 30-day and long-term mortality (HR = 0.90, $P = 0.015$) [Cinq-Mars 2016]. Cerin's experiences revealed the same results, with a 75% mortality rate in patients operated on within the first week of VSD confirmation and 16% if the time of VSD confirmation was longer than three weeks [Cerin 2003]. Serpytis reported a 100% survival rate for 33 patients who underwent surgery after 3-4 weeks and a 100% mortality rate for those who underwent surgery within the first 10 days (N = 5) [Serpytis 2015]. Meanwhile, three weeks seemed to be another time point at which the surgical suture may be stable. Our study divided 14 patients into two groups, but the mortality rate did not seem to differ between groups. Despite the small volume of patients, we still believe that time matters.

It is not so much that time affects the effect of surgery; it is better to say that time is an indicator of hemodynamic conditions. The STS database reflected elective operations with a mortality rate of 13.2%, compared with 680 patients who died with an emergency status (mortality of 56.0%) and 173 salvage patients (mortality rate of 80.5%) who died. Surgical status determines an outcome that is easy to understand. Five

Table 3. Operative data and postoperative mortality and morbidity

Category	Total	Group 1 (9)	Group 2 (5)	*P*-value
CPB, min	203.9±52.3	212.9±52.4	187.6±53.7	0.408
Aortic clamp, min	152.4±44.8	161.0±47.2	137.0±40.0	0.357
Concomitant CABG, N/%	14/100.0%	9/100.0%	5/100.0%	-
Concomitant mitral valve repair, N/%	3/21.4%	3/33.3%	0	0.258
Intraoperative IABP, N/%	3/21.4%	0	3 (60.0%)	0.027
Intraoperative ECMO, N/%	2/14.3%	0	2 (40.0%)	0.110
ICU, day	11.3±9.5	10.6±9.1	12.8±11.7	0.736
Ventilation, h	49.6±43.1	37.2±44.2	74.5±31.6	0.069
Reexploration, N/%	0	0	0	
Postoperative CRRT, N/%	2/14.3%	0	2 (40.0%)	0.110
Pulmonary infection, N/%	6/42.9%	3 (37.5%)	3 (60.0%)	0.592
Mortality, N/%	2/14.3%	1 (11.1%)	1 (20.0%)	1.000
Resistant shunt, N/%	0	0	0	-
Follow-up LVEF, %	41.0±9.7%	44.9±10.0%	34.6±5.0%	0.032

VSD, ventricular septal defect; AMI, acute myocardial infarction; LVEF, left ventricular ejection fraction; IABP, intra-aortic balloon pump; ECMO, extracorporeal membrane oxygenation; TTE, transthoracic echocardiography; CICU, cardiac intensive care unit; CPB, cardiopulmonary bypass; VAD, ventricle assist device

patients in Group 2 in our study received urgent procedures, whereas only one patient in Group 1 had a rapidly changed condition, while he was undergoing medical therapy on day 10. However, the mortality rate in the present study still is low compared with other reports; two of six patients with a mortality rate of 33.3% died: one patient in Group 2 and one in Group 1. Thus, another key point that ignores preoperative status should be raised, which is how to bridge the urgent procedure and stabilize patients' hemodynamic conditions.

A total of 65.0% of patients from the STS database received preoperative IABP support, but no data showed ECMO or VAD. In a review by Hobbs, limited experiences were reported in several articles about providing mechanical circulatory support for patients with post-AMI VSD. Peripheral ECMO or Impella are commonly used devices, with a 47% patient survival rate after a bridge to surgical correction or heart transplantation [Hobbs 2015]. In our cases, 42.9% of patients required preoperative IABP support: two patients in Group 1, and both patients were weaned from IABP before surgery, and four patients in Group 1, who had a rate of 80%. The remaining patient received ECMO support, which was successful in bridging to surgical repair. The results tell us that patients who require IABP support must have circulation shock, and the progression of their hemodynamic condition relies on the cardiac output and Qp/Qs induced by the shunt. Although one can recover from acute conditions if he/she responds well to vasoactive drugs or IABP, a longer time period is reasonable. However, if the hemodynamic condition does not recover well, even with mechanical device support, then an urgent procedure is required. Therefore, a mechanical circulation support device should be the first choice for patients with VSD with

hemodynamic instability, and then, the surgical timing can be chosen based on the response after mechanical support.

Time is not an indication that should limit the decision of surgical timing; the hemodynamic state is. For patients who insist on longer times, a mechanical circulation support device should be the first choice before urgent surgery.

Surgical method and resistant VSD: Daggett described repair methods 40 years ago [Daggett 1977]. Overall, the operative mortality rate was 33% (12/36) and the mortality rate was even lower at 18% (3/17) after 1973, when he modified the surgical methods. Briefly, ventriculotomy was positioned in the center of the infarcted area, and the VSD was repaired through a direct suture with a felt-buttressed suture. The infarct myocardium was resected and closed with or without a woven Teflon graft fabric. Six patients (16.7%) had postoperative VSD, and five of them died because of rerupture of the ventricular septum or heart failure. David introduced the infarct exclusion method for VSD repair with acceptable results. The infarcted septum (including VSD) and free wall myocardium are excluded using a large patch of bovine pericardium in David's method, and buttressed sutures are used to close the ventriculotomy without infarctectomy [David 1995]. In a group of patients on whom he reported, the overall mortality rate was 13.3% (6/45) and the actuarial survival rate was 66%±7% at six years. Only one patient suffered a minor resistant VSD. This ideal result made it the general surgical approach worldwide [Pojar 2018; Papadopoulos 2009]. The rate of postoperative VSD was 13% in Pojar's series [Pojar 2018] and 3.1% in Papadopoulos's series [Papadopoulos 2009]. No patients received further treatment unless they had severe negative outcomes. Lundblad compared the effect

of David infarct exclusion and Daggett direct septal closure on early and late outcomes, and the results showed that the infarct exclusion method was superior. However, the rate of residual or recurrent shunts was 16.7% in the David group and 48.5% in the Daggett group [Lundblad 2014].

We used David's method and achieved good results. During the follow-up period, no residual or recurrent VSD was found. We observed that David's method can avoid excessive suture tension and preserve left ventricular structure. Although some reports have shown resistant VSD, the persistent shunt does not cause significant hemodynamic abnormalities. However, the persistent shunt still carries risks of endocarditis and heart failure. Several patch-repair methods have been proposed. Okamoto used three modified patches to close the VSD and exclude the infarct area, and the cavity between the septum and free wall was filled with fibrin glue [Okamoto 2016]. Residual or recurrent VSD was observed in three patients (14%) but disappeared in two of the three patients. This finding tells us that the occurrence of resistant VSD may not originate from the anastomotic area. Although all clinical studies analyze the size and location of VSD, no study analyzed the location on residual VSD. According to our experience, the left ventricular incision easily exposes the VSD for anterior apical VSD, and the VSD edge can be defined at the time of anastomosis. However, for a VSD located on the posterior inferior part, it is often not easy to reveal, and the edge cannot be found when the patch is isolated. We tried a bilateral repair method for cases in which the VSD was located in the posterior inferior part in addition to the conventional patch suture from the myocardial incision. The VSD was exposed from the right atrial-tricuspid valve approach, and the patch was sutured on the other side. Although the number of cases is limited, we have achieved good results so far. There are some reported methods similar to ours as well as focused on the impact of the VSD location on surgical repair [Balkanay 2005; Labrousse 2006].

CONCLUSION

Even if myocardial revascularization has contributed to significantly improving the survival rate after myocardial infarction, ventricular post AMI is still be a great challenge for cardiac surgeons. Surgical timing is the major factor influencing the outcome, but longer waiting times for surgical correction means more patients died from hemodynamic dysfunction. Despite the time interval, we insist that the hemodynamic status is the first important factor. Urgent surgery is necessary if circulation status get worse and a mechanical assist device is useful for a bridge to surgery. Surgical methods seem different with similar results and resistant shunt rate, but different methods have no significant benefit for outcomes and hemodynamic status.

ACKNOWLEDGEMENT

REFERENCES

Arnaoutakis GJ, Zhao Y, George TJ, et al. 2012. Surgical repair of ventricular septal defect after myocardial infarction: outcomes from the Society of Thoracic Surgeons National Database. Ann Thorac Surg. 94(2): 436-43; discussion 443-4.

Balkanay M, Eren E, Keles C, Toker ME, Guler M. 2005. Double-Patch Repair of Postinfarction Ventricular Septal Defect. Texas Heart Institute Journal. 32(1):43-46.

Cerin G, Di Donato M, Dimulescu D, et al. 2003. Surgical treatment of ventricular septal defect complicating acute myocardial infarction. Experience of a north Italian referral hospital. Cardiovasc Surg. 11(2): 149-54.

Cinq-Mars A, Voisine P, Dagenais F, et al. 2016. Risk factors of mortality after surgical correction of ventricular septal defect following myocardial infarction: Retrospective analysis and review of the literature. Int J Cardiol. 206: 27-36.

Coskun KO, Coskun ST, Popov AF, et al. 2009. Experiences with surgical treatment of ventricle septal defect as a post infarction complication. J Cardiothorac Surg. 4:3.

Daggett WM, Guyton RA, Mundth ED, Buckley MJ, McEnany MT, Gold HK, Austen WG. 1977. Surgery for Post-Myocardial Infarct Ventricular Septal Defect. Annals of Surgery, 186(3), 260–270.

David TE, Dale L, Sun Z. 1995. Postinfarction ventricular septal rupture: repair by endocardial patch with infarct exclusion. J Thorac Cardiovasc. Surg. 110(5): 1315-22.

Hobbs R, Korutla V, Suzuki Y, et al. 2015. Mechanical circulatory support as a bridge to definitive surgical repair after post-myocardial infarct ventricular septal defect. J Card Surg. 30(6): 535-40.

Labrousse L, Barandon L, Choukroun E, Deville C. 2006. 'Double patch and glue' technique for early repair of posterior post-infarction ventricular septal defect, Interactive CardioVascular and Thoracic Surgery, Volume 5, Issue 3, 1 June, Pages 195–196.

Lundblad R, Abdelnoor M. 2014. Surgery of postinfarction ventricular septal rupture: the effect of David infarct exclusion versus Daggett direct septal closure on early and late outcomes. J Thorac Cardiovasc Surg. 148(6): 2736-42.

Moreyra AE, Huang MS, Wilson AC, et al. 2010. Trends in incidence and mortality rates of ventricular septal rupture during acute myocardial infarction. Am J Cardiol. 106:1095–1100.

Okamoto Y, Yamamoto K, Asami F, et al. 2016. Early and midterm outcomes of triple patch technique for postinfarction ventricular septal defects. J Thorac Cardiovasc Surg. 151(6): 1711-6.

Papadopoulos N, Moritz A, Dzemali O, et al. 2009. Long-term results after surgical repair of postinfarction ventricular septal rupture by infarct exclusion technique. Ann Thorac Surg. 87(5): 1421-5.

Pojar M, Harrer J, Omran N, et al. 2018. Surgical treatment of postinfarction ventricular septal defect: risk factors and outcome analysis. Interact Cardiovasc Thorac Surg. 26(1): 41-46.

Serpytis P, Karvelyte N, Serpytis R, et al. 2015. Post-infarction ventricular septal defect: risk factors and early outcomes. Hellenic J Cardiol. 56(1): 66-71.