CLINICAL CHARACTERISTICS AND SHORT-TERM OUTCOMES OF POST-MYOCARDIAL INFARCTION VENTRICULAR SEPTAL RUPTURE- A RETROSPECTIVE STUDY

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ABSTRACT

BACKGROUND

We wanted to evaluate the patient characteristics, risk factors, short-term outcomes and predictors of poor outcomes in patients with ventricular septal rupture developed as a complication of acute myocardial infarction.

METHODS

This was a single-centre, retrospective study which included 45 patients with ventricular septal rupture developed post-acute myocardial infarction, admitted to a tertiary centre in India, between April 2012, and February 2017. Ventricular septal rupture was diagnosed and localized/characterised using echocardiography. The comparison of survivor and non-survivor patients was done for demographic, lesion and procedural characteristics, effect of time of surgery on mortality in patient with ventricular septal rupture.

RESULTS

The mean age of the patients was 62.5 ± 9.77 years. Anterior wall myocardial infarction and apical location of ventricular septal rupture were present in most of cases. The median time from onset of symptoms to the diagnosis of the ventricular septal rupture was 2 days. The overall 30-days mortality was 80%. Medically treated patients (n =37) had a 30 days mortality of 94.6%. Among surgically treated patients (n=8), the survival at 30 days was 87.5%. Low left ventricular ejection fraction, high TIMI score and shorter duration between the onset of myocardial infarction and occurrence of ventricular septal rupture were found to be associated with poor outcomes and high mortality rate.

CONCLUSIONS

Despite improvements in medical, surgical as well as interventional techniques, the short-term prognosis of post-myocardial infarction ventricular septal rupture remains poor.

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BACKGROUND

Acute myocardial infarction (AMI) may instigate various haemodynamic, electrical and mechanical complications. Ventricular septal rupture (VSR) is one of most common and lethal mechanical complication which develop post AMI with the prevalence rate of 0.15-0.4%.[1] The severity of this complication has always remained high with 80-100% mortality in patients on medical therapy and 20-40% in patients who underwent surgical treatment.[1-3] However, the incidence of VSR post-AMI has markedly reduced by 10 folds with the development of efficacious revascularization therapies. Anterior wall myocardial infarction (AWMI) most likely causes apical rupture, however inferior or lateral wall myocardial infarction (IWMI or LWMI) commonly causes basal rupture.[4]

The pathology of septal rupture embroils neutrophil infiltration at ischemic site causing coagulative necrosis which ultimately weakens the septal myocardium. Factors associated with increased risk of VSR in patients with AMI include older age, female sex, hypertension, congestive heart failure, chronic kidney disease, thrombolytic therapy and AWMI.[1,5] The standard guideline suggest the immediate closure of the VSR to reduce the left-to-right shunting, pulmonary over-circulation and systemic hypo-perfusion which may cause multiple organ damage or even death.[6,7] Although various advanced techniques are available for management of AMI, VSR development post-AMI still exists with higher mortality rate. Hence, the present study aimed

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to assess the patient characteristics, risk factors, the short-term outcomes (30 days) and predictors of poor outcomes in patients with VSR developed post-AMI.

METHODS

This was a retrospective study which included 45 patients admitted to the tertiary care centre in India between April 2012 and February 2017. It included patients with AMI complicated with VSR. The characteristic clinical symptoms, electrocardiographic signs of infarction and elevated cardiac enzymes were used as diagnostic criterion for AMI. Echocardiography was used for diagnosis of VSR. Demographic details, past medical history, electrocardiographic patterns, hemodynamic data and echocardiographic parameters for each patient were noted. Left ventricular systolic function and location/characteristics of the ventricular septal defect were assessed using 2D-Doppler echocardiography. The details of medical treatment given to each patient and scheduled time of surgery were noted for individual patient. The difference between patient in need for acute/sub-acute operation was made as early surgery (≤7 days from diagnosis of ventricular septal defect) and late surgery (>7 days from diagnosis of ventricular septal defect), as such patients were decompensated and were too unstable at the time of diagnosis from those who underwent scheduled surgery.

All the data were evaluated using statistical package for the social sciences version 15 (Chicago, IL, USA). Quantitative data were summarized as mean ± standard deviation and difference in mean was analysed using student t- test. Qualitative variables were articulated as frequency and percentage and were analysed using chi-square test. Level of significance was considered as 5%.

RESULTS

This was a retrospective study which included 45 patients with AMI complicated with VSR. The mean age of patients was 62.5 ± 9.7 years which included 22 (48.9%) male and 23 (51.1%) female patients. Among all, 25 (55.6%) had hypertension, 17 (37.8%) had diabetes, 13 (28.9%) were smokers and 8 (17.8%) had dyslipidaemia. No patients had a history of any previous cardiac events. The demographic details are displayed in Table 1.

The detailed hemodynamic and other diagnostic parameters are mentioned in Table 2. Thirty-eight (84.4%) patients were diagnosed with AWMI and 7 (15.6%) patients with IWMI, which involved proximal left anterior descending coronary artery in about 55% patients. About 50.4% patients were diagnosed with VSR within 2 days of AMI symptoms onset. Echocardiography showed that 73.3% of VSR were located in apical region followed by 15.6% in basal and 11.1% mid septal region. Thirty-three (73.4%) patients displayed TIMI-score 6-10. The mean left ventricular ejection fraction (LVEF) of all the patients was found to be 45.1 ± 14.2%.

Reperfusion was achieved through thrombolysis therapy in 19 (42.2%) patients and via percutaneous trans-luminal coronary angioplasty in only 2 (4.4%) patients. Intra-aortic balloon counter pulsation (IABP) therapy was used in 3 (6.7%) patients. Surgical repair of VSR was performed in 8 (17.8%) patients with concomitant coronary artery bypass grafting as they have more than one diseased vessel and remaining 37(82.2%) patients were managed using conservative medical treatment. The average time taken for surgery was 8 days, after diagnosis of VSR. Table 3 displays the procedure details among all the patients.

In this study, short-term clinical outcomes at 30 days of treatment were determined. The over-all 30 days mortality was found to be 80% and only 20% patients survived. Among the survived patients, 5.4% patients were treated with conservative medical treatment and 87.5% patients had undergone surgery. The multi-variant analysis (Table 4) for the survival after 30 days of treatment demonstrated that presence of AWMI, higher TIMI score and lower LVEF were independently associated with the higher mortality and poor clinical outcomes. The surgical repair of VSR was also found to be independently associated with the better survival in patients underwent surgery compared to medically managed patients.

Variables	Patients (N=45)
Age (Mean ± SD, years)	62.5 ± 9.77
Gender, n (%)	
Male	22 (48.9%)
Female	23 (51.1%)
CAD risk factors, n (%)	
Hypertension	25 (55.6%)
Diabetes mellitus	17 (37.8%)
Dyslipidaemia	8 (17.8%)
Smoking	13 (28.9%)
Comorbidities, n (%)	
COPD	1 (2.2%)
Associated symptoms, n (%)	
Dyspnoea	29 (64.4%)
Fatigue	1 (2.2%)
Palpitations	1 (2.2%)
Syncope	3 (6.7%)

Table 1. Demographic Details of All the Patients

CAD: Coronary Artery Disease; CKD: Chronic Kidney Disease; CVA: Cerebrovascular Accident; COPD: Chronic Obstructive Pulmonary Disease and PAD: Peripheral Arterial Disease.

Variables	Patients (N=45)
Type of MI, n (%)	
AWMI	38 (84.4%)
IWMI	7 (15.6%)
S3, n (%)	5 (11.1%)
Chest Crept, n (%)	37 (82.2%)
Location of VSR, n (%)	
Apical	33 (73.3%)
Basal	7 (15.6%)
Mid Septal	5 (11.1%)
Size of VSR (mean ± SD, mm)	10.31 ± 3.98
Killip Class, n (%)	
Class-I	3 (6.7%)
Class-II	19 (42.2%)

Class-III	9 (20%)
Class-IV	14 (31.1%)
TIMI score (6-10), n (%)	33 (73.4%)
LVEF (mean ± SD, %)	45.13 ± 14.23
Jugular Venous Pressure, n (%)	
Normal	24 (53.3%)
Elevated	21 (46.7%)
Systolic Blood Pressure (mean ± SD, mmHg)	105.11 ± 23.99
Diastolic Blood Pressure (mean ± SD, mmHg)	64.71 ± 27.86
Heart Rate (mean ± SD, beats/min)	98.87 ± 23.00
Laboratory Findings (mean ± SD)	
Haemoglobin, g/dL	12.27 ± 1.71
Total leucocyte count, cells/mm^3	13300 ± 3532.30
Sodium level, mEq/L	132.78 ± 5.28
Potassium level, mEq/L	4.18 ± 0.65
Serum creatinine level, mg/dL	1.56 ± 0.77
Random blood sugar, mg/dL	164.44 ± 75.38

Table 2. Haemodynamic Profile and Other Diagnostic Characteristics of All the Patients

MI: Myocardial Infarction; AWMI: Anterior Wall Myocardial Infarction; IWMI: Inferior Wall Myocardial Infarction; VSR: Ventricular Septal Rupture; TIMI: Thrombolysis In Myocardial Infarction and LVEF: Left Ventricular Ejection Fraction.

Characteristics	Patients (N=45)
Reperfusion, n (%)	
Thrombolysis	19 (42.2%)
Primary PTCA	2 (4.4%)
No reperfusion	21 (46.6%)
IABP Therapy Support, n (%)	3 (6.7%)
Surgical Repair, n (%) (CABG + VSD patch repair)	
Done	8 (17.8%)
Not done	37 (82.2%)
Outcomes (30 Days Mortality), n (%)	
Expired	36 (80%)
Survived	9 (20%)
Median Duration of MI to VSR	2 days
Median Time to First Hospital Contact	7 hours
Median Time of Surgery from Diagnosis	8 days
Median Time from VSR Detection to Death	4.5 days

Table 3. Procedural Characteristics of All the Patients

PTCA: Percutaneous Transluminal Coronary Angioplasty; IABP: Intra-aortic Balloon Counter Pulsation; CABG: Coronary Artery Bypass Grafting; VSD: Ventricular Septal Defect; MI: Myocardial Infarction and VSR: Vascular Septal Rupture.

Parameter	Survivors (N=9, 20%)	Non-Survivors (N=36, 80%)	p Value
Age (mean ± SD, years)	59.33 ± 8.8	63.3 ± 9.9	0.27
Gender, n (%)			
Male	5 (22.7%)	17 (77.3%)	0.65
Female	4 (17.4%)	19 (82.6%)	
Type of MI, n (%)			
AWMI	7 (18.4%)	31 (81.6%)	0.53
IWMI	2 (28.6%)	5 (71.4%)	
Location of VSR, n (%)			
Apical	6 (18.2%)	27 (81.8%)	0.82
Basal	2 (28.6%)	5 (71.4%)	
Mid septal	1 (20%)	4 (80%)	
Killip Class, n (%)			
Class-I	1 (33.3%)	2 (66.7%)	0.28
Class-II	6 (31.6%)	13 (68.4%)	
Class-III	1 (11.1%)	8 (88.9%)	
Class-IV	1 (7.1%)	13 (92.9%)	
TIMI Score (mean ± SD)	6.7 ± 1.7	8.6 ± 2.4	0.038

Size of VSR (mean ± SD, mm)	12.4 ± 5.9	9.7 ± 3.2	0.07
LVEF (mean ± SD, %)	58.2 ± 11.2	41.8 ± 13	0.001
Thrombolysis (streptokinase), n (%) No Yes	 6 (23.1%) 3 (15.8%)	 20 (76.9%) 16 (84.2%)	0.546
Surgery, n (%) Done (N=8) Not done (N=37)	 87.5% 5.4%	 12.5% 94.6%	0.001
Surgery (N=8), n (%) ≤7 days (N=3) >7 days (N=5)	 2 (25%) 5 (62.5%)	 1 (12.5%) 0	0.17
Trans-catheter closure (N=3), n (%)	3 (100%)	0	-
Systolic blood pressure (mean ± SD, mmHg)	114 ± 14	102 ± 25	0.195
Diastolic Blood Pressure (mean ± SD, mmHg)	72 ± 9	61 ± 30	0.117
Heart Rate (mean ± SD, beats/min)	94 ± 9	100 ± 25	0.484
Haemoglobin (mean ± SD, g/dL)	11.8 ± 1.4	12.3 ± 1.7	0.436
Sodium level (mean ± SD, mEq/L)	130.6 ± 5.8	133.0 ± 5.0	0.183
Potassium level (mean ± SD, mEq/L)	4.0 ± 0.7	4.2 ± 0.6	0.768
Serum Creatinine Level (mean ± SD, mg/dL)	1.2 ± 0.4	1.6 ± 0.8	0.109
Random Blood Sugar (mean ± SD, mg/dL)	165 ± 93	164 ± 71	0.965
Time to First Hospital Contact (mean ± SD, hours)	69 ± 121	20 ± 30.5	0.031
Duration of MI to VSR Detection (mean ± SD, days)	10.2 ± 13.7	3.2 ± 3.6	0.008
Time of Surgery from Diagnosis (mean ± SD, days)	9.0 ± 5.4	3.0 ± 0.0	0.340

Table 4. Comparison of Survivor Versus Non-Survivor Patients with Post-Myocardial Infarction Ventricular Septal Rupture

MI: Myocardial Infarction; AWMI: Anterior Wall Myocardial Infarction; IWMI: Inferior Wall Myocardial Infarction; VSR: Ventricular Septal Rupture; TIMI: Thrombolysis in Myocardial Infarction and LVEF: Left Ventricular Ejection Fraction.

	Historical Data	**MIDAS (19) (n=148881) (STEMI)**	**GUSTO-1 (8) (n=41021) (STEMI)**	**GRACE (20) n=60198 (ACS)**	**APEX-AMI(21) (n=5745) (STEMI)**	**SHOCK Registry(9)**	**Present Study**
Treatment (Overall Cohort)	Pre-thrombolysis	PCI	Thrombolysis	Primary PCI	Primary PCI	--	Thrombolysis (42%)
Incidence of VSR	1-2%	0.25-0.31%	0.20%	0.25%	0.17%	--	--
Median Time to VSR Detection	3-5 days	Not reported	1 day	Not reported	7.7 hours	16 hours	2 days
30 Days Mortality	--	--	73.8%	--	80%	--	80%
In-hospital Mortality ● Conservative ● Surgical	 90% 45%	41%	 94% 47%	41%	--	 96% 81%	 95% 12.5%
In-hospital Survival on Surgical Management	--	--	53%	--	--	19%	87.5%

Table 5. Clinical Scenario of Ventricular Septal Rupture in Various Large Clinical Studies and Present Study

VSR: Ventricular Septal Defect; STEMI: ST-Elevated Myocardial Infarction; and ACS: Acute Coronary Syndrome

DISCUSSION

The present study evaluated the short-term (30 days) outcomes of 45 patients with VSR developed post-AMI. In this study the ratio of male and female was found to be nearly equal however, the GUSTO-I[8] and SHOCK[9] studies reported female predominance for VSR development post-AMI.

It has been reported in various studies that in thrombolytic era the time of VSR formation has reduced which may indicate that rupture might occur sooner compared to pre-thrombolytic era.[5,8,9] It has been proved that thrombolytic therapy decreases the size of infarct, however reperfusion may stimulate the formation of haemorrhage or dissection in the myocardium which potentially escalate the risk of rupture. In the present study also, 50.4% of the patients were diagnosed with VSR within 2 days of AMI onset. Total 19 patients underwent conservative thrombolytic management with streptokinase and among them only 3 (15.8%) patients survived at 30 days depicting 84.2% mortality in patients who underwent thrombolysis. Therefore, conservative thrombolytic management did not improve survival rate in patients with VSR post-AMI as it may leads to the formation of more complex ruptures that are more difficult to repair.[4]

Anterior wall infarcts have in some studies been associated with a more frequent development of septal rupture than inferior-posterior infarcts.[1,4,10] In the present study, the ECG location of the AMI and the location of the septal rupture by echocardiography were much more common in anterior wall (84.4%) than inferior wall, which was in contrast to certain studies.[11] IABP was used in 3 (6.7%) patients for stabilization of haemodynamic conditions. Although no definite documentation exists that IABP improves survival, the use of IABP has been widely accepted as a favourable support in the treatment of myocardial septal rupture. Use of IABP decreases left ventricular afterload, reduces the magnitude of the left-to-right shunt, and increases the coronary perfusion. Thus, IABP may stabilize and improve the clinical and hemodynamic condition in a number of patients.

In contrast with previous reports, this study demonstrated that clinical signs of heart failure, such as increased Killip class and increased heart rate, were not found to be the independent predictors of short term mortality.[8-10] Other demographic characteristics such as advanced age and history of hypertension were also not found to be independently associated with mortality. Hospital survival in surgically treated patients in the SHOCK trial[9] and GUSTO-I trial[8] was 19% and 53%, respectively. However, the present study depicted 87.5% survival in surgically treated patients at 30 days. Moreover, in-hospital mortality (95%) following conservative management in the present study was found to be similar to that reported in the GUSTO-I trial (94%) and in the SHOCK Registry (96%).[8,9] (Table 5)

In accordance with the other studies,[8,12-15] the present study also reported high mortality (33.37%) in early operated (≤7 days after diagnosis) patients compared to none (0%) in late operated patients (>7 days after diagnosis). The fragile necrotic myocardium is a major concern while operating on an urgent basis and the patients who underwent early surgery usually referred to have marked haemodynamic instability and circulatory compromise. However, in the current study the difference was non-significant between survivors and non-survivors patients with early and late surgery, as the patients who underwent surgery were really less (n=8). Literature also state that better survival in patients with late surgical repair might be due to development of fibrotic and scar tissues around the VSR, which is a result of natural healing tendency of the body. Thus, various investigators use mechanical circulatory support with ventricular assistance device in severely hemodynamically compromised patients until surgical repair. However, in the current study, IABP was used to provide mechanical support in only 3 patients. Furthermore, the use of a trans-catheter closure device should be considered, if the patient is not considered for concomitant coronary artery bypass surgery, if the ventricular septal defect has a simple structure (predominantly anteriorly located) and if it is not located close to the mitral valve apparatus. However, very limited data are available which have documented the yield of these devices that may bring out significant future treatment options.[16-18] In this context, three patients with septal rupture was recently treated in our department with an Amplatz Occluder and the outcome was successful.

In this study, some additional independent prognostic markers like low LVEF, high TIMI scores and shorter duration between acute MI and VSR occurrence were also found to be associated with lower survival rate of VSR patients in addition to various other prognostic markers already studied in previous studies. It helps in better understanding and risk stratification of patients with VSR and provide an early institution of appropriate management. Although large studies with more sample size are needed to confirm these findings.

Study Limitation

The main limitation of the present study is its study design i.e. a single-centre, retrospective study with relatively small sample size. Furthermore, it had higher selection bias generally for surgical repair of VSR and limited use of mechanical support such as IABP device. Only short-term (30 days) mortality rate have been mentioned.

CONCLUSIONS

Although various advanced treatment options are available, post-MI VSR is associated with significant mortality. Low LVEF, high TIMI score and shorter duration between the onset of MI and occurrence of VSR are associated with poor outcomes in patients with post-MI VSR. Surgical correction brings significant change in the prognosis. Transcatheter closure can be considered in elderly age and hemodynamically unstable patients who are with high risk of surgical closure.

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