Surgical Repair of Post Infarction Ventricular Septal Rupture: An 18 Years' Retrospective Multicenter Study

Running Title: Post MI VSR Closure

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Abstract

Background: Ventricular Septal Rupture (VSR) is a rare but challenging complication after myocardial infarction (MI). In the presence of acute MI, volume and pressure overload lead to acute heart decompensation. The present study was designed to evaluate the early surgical outcome of VSR over 18 years.

Method: This multicenter study was done during 2000-2018, in which 99 patients with post MI VSR were included.

Results: The patients (n=11) presenting hemodynamic deterioration at the time of hospital admission, died before any attempt for surgery. A consecutive series of 88 patients with surgical repair of VSR was evaluated. Mean interval from MI to VSR diagnosis was 7.5±7.2 days and from admission to operation was 5±5 days. VSR location did not influence the outcome (p=0.1). Concomitant coronary bypass was done for all patients; two vessel disease were more prevalent (39%). Only 25 patients survived and left the hospital (13 patients died in the operating room due to the failure of pump weaning and 50 patients in the ICU due to low cardiac output). Predictors of poor prognosis included low ejection fraction (p=0.01), prolonged pump time (p=0.01) and operation in the second half of this period (p=002).

Conclusion: Despite the improvement in perioperative management and cardiac surgery techniques, the perioperative mortality rate of VSR has remained high where assist device is not

accessible. We suggest VSR repair limited to certain centers with adequate experiences because of the low average annual number.

Key words: Acute Myocardial Infarction; Left Ventricular Function; Mechanical Myocardial Infarction Complications; Ventricular Septal Rupture.

Introduction

Ventricular Septal Rupture (VSR) as a serious and known mechanical complication occurs in 1-3% of cases with transmural Myocardial Infarction (MI) [1-5]. Its incidence has decreased significantly during the recent two decades due to development and routine use of early reperfusion treatment (thrombolytic therapy and percutaneous coronary intervention) [3, 6-8]. Also, it is a life threatening complication and one of the most challenging emergencies for cardiac surgeons.

In the natural course of MI without reperfusion therapy, coagulation necrosis may occur with neutrophils accumulation in the ischemic zone. The neutrophils apoptosis and the released lytic enzymes may contribute to split up of the myocytes into necrotic part and lead to the VSR formation [6, 8, 9].

In patients complicating by VSR, the combination of myocardial dysfunction and following low cardiac output, acute right ventricular volume and pressure overload leads to the acute heart failure. Traditionally, surgical defect closure is the only definitive treatment for post- MI VSR that is also disappointing. From the first surgical repair reported by Cooley in 1957, the perioperative mortality has remained high despite numerous advances in cardiac surgery techniques and perioperative care [10-12]. Indeed, it has the highest mortality rate among all types of the cardiac operations. Also it is a major source of concern, as without defect closure, the mortality rate would be as high as 90% and considered as class I indication for surgical repair [2, 3, 5, 6, 8-10, 12-14].

The appropriate time for surgery is still under debate. The surgical timing and associated co-morbidities play an important role in determining the patients' outcome [4, 12, 15]. Current

guidelines suggest the immediate surgery, regardless of the patient's clinical status, in order to prevent further hemodynamic deterioration and organs failure. However, some studies have recommended the delayed surgery by 2-4 weeks, if the hemodynamic status is allowed [4, 9, 10].

VSR is a rare complication with variation in natural course of disease, so the available VSR literature is scattered [4, 15]. There are limited reports addressing the experiences regarding challenging operation of VSR patients in the Iranian population. The aim of this study was to evaluate the early surgical outcome and the risk factors of VSR over a period of 18 years in the three tertiary university hospitals.

Methods

A retrospective data base review was performed on consecutive patients who had undergone surgical repair of post-MI VSR in the three tertiary high volume university hospitals (Modarres Hospital, Imam Hospital, and Rajaei Hospital) in Tehran, Iran during 2000- 2018. The mentioned timeline was chosen with regards to availability of acceptable medical records. The study has been approved by the Ethical committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.REC.1397.014). The patients informed consent was waived due to the retrospective design of the study.

This an all-comers retrospective analysis which included the patients presenting with ST-segment elevation MI whose echocardiographic or angiographic findings showed the presence of interventricular shunt. The exclusion criterion was the presence of congenital VSR.

The demographic and clinical data of the patients including traditional cardiovascular risk factors, angiographic findings, perioperative data, time interval between MI and hospital admission and time interval between admission and operation, Intra- Aortic Balloon Pump

(IABP) usage, extent of coronary artery disease and simultaneous coronary artery bypass graft (CABG), and operative and in-hospital mortality rates were obtained from the medical records. After the diagnosis, medical care was started to reduce systemic vascular resistance and left-to-right shunt, and maintaining the cardiac output to ensure adequate end-organ perfusion.

Surgical Treatment

VSR surgical management has been consistent between the studied centers. All the patients had midline sternotomy, moderate hypothermic cardiopulmonary bypass using bicaval cannulation and antegrade bloody cardioplegic solution. The longitudinal ventriculotomy approach was done through the infarcted area with direct access to septal defect. The defect was repaired by one of the two routine techniques: Daggett technique of patch closure or David infarct exclusion technique according to the local routines. A large prosthetic patch and interrupted pledget 3-0 polypropylene suture were used by keeping the pledgets on the right ventricular side with attention to prevent sutures from cutting through. Infarct exclusion technique was used for friable margins and too inflamed tissue. In case of the of large ventricular aneurysm, it was resected and ventriculotomy was closed by 2-0 polypropylene suture with felt strip placed on each side of the ventriculotomy for reinforcement.

If the patients had other stenotic coronary arteries, saphenous vein grafts were used on the cardioplegic heart before ventriculotomy, and proximal anastomoses were performed after removal of aortic clamp. Routine rewarming, de-airing, cardiopulmonary bypass weaning, and primary sternal closure were done. The left internal thoracic artery was not used. There was no record showing cardiac output measurement during the intraoperative and post-operative periods.

Statistical analysis

Data was assessed by descriptive statistics (frequency and percentage, mean and standard deviation). Associations between categorical variables were analyzed by the Chi-square test or the Fisher's exact test. The Kolmogorov-Smirnov test was applied to evaluate the normal distribution of quantitative variables and the Mann–Whitney test was carried out for non-normally distributed variables. All statistical analyses were performed using SPSS (version 11.5; SPSS Inc, Chicago, IL, USA). P values < 0.05 were considered statistically significant.

Results

A consecutive series of 99 patients with diagnosis of post-MI VSR were recruited from the three allocated hospitals between March 2000 and March 2018. Of them, 11 patients had hemodynamic deterioration at the time of hospital admission and died before any attempt for surgery. Consequently, a total of 88 patients (40 males; 48 females) were included in the study and underwent the surgery in the three tertiary centers. Table 1 shows the distribution of risk factors and preoperative characteristic of the patients.

There was no significant difference in cardiovascular risk factors, VSR location and size, number of stenotic coronary arteries and need to IABP support between groups (Table 1). The survivors had statistically significant higher left ventricular ejection fraction (38.8% ± 8.6 vs 33.6% ± 9.3 in non-survivors, p= 0.01), and lower pump time (113.9 min ± 42.4 vs 147min ± 44.6, p= 0.01). The mortality rate was similar for the posterior and the anterior VSRs (p=0.07).

The IABP was not used in 36 patients (36.3%) that 11 of them were among non-operated patients (100% of non-operated patients), and 25 of them were among operated patients (28.4% operated patients), either because it was judged unnecessary due to hemodynamic stability or

failure of the balloon insertion into the femoral artery. Among operated patients with IABP support, the mortality rate was 20 in survived and 43 in non-survived patients that this difference was statistically insignificant (p= 0.3).

The diagnosis of MI was based on the 4th Universal Definition of Myocardial Infarction and MI to VSR diagnosis time was defined as the time from diagnosis of MI to time of VSR diagnosis by transthoracic echocardiography.

There was a trend of longer MI to VSR diagnosis time in survivors compared to non-survivors (10.5 ± 8.5 versus 6± 6 days, p value = 0.06).

Among operated patients, 13 patients (14.77%) had a failure in weaning from cardiopulmonary bypass due to cardiac failure in the operating room and 50 patients (56.81%) expired during the postoperative period in the ICU due to the low cardiac output and multi-organ failure predominantly. There was no access for ventricular assist device for them. Remaining patients (n=25, 28.4%) survived and were discharged from the hospitals. Comparing the two operative techniques (patch closure vs. exclusion technique) showed no difference in early mortality.

Table 2 shows the results obtained from the comparison of operated patients data according to time division. All the 11 patients (11.1% of all patients) with cardiogenic shock who died before operation belonged to the first half of the study period. The frequency of VSR was similar between the first and second half of the study period (18 years) but most survivors were the operated patients in the first half (p=0.02). The routine uses of IABP increased in the second half of our series without any statistically difference (p= 0.1). During the second half, VSR patients had been referred faster to the referral hospitals (p=0.03), had been underwent the thrombolytic

therapy further in primary centers before transfer (p=0.01), and had statistically significant longer operation time (p=0.002).

Discussion

In the present study, a consecutive series of 99 patients with post-MI VSR was studied for 18 years. To the best of our knowledge this is the first multicenter study on surgical repair of VSR in Iran. The significant early mortality after surgical repair of post MI-VSR was the main finding in the present study.

VSR is a well-recognized mechanical complication of acute MI. Its incidence is very low in the recent decades thanks to the revascularization. However, it has remained as one of the most serious complications. Development of acute decompensated heart failure is the most important determinant of early outcome following VSR. Timing of surgery (immediate surgery vs delay operation) and type of closure (direct patch closure vs exclusion technique) are the two important debates about surgical treatment of VSR. Comparing these two operative techniques showed no difference in early morbidity and residual shunt [1, 7, 9, 11, 13].

There is a reverse association between VSR mortality and timing of surgery [6, 10, 12]. VSR closure in the necrotic tissue would be technically difficult. It is believed that in case of stable hemodynamic status, it is better to have an interval to achieve a firm and fibrotic margin of VSR in order to support the tension of sutures. If there is cardiogenic shock, the patient should be operated without delay to get a better outcome. Under rare conditions where the patient has neglected the VSR and refers with multi-organ failure, every attempt may be futile. Less mortality in delayed closure means that the patients have been in more hemodynamically stable condition and provide a chance for a more effective repair. On the other hand, the need for early

surgery means the immediate operation on decompensated heart failure and suturing in inflamed, fragile tissues. The highest operative mortality rate has been reported among these patients who had to undergo surgery to survive [10, 16].

The mortality in our study was comparable to previous studies. The mortality rate for post-MI VSR emergency surgical repair is depends on the selection population (0– 80 %) [1, 4, 9, 12, 17]. According to the society of thoracic surgeons' data base, the operative mortality rate is more than 40% with an inverse association between MI and repair time [16].

The recent guideline recommends urgent repair of post MI-VSR as a class I indication irrespective of the hemodynamic status [9]. The STS data base has introduced the timing of surgery as an important factor influencing the mortality, given the 7-day cut off (54% mortality compared to 18%) [11]. In another report, surgical repair was associated with 100% mortality during the first 10 days, however, all the patients survived when the operation was performed 3-4 weeks later [11]. In contrast, in a similar study conducted in a high volume tertiary center in France, their therapeutic management was early surgery as soon as possible without considering the hemodynamic status along with prophylactic preoperative IABP implantation for all the patients [13]. Although there is a discrepancy in timing surgery of VSR, all the efforts should be done to prevent further hemodynamic deterioration. It seems that the hemodynamic status is the most determinant of outcome, while the timing (early vs. late) has no such role.

Simultaneous CABG did not influence the early outcome of the patients although, other studies have shown that it increases the survival rate and prevents deterioration of left ventricle function in the patients with three- vessel diseases in the long term [11, 15]. The number of coronary vessels involved does not seem to have a significant effect on the immediate surgical outcome of

the patients, as the prevalence of two and three- vessel disease were similar in the non-survivor group compared to the survivor group as observed in other researches [12, 18, 19].

Some reports attributed the high mortality rates in posterior VSR due to the difficult in operative exposure and concomitant both ventricular dysfunction. The location of VSR did not influence the outcome of our patients, but it was helpful in determining the ventriculotomy site [1, 2, 5, 13, 16].

The Extracorporeal Eembrane Exygenator (ECMO), as a bridge to recovery from the acute phase can be applied to stabilize the patient's condition and to avoid further deterioration [20]. ECMO was not accessible easily in our centers and has been used with limitations in a few centers. However, in this study, all the VSR patients treated with only intravenous inotropic support and IABP alone, and the patients with cardiogenic shock refractory to these primary treatments did not survive by this opportunity. Some studies have suggested that delayed surgery could be an important option for the centers without ECMO support to improve the outcomes [15]. IABP decreases the afterload of the left ventricle and improves coronary circulation. Herein, the IABP was used in 47 patients preoperatively. Although IABP use did not show a survival benefit, IABP provided relative and transient mechanical support. It is not recommended for prolonged use [15].

Recent studies have suggested the possibility of using mechanical circulatory support (Impella) to decrease the Qp/Qs and the pulmonary artery and capillary wedge pressure, as well as increasing the cardiac index [19]. This mechanical assistance can be introduced percutaneously. Although it has been used for small series of patients, its benefits seem to be exceeding of the IABP. Results of another study on 64 VSR patients conducted in another state of Iran during

2005-2015 confirmed that the in hospital mortality could be more than 80% without using the assist device [21].

Trans-catheter closure of post-MI VSR has been demonstrated in case reports and limited single-center series with varying results. Despite using the less invasive techniques, mortality has remained high [22]. Percutaneous trans-catheter repair has been suggested in the defects less than 15mm as temporary option to decrease the shunt, and help to stabilize hemodynamic condition before the surgery [1, 4, 8, 10, 11, 14]. It is especially true for the patients who are deemed poor surgical candidates, such as those with advanced age and multiple comorbidities. However, in some carefully selected patients, it could be a destination therapy [9]. There are a few cases reports regarding percutaneous closure of VSR in our hospitals [23].

The mortality rate was statistically significant in the second half of study period. There has been a significant shift to junior surgeons in all the centers after a decade. VSR is a rare issue requiring surgical expertise, which is achieved difficulty. Few surgeons may observe more than a few VSR cases per year. Despite the progress in surgical techniques and perioperative care in coronary bypass surgery during the last years, the surgeons are slowly losing their skills in the treatment of such patients (we found less than 2 patients per year were found in every center during the study period) suggesting that VSR patients in a stable condition should be transferred to a selected center to improve outcome.

In this retrospective study, small sample size attributing to the rare occurrence of the disease, as well as lack of follow up of living patients, missing and incomplete information were all considered as limitations of the study. Given the multicenter design of the study, it needs a simplified form of data collection with a limited number of variables to avoid further missing data. In this study, the data of patients undergoing surgical repair of post-MI VSR was prepared

from the three high-volume centers, during an 18- year's period, which was a strength of the study.

Conclusion

The therapeutic management has not changed during the recent two decades, and is limited to the surgery as trans-catheter VSR closure and ECMO are not accessible easily in our centers. Emergent surgery is required for refractory hemodynamic instability. It is suggested to limit the VSR repair to certain centers with adequate experiences because of the low average annual number.

Authors contributions:

Conception- Foroughi, Mohammadi**.** Design- Foroughi**.** Supervision- Rostambeigi**.** Data collection- Foroughi, Mohammadi, Ghorbani **.** Analysis-Pourmotahari**.** Literature review- Foroughi, Sadeghipour, Tavousi**.** Critical review- Foroughi, Mohammadi, Sadeghipour, Majidi.

The manuscript has been read and approved by all the authors, the requirement for authorship have been met and that each author believe that the manuscript represent honest work.

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