Original Research

Post-Infarction Ventricular Septal Defect: Risk Factors and Early Outcomes

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Background: Rupture of the ventricular septum complicates acute myocardial infarction in 0.2% of cases in the thrombolytic era. Ventricular septal defect (VSD) has a mortality of 90-95% in medically managed and 19-60% in surgically treated patients.

Methods: A retrospective analysis was performed of 41 patients, 26 females (63.4%) and 15 males (36.6%), average age 67.5 ± 15 years, with post-infarction VSD who were treated in the VUL SK intensive cardiology unit between 1991 and 2007.

Results: Thirty-seven patients had hypertension (90.2%); anterior wall acute myocardial infarction (AMI) was found in 27 patients (68%). VSD was more frequent in women than in men (p=0.043). In 36 patients (87%) treatment was started 24 hours or later after the development of AMI symptoms. In 34 patients (83%) the rupture occurred during the first episode of AMI and in the majority of these (19 patients, 46.3%), preoperative coronary angiography demonstrated disease of only one coronary artery. During the first 10 days after the onset of AMI, 5 patients (12.2%) were treated surgically but did not survive the operation; 33 patients (80.5%) underwent operation 3-4 weeks after the onset of AMI and all survived.

Conclusions: Female sex, advanced age, arterial hypertension, anterior wall AMI, absence of previous AMI, and late arrival at hospital are associated with a higher risk of mortality from acute VSD. The most important factor that determines operative mortality and intra-hospital survival is the time from the onset of AMI to operation.

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Ventricular septal defect (VSD) is a rare, but life-threatening complication of acute myocardial infarction (AMI). In the pre-thrombolytic era, its incidence amounted to 1-2%; the use of thrombolytic agents reduced this to 0.2%.[1,2] Known risk factors for ventricular septal rupture are advanced age, female sex, arterial hypertension (PAH), anterior AMI, absence of previous MI, and angina pectoris.[2,3] Despite progress in pharmaceutical therapy, invasive cardiology, and surgical technique, the mortality rate after the development of this complication still remains high.[2] When conservative treatment is applied alone, the mortality rate reaches 90-95%, while for surgical intervention it varies from 19% to 60%.[1] Results from different medical centers have varied. Moreover, it is still not clear how the timing of surgical treatment is related with outcomes.

The aim of this study was: 1) to assess the impact of risk factors for coronary artery disease (CAD) and their progress on the development of ventricular septal rupture; 2) to identify those risk factors which increase operative and in-

hospital mortality after the development of VSD; 3) to identify the optimal timing for surgical treatment; and 4) to compare the data of our center with data from other centers.

Materials and methods

Patient population and data collection

A retrospective data analysis was performed on 41 patients who were treated between 1991 and 2007 in the intensive cardiology unit of Vilnius University Hospital Santariskiu Klinikos (ICU VUL SK), developed a post-infarction VSD and received surgical treatment. The average age of the group was 67.5 ± 15 years (range 52-82 years). The AMI diagnosis was based on clinical ischemic symptoms, electrocardiographic (ECG) changes, and a typical rise in the levels of biomarkers of myocardial necrosis. Coronary angiography and echocardiographic data were also assessed. In all cases, post-infarction VSD was suggested by findings on physical examination (a new rough systolic murmur) and confirmed by echocardiography. Demographic data characterizing patients, including age, sex, CAD risk factors and prior MI, were collected. Clinical status, acute left ventricular (LV) failure according to the Killip classification upon arrival, ECG, coronary angiographic findings (>50% coronary artery stenosis was considered to be significant), and echocardiographic data were assessed. The times from the appearance of AMI symptoms to the start of treatment and to the development of ventricular septal rupture were measured.

Surgical timing

A number of patients developed cardiogenic shock and deteriorating hemodynamic status in spite of conservative treatment, including intra-aortic balloon counterpulsation (IABC). These patients were operated on within the first 10 days after the onset of AMI. The other patients underwent operation 3-4 weeks after the onset of AMI. Their clinical status was stabilized and maintained by conservative means in the ICU. In all operated patients, the septum was approached through a left ventriculotomy at the level of the infracted area. Reconstruction of the ventricular septum and closure of the defect were performed with Dacron, Teflon or pericardial patch, or by direct suture.

Endpoints

The primary endpoint was the impact of demographic and clinical data on the development of VSD. Secondary endpoints included early in-hospital mortality, defined as death occurring during hospitalization, and factors leading to operative mortality, defined as death during cardiac surgery.

Statistical analyses

Standard statistical software SPSS (version 16 for Windows) was used for calculations. Quantitative variables are presented as mean ± standard deviation (SD). Categorical variables are presented as both absolute and relative (%) values. Non-survivors and discharged patients were compared using chi-square or Fisher's exact tests (where appropriate). A p-value <0.05 was considered significant.

Results

Over a 16-year period, 41 patients were treated for post-infarction VSD in the VUL SK intensive cardiology care unit. In all cases, this complication was diagnosed within seven days (100%) from the development of AMI symptoms. Women developed this complication more often than men ($p=0.043$). Patients with post-infarction VSD were more likely to have an anterior wall AMI. In all cases, treatment was started 24 hours or later following the onset of AMI. Thirty-four patients (83%) developed post-infarction VSD during their first episode of AMI. These patients had never been diagnosed with an acute coronary syndrome (ACS). The majority of patients with VSD had hypertension and type II diabetes mellitus. Coronary angiography was performed in all patients. Most patients with VSD had single-vessel (left coronary artery) disease, while the remainder had two- or three-vessel CAD, both occurring with equal frequency (Table 1).

Overall in-hospital mortality was 19.5% (n=8) (Table 2). Thirty-eight (92.7%) patients were treated surgically. Three patients died before operation: two women and one man. An 80-year-old woman died from hospital-acquired pneumonia 3 weeks after the onset of AMI. A 64-year-old woman died from an ischemic brain stroke 2 months after AMI. These women came to hospital more than 24 hours after the onset of ACS symptoms. All developed cardiogenic shock, and coronary angiography disclosed hemody-

Table 1. Baseline characteristics of patients with a ventricular septal defect.

Number of patients	n = 41
Age, years	67.5 ±15
Female/male sex	26/15 (63.4%/36.6%)
PAH	37 (90.2%)
Diabetes, type II	28 (65.5%)
Location of infarction:	
Anterior	27 (68%)
Inferior – lateral	14 (34.1%)
Previous AMI	7 (17%)
Killip class:	
III	6 (12.2%)
IV	36 (87.8%)
Diseased vessels:	41 (100%)
1 vessel	19 (46.3%)
2 vessels	11 (26.8%)
3 vessels	11 (26.8%)
Infarct related artery:	
Left coronary artery	25 (61.0%)
Left circumflex	9 (22.0%)
Right coronary artery	7 (17.0%)
Time from symptoms to treatment:	
<24 hours	6 (14.6%)
>24 hours	35 (85.4%)
IABC	15 (36.6%)

PAH – primary arterial hypertension; IABC – intra-aortic balloon counterpulsation.

namically significant stenoses in more than one vessel. A 67-year-old man with type II diabetes mellitus and known CAD arrived 6 hours after the onset of AMI in cardiogenic shock. He died of hospital-acquired pneumonia during the third week of hospitalization. Five patients developed sudden hemodynamic deterioration that failed to respond to medical therapy. These patients were operated on during the first 10 days after the onset of AMI. None of them survived the operation. On the other hand, all patients who were operated on 3-4 weeks after the onset of AMI survived (Table 3). There was a direct relationship between operation timing and mortality ($p<0.001$). The significant predictors of operative mortality were age and the time between the onset of MI and the operation (Table 4).

Discussion

The frequency of post-infarction VSD has decreased as a result of myocardial reperfusion therapy. Results of recent studies suggest that early and complete restoration of circulation in the infarcted artery using thrombolytic agents or primary percutaneous

Table 2. In-hospital mortality.

		Number of survivors (n=33)		Number of deaths (n=8)		p
Sex	Male	12	36.4%	3	37.5%	1.000
	Female	21	63.6%	5	62.5%	
IABC	Applied	10	30.3%	5	62.5%	0.117
	Not applied	23	69.7%	3	37.5%	
MI type	Inferior-lateral	11	33.3%	3	37.5%	1.000
	Anterior	22	66.7%	5	62.5%	
KILLIP	III	5	15.2%	-		0.563
	IV	28	84.8%	8	100.0%	
Cardiogenic shock		33	100.0%	8	84.8%	0.563
CA	LCA	19	57.6%	6	75.0%	0.217
	LCx	9	27.3%	-		
	RCA	5	15.2%	2	25.0%	
Age group	<=70	14	42.4%	7	87.5%	0.045
	>70	19	57.6%	1	12.5%	
Diabetes type II		23	69.7%	5	62.5%	
PAH		30	90.9%	7	87.5%	
Start of treatment	<=24 hours	5	15.2%	1	12.5%	1.000
	>24 hours	28	84.8%	7	87.5%	
Died before operation		-		3	37.5%	
Operated during first 10 days		-		5	62.5%	<0.001
Operated after 3-4 weeks		33	100.0%	-		<0.001

IABC – intra-aortic balloon counterpulsation; AMI – acute myocardial infarction; CA – coronary artery; LCA – left coronary artery; LCx – left circumflex; RCA – right coronary artery; PAH – primary arterial hypertension.

Table 3. Operation time and in-hospital mortality.

Number of patients (n)		
Operated within first 10 days	5	(12.2%)
Operated after 3-4 weeks	33	(80.5%)
Survived	33	(80.5%)
Died:		
Before operation	3	(7.3%)
During operation	5	(12.2%)

coronary intervention (PCI) reduces the ischemic insult in the myocardium and helps to preserve left ventricular function, as well as decreasing the frequency of development of VSD.[3] Earlier studies reported that VSD usually occurs during the first 10-14 days following AMI.[4,8] However, recent reports show that the time between AMI and VSD development has shortened.[3,5,9] Currently, VSD occurs approximately 3-5 days following AMI.[3,5,9] Thrombolytic therapy reduces myocardial ischemic volume, but reperfusion can potentially lead to myocardial hemorrhage and dissection in the zone of necrotic myocardium, thereby facilitating the development of rupture within 24 hours after the onset of AMI.[2,3,5] With primary PCI, VSD develops earlier than in the pre-thrombolysis era, but later than with thrombolysis.[3] In our study, all cases of VSD (100%) were diagnosed within 7 days after the onset of AMI. Our patients came to hospital late, with 35 (85.4%) arriving more than 24 hours after the onset of AMI symptoms. Therefore, successful reperfusion after PCI occurred more rarely and the time to the development of VSD was longer compared with the data from other recent studies.

Our data, as well as reports from GUSTO-1, SHOCK, Crenshaw et al, Yip et al, Birnbaum et al, and Barker et al, found female sex to be a risk factor for the development of VSD.[1,5-8,10,20,21] In the present study the male/female ratio was 1.75. Although VSD may develop at a wide range of ages, older age (60-69 years) was found to be an independent predictor of VSD-related MI both during the pre-thrombolytic era and in the current series.[3,4] In this survey, the average age of patients who developed post-infarction VSD was 67.5 ± 15 years. In earlier studies, the average age was approximately 65 years, but more recently the average age of patients with VSD has been in the range

Table 4. Operative mortality.

		Number of survivors (n=33)		Number of deaths during operation (n=5)		p
Sex	Male	12	(36.4%)	2	(40%)	1.000
	Female	21	(63.6%)	3	(60%)	
IABC						
	Yes	10	(30.3%)	3	(60%)	0.315
	No	23	(69.7%)	2	(40%)	
AMI type	Inferior-lateral	11	(33.3%)	2	(40%)	1.000
	Anterior	22	(66.7%)	3	(60%)	
Killip	III	5	(15.2%)	-		0.592
	IV	28	(84.8%)	5	(100%)	
Cardiogenic shock	Yes	31	(86.1%)	5	(100%)	1.00
	No	5	(13.9%)	-		
CA	LCA	19	(57.6%)	3	(60%)	0.260
	LCx	9	(27.3%)	-		
	RCA	5	(15.2%)	2	(40%)	
Age group	<=70	14	(42.4%)	5	(100%)	0.046
	>70	19	(57.6%)	-		
Diabetes type II		23	(69.7%)	3	(60%)	0.643
PAH		30	(90.9%)	4	(80%)	0.446
Start of treatment	<=24 hours	5	(15.2%)	-		0.592
	>24 hours	28	(84.8%)	5	(100%)	
Operated during the first 10 days		-		5	(100%)	<0.001
Operated after 3-4 weeks		33	(100%)	-		<0.001

Abbreviations as in Table 2.

of 70-72 years.[2,5,7,10,12] Arterial hypertension is a significant risk factor for the development of post-infarction VSD and it was commonly observed in our patients.[3,8,9,10] In our study, as well as in earlier reports, the absence of previous MI or angina pectoris was noted.[6,8,9,12-14] Angina pectoris or prior infarction might lead to myocardial preconditioning, as well as to development of coronary collaterals, both of which could reduce the likelihood of septal rupture.[10] Although type II diabetes is not a risk factor for the development of VSD, it is worth mentioning that in our study it was present in 65.5% of patients. In previous studies and in our clinical observations, anterior AMI was a significant risk factor for the development of VSD.[2,3,5,10,15] When post-AMI VSD occurs, paradoxical ventricular septal motion is often observed during systole.[3] Coronary artery disease involving the left anterior descending artery is also common.[3] A predominance of single-vessel disease with total occlusion of the infarct-related artery is associated with more frequent development of septal rupture.[5,9,12,15,16] Our observations are in accordance with these earlier findings. In this study, all patients had acute left ventricular failure (Killip class III-IV). We believe that the poor clinical status of our patients was determined by their late arrival at the hospital: 85.4% came more than 24 hours after the onset of AMI symptoms and 87.8% presented with cardiogenic shock (Killip class IV).

In the present study, the management strategy for post MI VSD was initial stabilization with medical therapy and/or IABC in the intensive cardiac care unit. It has previously been reported that patients who undergo operation early after septal rupture have a more adverse outcome compared with patients who undergo late surgery.[5,9,11,12,16,18] Five of our patients underwent operation during the first ten days after the onset of AMI. None of them survived. Sudden hemodynamic deterioration between admission and a scheduled later operation, as well as shock prior to surgery, were both strong predictors of early mortality.[10,12] Urgent surgical repair is needed if conservative attempts fail to stabilize the patient, and operation then remains the only option, though survival is known to be poor.[13] The current recommendations of the European Society of Cardiology state that urgent surgical repair offers the only chance for survival with large post-infarction VSD and cardiogenic shock.[19] The American Heart Association/American College of Cardiology guidelines also recommend urgent surgical repair. This recommendation is based on the fact that a septal defect grows during a waiting period, and sudden hemodynamic deterioration may develop.[17] However, it is possible to delay operation for those patients who do not develop cardiogenic shock, despite the presence of congestive heart failure.[17] Surgical timing in post-MI VSD patients is the critical issue.[5,9,11,12,16] Our results confirm that both operative and late survival are favored by delayed surgery. During the current study, all patients who were operated on 3-4 weeks following the onset of AMI survived, regardless of their clinical status on admission.

The number of patients in this study was relatively small, limiting its statistical power. Nevertheless, urgent surgery and younger age were statistically significant predictors of higher operative and intra-hospital mortality ($p<0.001$). In some studies, older age (more than 70 years) was related to a worse outcome in surgically treated patients.[2,5] However, not all observers report age as a consistent risk factor for survival.[1,16,10] Some studies have reported that patients with inferior infarcts and VSD tend to have a worse outcome than those with an anterior AMI.[2,4,10] We were unable to demonstrate any effect of AMI location on VSD survival.

Post-ischemic rupture of the ventricular septum still represents a major challenge for cardiologists and cardiac surgeons. Operation through the infarcted ventricular zone along with IABC support is currently the standard surgical approach.[18] This method was used in our series.

Conclusions

The frequency of post myocardial VSD has recently decreased as a result of early reperfusion therapy. Female sex, advanced age, arterial hypertension, anterior wall AMI, first AMI, and late arrival at hospital are associated with a higher VSD risk. The most important factor determining operative and late survival is the time from the onset of AMI to operation.

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