Clinical update

Ventricular septal rupture complicating acute myocardial infarction: a contemporary review

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Ventricular septal rupture (VSR) after acute myocardial infarction is increasingly rare in the percutaneous coronary intervention era but mortality remains high. Prompt diagnosis is key and definitive surgery, though challenging and associated with high mortality, remains the treatment of choice. Alternatively, delaying surgery in stable patients may provide better results. Prolonged medical management is usually futile, but includes afterload reduction and intra-aortic balloon pump placement. Using full mechanical support to delay surgery is an attractive option, but data on success is limited to case reports. Finally, percutaneous VSR closure may be used as a temporizing measure to reduce shunt, or for patients in the sub-acute to chronic period whose comorbidities preclude surgical repair.

Keywords
VSR • Ventricular septal rupture • Acute myocardial infarction • Percutaneous closure

Introduction

Ventricular septal rupture (VSR) is a rare but lethal complication of acute myocardial infarction (AMI). As acute reperfusion strategies for AMI have evolved, VSR has become increasingly rare and is identified earlier in the post-MI course. Despite significant improvements over the last two decades in overall mortality for patients with AMI, the outcome of patients who develop VSR remains poor. In this paper, we will review the incidence and pathophysiology of VSR in the current era of aggressive reperfusion with dual antiplatelet therapy and primary percutaneous coronary intervention (PCI), and provide a current perspective on the surgical and percutaneous management of VSR.

Epidemiology

The advent of emergent reperfusion strategies for AMI, including thrombolysis and PCI, has led to a decline in the incidence of VSR in contemporary series. Restoration of flow in the infarct related artery leading to myocardial salvage and reduced incidence of transmural infarct may account for this observation. In the pre-thrombolytic era, VSR was thought to complicate ~1–2% of AMI presentations. More contemporary series, however, show it to be increasingly rare, complicating between 0.17 and 0.31% of patients presenting with AMI (Table 1).

It is logical to think that mechanical complications would be less frequent in patients treated with primary PCI when compared with thrombolysis or medical therapy alone. In contrast to thrombolysis, optimal PCI results in increased TIMI 3 flow, increased salvage index, and less haemorrhagic transformation of the infarct zone. In the Global Registry of Acute Coronary Events (GRACE) registry, patients presenting with ST-elevation MI (STEMI) were evaluated for heart rupture (VSR or free-wall rupture) based on reperfusion strategy. Although neither thrombolytic use nor PCI were independent predictors of heart rupture, there was an overall trend favouring patients treated with PCI (0.7% incidence of heart rupture) vs. those treated with thrombolysis (1.1%) vs. neither lytic or PCI (1.2%).

There was also a significant linear relationship between shorter time to thrombolysis infusion and lower incidence of heart rupture ($P = 0.02$). Finally, it has been shown that the incidence of VSR is lower in patients who undergo primary PCI compared with those who undergo delayed or elective PCI after recent AMI. Thus, strategies aimed at reducing door-to-balloon time for STEMI, including pre-hospital electrocardiogram and bypass of the emergency department, may contribute to the observed reduction in heart rupture. Unfortunately though, despite a declining incidence, current mortality among patients with VSR...
remains high (41–80% in current series), and appears mostly unchanged over the last few decades (Table 1).²,³,⁵

<table>
<thead>
<tr>
<th>Source</th>
<th>MI treatment (overall cohort)</th>
<th>Incidence of VSR, % (n)</th>
<th>Time to VSR identification</th>
<th>Mortality, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Historical data</td>
<td>Pre-thrombolysis</td>
<td>1–2</td>
<td>3–5 days</td>
<td>With surgery: 45</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Without: 90</td>
</tr>
<tr>
<td>MIDAS²</td>
<td>PCI (19%)</td>
<td>0.25–0.31 (408)</td>
<td>Not reported</td>
<td>In-hospital: 1990–92: 41</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2005–07: 44</td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td>1-year: 1990–92: 60</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2005–07: 56</td>
</tr>
<tr>
<td>GUSTO-1³</td>
<td>Thrombolysis (100%)</td>
<td>0.20 (84)</td>
<td>1 day</td>
<td>30-day: with VSR: 73.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>without VSR: 6.8</td>
</tr>
<tr>
<td>GRACE³</td>
<td>Primary PCI (15% overall; 38% for STEMI)</td>
<td>0.25 (155)</td>
<td>Not reported</td>
<td>In-hospital: 1990–92: 41</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2005–07: 44</td>
</tr>
<tr>
<td></td>
<td>Lysis (12% overall; 28% for STEMI)</td>
<td></td>
<td></td>
<td>1-year: 1990–92: 60</td>
</tr>
<tr>
<td>APEX-AMI⁶</td>
<td>Primary PCI (94%)</td>
<td>0.17 (10)</td>
<td>7.7 h (range 5.5–23.5)</td>
<td>30-day: 2004–2006: 80</td>
</tr>
</tbody>
</table>

VSR, ventricular septal rupture; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Pathophysiology

Rupture develops after full-thickness (transmural) infarction of the ventricular septum and can occur at any anatomic location. Infarctions involving the left-anterior-descending, dominant right-coronary, or dominant left-circumflex arteries can all involve septal branches. Ventricular septal rupture seems to occur with similar frequency in anterior and inferior/lateral infarctions.³ Anterior infarctions are more likely to cause apical defects and inferior or lateral infarctions are more likely to cause basal defects at the junction of the septum and the posterior wall. Regardless of location, the newly formed communication results in left to right shunting of oxygenated blood from the high-pressure left ventricle (LV) to the lower-pressure right ventricle (RV). Clinical presentation varies from complete haemodynamic stability to frank circulatory collapse depending on the size of the defect, presence of RV infarction, ongoing RV ischaemia, or stunning of the RV from volume overload. Unpredictable haemodynamic deterioration is the norm in most patients in the days and weeks following VSR, and reports of long-term survival independent of corrective surgery are extremely rare.

The conventional mechanism of septal rupture involves coagulation necrosis of ischaemic tissue with neutrophilic infiltration, eventually causing thinning and weakening of the septal myocardium.¹ This sub-acute process requires 3–5 days, likely accounting for the traditional timing reported in the early surgical literature. Rupture occurring within 24 h of presentation is more likely due to dissection of an intramural haematoma or haemorrhage into ischaemic myocardium. This classically occurs due to physical shear stresses at the border of an infarct zone, combined with a hypercontractile, remote myocardial segment. Clinically, it is most commonly seen in the setting of an inferior infarction with the VSR noted in the basal inferior septum, abutting the hyperdynamic mid-septum that is perfused by the LAD. Ventricular septal rupture can also present in
concert with other mechanical complications such as ventricular aneurysm, free wall rupture, or papillary muscle rupture.

Becker and Mantgem\(^1\) classified the pathological features of cardiac free wall rupture (similar in pathophysiology and therefore applicable to VSR) into three types. Type I rupture shows an abrupt, slit-like tear, and is associated with acute infarcts <24 h in age. Type II rupture demonstrates erosion of the infarcted myocardium, and correlates clinically with a sub-acute presentation. Type III rupture exhibits concomitant aneurysm formation with significant thinning of the septum and subsequent rupture, a process associated with older infarcts. Septal ruptures are further classified as simple or complex.\(^1\) Simple ruptures have a direct connection between the left and right ventricles, occurring at the same level in both chambers, while complex ruptures take a serpigenous course and are more likely to be caused by haemorrhage and irregular tears within the necrotic septum (Figure 1).

**Diagnosis**

It is critical that all patients with AMI have a brief evaluation for mechanical complications prior to primary PCI. All patients who develop haemodynamic compromise during AMI should be rapidly examined for the characteristic, harsh, systolic murmur over the precordium, as well as a palpable thrill, both of which may be difficult to detect in patients with a low output state. Other physical exam findings result from augmented right-sided flow, and may include a loud pulmonary component of the second heart sound, left or right S3 gallop, or tricuspid regurgitation.

Left ventriculography performed in the left-anterior oblique (LAO) projection in a patient with VSR may demonstrate shunting of contrast from the LV to the RV. If a PA catheter is placed, the diagnosis should be suspected in patients who have acutely rising mixed

![Figure 1](https://academic.oup.com/eurheartj/article-abstract/35/31/2060/2293126/2062)
venous O₂ saturations, which could be reflective of a left-to-right shunt.

Usually, the diagnosis is made by a prompt transthoracic echocardiogram identifying drop-out of the ventricular septum in the 2D image and demonstration of flow across the septum using colour Doppler (Figure 1). Evidence of right-ventricular dilation and pulmonary hypertension are also important clues to the diagnosis. The remaining portions of the left ventricle are often hypodynamic unless there is a large territory of infarction, or previous ischaemic insults have led to compromised function. Colour Doppler evaluation can also be useful to assess the anatomical size of the defect. When the patient has poor acoustic windows due to mechanical ventilation or body habitus, a TEE should be considered.

When a diagnosis of VSR is made prior to primary PCI, strategies for prompt restoration of coronary flow must be approached with consideration towards the competing need for emergent surgery and the associated risks of surgical bleeding after the administration of dual-antiplatelet therapy. It remains key to limit the ischaemic burden in the infarct-related artery, especially if there is right-ventricular involvement, so immediate collaboration between the interventional cardiologist and cardiac surgeon is critical to develop a case-specific approach. Ideally, VSR would be diagnosed prior to PCI. Flow may be restored in the infarct related artery with aspiration thrombectomy and/or balloon angioplasty, with preparations made for immediate VSR repair with coronary artery bypass grafting. If surgery is delayed, consideration should be given to bare-metal stent placement to minimize dual-antiplatelet therapy duration.

**Surgical management**

Operative management of patients can be complex, and having a systematic approach is helpful. For an anterior VSR, it is important to assess the severity of LV dysfunction, presence of coexisting CAD, suitability of potential revascularization targets, and anatomy of previous infarctions. For a posterior VSR, an additional understanding of RV function and the presence of mitral regurgitation is important.

Most patients with acute post-MI VSR are in cardiogenic shock, and once in the operating room cardiopulmonary bypass with bicaval cannulation should be initiated expeditiously. Many surgeons prefer a left ventriculotomy through the infarct (generally 1 cm lateral to the LAD) to access the VSR as it allows the most direct view of the defect, and infarctectomy or aneurysmectomy can be more easily performed if needed. There are two common techniques used for repair of VSR, the Daggett and David procedures (Figure 2). The Daggett is a single or double patch technique which closes the VSR by placing a patch over the defect and sewing to the RV and LV. In contrast, the David technique is an infarct exclusion procedure with all sutures placed in the LV. 13

In the acute setting, infarcted myocardium is weak and friable, and holds sutures poorly leading to increased risk of tearing and recurrent septal defects. Principles of successful repair include debridement of infarcted tissue back to healthy myocardium (even if it involves enlarging the defect), and avoiding tension on the repair by using an appropriately sized patch. Large, 1 cm bites of tissue and buttressing of suture lines with pericardium or felt can improve the strength of the repair. This is especially important when the infarct is <24 h old as it may be difficult to differentiate viable and infarcted myocardium visually. In a large VSR there may not be enough anterior septum to allow adequate suturing of the patch. In this case, horizontal mattress sutures can be placed through the right ventricular wall.

Posterior VSRs pose additional technical challenges, as the heart must be elevated for adequate exposure. Additionally, the PDA and posteromedial papillary muscle are in close proximity. The transinfarct ventriculotomy is made 1 cm lateral to the PDA and care is taken to preserve the mitral subvalvular apparatus. In both anterior and posterior VSRs, the ventriculotomy is closed primarily or with a patch (usually Dacron) carefully to avoid post-operative free wall rupture. If surgical revascularization is planned, the grafts are placed prior to addressing the VSR to allow for more complete myocardial protection and to minimize handling the heart after the defect is repaired. 15 The use of saphenous vein as conduit for all grafts is common.

**Outcomes of surgical ventricular septal rupture repair**

Medical management of VSR is usually futile with rare exception (Figure 3). Definitive surgery remains the treatment of choice, but remains a challenging operation associated with high early mortality. A recently published review of the Society of Thoracic Surgeons National Database (STS Database) identified 2876 individuals aged ≥18 years who underwent post-MI VSR repair between 1999 and 2010. Overall operative mortality was 42.9%, which represented the highest mortality rate of any cardiac surgery. Patients who did not survive to 30 days tended to be older, female, had higher serum creatinine levels, and higher acuity of disease (cardiogenic shock, reduced LVEF, triple-vessel CAD, or requirement for pre-operative IABP). Operative mortality was much lower for procedures considered elective (13.2% mortality) vs. emergent (56.0% mortality) vs. salvage (80.5% mortality).

A smaller study of 68 consecutive patients, 85% of which underwent surgery <48 h after VSR diagnosis, investigated determinants of post-surgical outcomes. 17 In this group, residual interventricular communication was present in 22 of 63 patients (35%) who survived the initial surgery, and was an independent predictor of post-operative CHF. It was due to patch dehiscence in all 11 patients who underwent repeat surgery due to haemodynamic instability (percutaneous closure for residual VSR is discussed subsequently).

**Timing of surgery**

Mortality of patients in the STS database varied significantly depending on timing of surgery. Patients who underwent surgery within 7 days of presentation had a 54.1% mortality compared with 18.4% mortality if repair was delayed until after 7 days. Mortality was highest (>60%) in patients who underwent operation in the first 24 h, consistent with other investigators. 18 The improved outcome with delayed surgery may be related to evolution of the infarct and improved stability of the cardiac tissue allowing a more effective repair, but is also a representation of survival bias, as early surgery is usually performed on individuals with marked haemodynamic instability and circulatory compromise. Ultimately, only 886 of the 2876 patients (30.8%) in the STS database...
had surgery more than 7 days after presentation, suggesting that a minority of patients survive until elective repair. Also, the number of patients turned down for surgery is unreported. Similarly, the GUSTO-I trial demonstrated a 47% mortality at 30-days among 34 patients who underwent prompt surgical repair (median time 3.5 days, 95% CI, 1–7) vs. 94% mortality for the 35 patients treated without surgery (although again, selection bias must be considered).3

Taken together, the evidence demonstrates that although surgical mortality remains very high, non-surgical mortality is certainly higher. Thus, the clinician must weigh the known risk of expedient surgery against the unknown risk of postponing surgery and developing further clinical deterioration. A simplified version of our own multidisciplinary strategy for managing these patients is included, with the caveat that each case requires a tailored approach (Figure 4).

Medical management and mechanical support

The cornerstone of medical management of VSR is afterload reduction to increase effective LV stroke volume by reducing left-to-right shunting. Intravenous afterload-reducing pharmacotherapy such as sodium nitroprusside has the advantage of being rapidly titrated or emergently discontinued compared with oral agents. Intra-aortic balloon counterpulsation (IABP) provides mechanical afterload reduction and augmentation of cardiac output, and may be considered routine care, even in patients who remain haemodynamically stable, as development of haemodynamic compromise is often unexpected, rapid, and fatal. Of the 2876 patients in the STS database, 65% had an IABP placed pre-operatively, and another 8% had an IABP placed...
during surgery. IABP utilization was significantly higher in emergent (84.7%) and salvage (87.9%) cases when compared with elective cases (18.6%).

Several case studies in the literature have documented the use of extracorporeal membrane oxygenation systems to stabilize patients until surgery can be performed. Other options include placement of a percutaneous or surgical left-ventricular assist device as a bridge to surgery or transplant. The data detailing the success of these strategies in patients with acute VSR is currently limited to case reports.
Table 2  Major trials of percutaneous closure of ventricular septal rupture

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of patients</th>
<th>Initial procedural success</th>
<th>Timing of closure (days after AMI)</th>
<th>30-day mortality, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assenza,32 2013</td>
<td>30 patients</td>
<td>Primary closure: 12</td>
<td>19 (11–27)</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Residual after surgery: 18</td>
<td>54 (22–173)</td>
<td>11</td>
</tr>
<tr>
<td>Maltias,34 2009</td>
<td>12 patients</td>
<td>Unspecified</td>
<td>12.2</td>
<td>42</td>
</tr>
<tr>
<td>Thiele,30 2009</td>
<td>29 patients</td>
<td>Cardiogenic shock: 16</td>
<td>1 (1–3)</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No shock: 13</td>
<td>6.5 (4–16)</td>
<td>38</td>
</tr>
<tr>
<td>Bialkowsk,35 2007</td>
<td>19 patients</td>
<td>Primary closure: 17</td>
<td>14/19</td>
<td>26.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Residual after surgery: 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demkow,36 2005</td>
<td>11 patients</td>
<td>10/11</td>
<td>2/10 patients: ‘acute’</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>8/10 patients: 24–392</td>
<td>0</td>
</tr>
<tr>
<td>Holzer,33 2004</td>
<td>18 patients</td>
<td>Primary closure: 8</td>
<td>16/18</td>
<td>25 (2–95)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Residual after surgery: 10</td>
<td></td>
<td>28</td>
</tr>
</tbody>
</table>

AMI, acute myocardial infarction.

As another strategy, a small series of five patients demonstrated successful use of the Impella 5.0 L system (Abiomed, Danvers, MA, USA) for a mean of 14.4 ± 6 days as a bridge to surgery with a 30-day mortality of 40%. The TandemHeart pVAD system has been shown to reverse cardiogenic shock in 117 patients, but the cohort included only five patients with acute STEMI, and an unknown number of VSRs. Finally, a single case report from Germany documents the use of a total artificial heart followed by a successful cardiac transplant 14 weeks later. In the absence of large trial data, these reports provide an interesting, albeit limited, perspective. Short-term mechanical circulatory support is a bridge to recovery in a IIa (LOE C) recommendation in patients with VSR and persistent shock according to current ESC guidelines.

Percutaneous ventricular septal rupture closure

The past decade has witnessed an exciting evolution in structural cardiac interventions. As a result, attention has turned to percutaneous options for the closure of VSR in patients with significant risk for surgical repair, either as a definitive strategy, or as a bridge to surgery after initial stabilization. Several case series have been published documenting single institution experience with both primary percutaneous VSR closure as well as closure of residual defects after surgery (Table 2). Similar to the surgical literature, outcomes improve as patients progress from the acute to chronic phase. The primary goal is a reduction in residual left-to-right shunting (Qp:Qs), which in the largest series of primary VSR closure, was reduced from 3.3 (IQR 2.3–3.8) to less than 1.5:1 in all but four of 29 patients.

There are several anatomic concerns in selecting patients for a percutaneous repair. Most authors suggest that a defect <15 mm is optimal, in large part due to the device sizes that are available, as well as the size of the septum. Inferior/posterior defects are especially challenging as they frequently lack an adequate tissue ‘rim’ to secure the device. The location of the adjoining tricuspid valve apparatus (especially the septal leaflet) makes closure of basal defects more difficult still. Serpigenous defects are not only difficult to cross with a wire, but can be complicated by significant leakage around the device since the path between the ventricles is not straight. Finally, freshly infarcted myocardium may exhibit ongoing necrosis and instability in the days following MI, making peri-device leakage or device embolization a concern. Thus, attempting device placement requires a thorough understanding of the defect’s size, shape, and borders, usually requiring characterization by both surface and transesophageal echocardiography. Intracardiac echocardiography is invasive and therefore not often used in the screening phase of management; however, it may be useful intra-procedurally, especially when the probe is advanced to the RV.

We favour a retrograde approach across the aortic valve. A soft wire (i.e. 0.035” Wholey wire) is passed across the VSR from the LV to the RV (along the direction of flow). The wire is then passed to the pulmonary artery to facilitate snaring. The snare may be advanced from the internal jugular or femoral venous approach. While the angle of the SVC to the VSR is more favourable than that of the IVC, we find that the inherent lack of sterility in operating from the neck is a limitation to this approach. Once the wire is snared in the PA, it is externalized. A delivery sheath is then advanced from the venous side and across the VSR into the LV. The intended device is then deployed across the septum.

Another novel approach is a combined surgical/percutaneous hybrid closure. Via a standard thoracotomy, a cannulating needle and introducer can be inserted directly into the RV or LV. Under fluoroscopic guidance, the defect is then crossed with a wire and the procedure conducted through the routine steps. Alternatively, a septal occlusion device can be placed under direct visualization. The hybrid approach has the theoretic advantages of easier crossing of the defect and better visualization than a fully percutaneous...
strategy, and conversely obviates the need for cardiopulmonary bypass. Furthermore, the surgeon need not suture into freshly infarcted and structurally poor myocardium. Patients who undergo percutaneous closure should receive dual anti-platelet therapy for 6 months followed by baby aspirin alone, and should receive appropriate antibiotic prophylaxis prior to invasive procedures.

Conclusions

Mortality due to AMI has fallen substantially over the past three decades. Nevertheless, patients who suffer VSR represent a subgroup with extraordinarily high mortality. Management of the patient who is in acute, decompensated cardiogenic shock should be directed at reducing left-to-right shunt with afterload reducing agents and IABP placement. There is no clear evidence to guide the surgical management of patients who are in shock, as all approaches have shown extremely high mortality. Possible strategies include emergent surgery, a period of percutaneous mechanical circulatory support prior to a delayed surgical or percutaneous intervention, or emergent placement of a percutaneous closure device to reduce the shunt. Percutaneous closure may also be a viable option for patients in the sub-acute to chronic period whose comorbidities preclude surgical repair, and whose septal anatomy is favourable to device placement. The management of VSR is complicated, and requires substantial critical care, imaging, interventional, and surgical expertise. It is therefore advisable, when clinically feasible, to transfer these patients to regional centres with adequate individual experience in the care of patients with VSR.

Conflict of interest: none declared.

References