Predictors of Mortality in Primary Surgical Repair of Postinfarction Ventricular Septal Defects: The Leipzig Experience

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ABSTRACT

Background: A postinfarction ventricular septal defect (pVSD) as a complication of acute myocardial infarction (AMI) is associated with high mortality. This retrospective, single-center study aimed to identify predictors of early and long-term outcomes in patients undergoing primary surgical repair of pVSD managed by various surgical techniques.

Methods: We reviewed data from 77 consecutive patients who underwent primary surgical repair after pVSD in our institution. Prospectively collected demographic and perioperative data were analyzed retrospectively. Predictors of 30-day mortality and long-term outcome were assessed.

Results: pVSD was anterior in 45 patients (58.4%) and posterior in 32 (41.6%). Buttressed mattress suture (n = 9, 11.7%), simple single septal patch (n = 34, 44.2%), simple double septal patch (n = 2, 2.6%), sandwich double patch (n = 1, 1.3%), and the infarct exclusion technique (n = 31, 40.3%) were performed for surgical closure. Fifty-three patients (68.8%) had preoperative cardiogenic shock. The 30-day mortality was 42.8% (33 patients). Independent risk factors of 30-day mortality were duration between AMI and surgery <7 days (odds ratio [OR] 5.229, P = .011), preoperative absence of diuretics (OR 6.913, P = .005), and preoperative cardiogenic shock (OR 3.558, P = .011). Cumulative survival rates at 1, 5, and 10 years were 57.1%, 57.1%, and 31.2%, respectively.

Conclusion: In pVSD, the 30-day mortality remains high, and preoperative cardiogenic shock significantly influenced mortality in our study. None of the surgical techniques or materials used in our investigation influenced the outcome.

INTRODUCTION

Acute myocardial infarction (AMI) remains one of the leading causes of death in developed countries. However, thanks to increasing progress in treatment options, its mortality rate has fallen significantly over the past 2 decades [Statistisches Bundesamt 2015]. The mechanical complications of AMI such as postinfarction ventricular septal defect (pVSD) occur seldom (0.17% to 0.34%) but are soon fatal with medical therapy only [Coskun 2009; Crenshaw 2000; Lee 1962; Moreyra 2010]. Notwithstanding the milestones in the gold-standard surgical treatment of pVSD [David 1995], 30-day mortality among these patients remains high: namely, 36.0% to 42.9% in recent studies [Arnaoutakis 2012; Lundblad 2014; Papadopoulos 2009; Takahashi 2015]. Not even the introduction of percutaneous, catheter-based closure of the pVSD has resulted in a real revolution, since the mortality rates for this procedure are similar and this method can currently only be used for small to medium-sized pVSDs [Schlotter 2016]. In addition, various risk factors are known to be responsible for a poor perioperative outcome, including cardiogenic shock (CS), emergency surgery, early repair, right ventricular dysfunction, posterior pVSD, renal impairment, and complex pVSD [Cinq-Mars 2016].

The different surgical approaches and the extent of the operation have regained renewed interest in recent years with the increasing use of percutaneous pVSD closure. The aim of this retrospective study was to determine the influence of different surgical methods, the extent of surgery, and the use of different materials on 30-day mortality. We also explored independent risk factors for 30-day mortality and long-term outcome to further optimize the perioperative outcome of these patients.

METHODS

Patient Cohort and Characteristics

At our institution, 77 patients underwent surgical closure for pVSD between October 1994 and January 2016. We only included patients in our study with a new diagnosis
of ventricular septal defect (VSD) due to myocardial infarction based on findings from right heart catheterization and/or transthoracic/transesophageal echocardiography. If a surgical or percutaneous interventional or surgical VSD occlusion had been attempted previously, the patient was excluded. We performed a retrospective analysis of the computerized hospital databases and the patient health records, considering demographics; pre-, intra-, and postoperative data; and survival at 30 days and the longest follow-up time point available.

**Definition of CS**
Cardiogenic shock was defined as persistent systolic blood pressure ≤90 mmHg or vasopressors required to maintain blood pressure >90 mmHg; evidence of end-organ failure (eg, urine output ≤30 mL/h, cold skin and extremities, serum lactate ≥2 mmol/l); evidence of elevated left ventricular filling pressures with clinical signs of pulmonary congestion; and/or the use of mechanical circulatory support devices (MCS).

**Operative Procedures**
All procedures were performed using a standard median sternotomy. The occlusion of the pVSD was performed using various techniques during cardiopulmonary bypass. A buttressed mattress suture without a patch was used in 9 patients (11.7%); a simple single-patch, simple double-patch, or sandwich double-patch was established in 34 (44.2%), 2 (2.6%), and 1 (1.3%), respectively. The infarct exclusion technique according to David et al [1995] was used in 41 (40.3%) patients, and 51 patients (66.2%) needed concomitant surgery.

**Statistical Methods**
Unless otherwise indicated, categorical variables are presented as numbers and percentages, and continuous parameters are expressed as mean ± standard deviation (SD). Fisher’s exact or χ² test was used to assess differences for categorical variables, and Student’s t test or the Wilcoxon rank-sum test was applied for continuous parameters, as appropriate. All-cause survival rates were analyzed by using the method of Kaplan–Meier. The log-rank test calculated statistical differences. Patients were divided into those who survived or did not survive 30 days after surgery for risk assessment. Multivariate analysis was performed using a logistic regression model to differentiate independent risk factors for 30-day all-cause mortality and Cox regression model for total all-cause mortality.

All tests were conducted 2-sided at the significance level α = 0.05. Unless otherwise stated, the analyses were performed using IBM SPSS Statistics for Macintosh, version 26.0 (IBM Corp., Armonk, NY).

**Ethical Concerns**
All authors had full access to datasets and maintained data integrity. They read and agree to the final paper as written. The local Ethics Committee approved the study. The study design, pseudonymous data acquisition, and data publication adhered to the Declaration of Helsinki.

**RESULTS**
Preoperative patient characteristics are summarized in Table 1 for all patients and according to 30-day survival. The mean age of the entire cohort was 68.7 ± 9.4 years. Left ventricular ejection fraction was 44.0% ± 15.0%, and the logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) was 42.4% ± 25.8%. Fifty-three patients (68.8%) presented in CS preoperatively and were implanted with an MCS; 36 patients (46.8%) received an intra-aortic balloon pump, and 4 (5.2%) extracorporeal life support (ECLS) preoperatively. The group of nonsurvivors was older (71.7 ± 8.8 versus 66.4 ± 9.3 years, P = 0.014) and had a shorter time of hospital admission to surgery (4.8 ± 7.6 versus 9.8 ± 9.4 days, P = 0.014) as well as of AMI occurrence to surgery (11.1 ± 14.9 versus 32.0 ± 39.2 days, P = 0.007). In addition, the nonsurvivor group was treated more frequently by emergency surgery (31.2% versus 18.2%, P = 0.001) and was more often in CS preoperatively (39.0% versus 29.9%, P = 0.01).

Periprocedural details are shown in Table 2. There were no differences between the group of nonsurvivors and survivors concerning surgical technique, extent of the procedure, or patch material used, but the group of nonsurvivors had a longer heart-lung machine time than the group of survivors (128.4 ± 52.6 versus 101.6 ± 49.6 min, P = 0.028). The infarct exclusion technique described by David et al [1995] had no impact on 30-day mortality in our cohort (P = 0.85). There was a tendency for surgical treatment of ventricular aneurysm to be more frequent (23.4% versus 9.1%, P = 0.087), access to pVSD occlusion to be via the left ventricle (33.8% versus 23.4%, P = 0.817), and incomplete revascularization to be less frequent (18.2% versus 22.1%, P = 0.103) in the group of survivors, but these differences were not significant.

Postoperative outcomes are summarized in Table 3. After surgery, 20 patients (26.0%) received a new or additional MCS. However, the nonsurvivor group had more frequent postoperative myocardial infarction (7.8% versus 1.3%, P = 0.038), need for resuscitation (10.7% versus 0.0%, P = 0.001), and requirement for dialysis (19.5% versus 10.4%, P = 0.013) compared with the survivor group. Furthermore, 6 patients (7.8%) had residual VSD after surgery and 13 (16.9%) at discharge. Because of a large persistent shunt, 9 patients (11.7%) had to undergo redo surgery; 4 of 5 of these patients who needed a reoperation within 30 days died. The other 4 patients, who all had >1 month between initial surgery and redo surgery, survived the reoperation.

The all-cause 30-day mortality of the population was 42.8% (33 patients). Figure 1A shows the Kaplan–Meier curve of the entire cohort, and Figure 1B illustrates the 30-day mortality of the patients with and without CS. The most common cause of death during the first 30 days after surgery was low cardiac output syndrome (20 patients; 26.0%). However, only 4 patients (5.2%) died of multiorgan failure, and 1 patient (1.3%) died of a neurological complication. In 10 other patients (13.0%), the ultimate cause of death could not be reconstructed reliably from the available...
Table 1. Preoperative Patient Characteristics*  

| Variable                                      | Entire Cohort (n = 77) | Nonsurvivor (n = 33) | Survivor (n = 44) | P Value |
|-----------------------------------------------|------------------------|----------------------|-------------------|---------|
| Age (y)                                       | 68.7 ± 9.4             | 71.7 ± 8.8           | 66.4 ± 9.3        | .014    |
| Glomerular filtration rate (Cockcroft–Gault)  | 65.9 ± 32.7            | 58.7 ± 34.8          | 70.5 ± 31.2       | .283    |
| Ejection fraction (%)                         | 44.0 ± 15.0            | 47.0 ± 17.8          | 41.8 ± 12.4       | .192    |
| Body mass index (kg/m²)                       | 27.0 ± 4.0             | 26.3 ± 3.4           | 27.5 ± 4.4        | .192    |
| Log EuroSCORE (%)                             | 42.4 ± 25.8            | 48.9 ± 26.0          | 37.6 ± 24.8       | .055    |
| Shunt volume (%)                              | 54.4 ± 16.8            | 57.1 ± 13.0          | 52.8 ± 18.6       | .407    |
| Time from hospital admission to surgery (d)   | 7.6 ± 8.9              | 4.8 ± 7.6            | 9.8 ± 9.4         | .014    |
| Time of AMI occurrence in surgery (d)        | 22.6 ± 32.3            | 11.1 ± 14.9          | 32.0 ± 39.2       | .007    |
| Female                                        | 32 (41.6)              | 17 (22.1)            | 15 (19.5)         | .163    |
| Age >60 y                                     | 62 (80.5)              | 29 (37.7)            | 33 (75.0)         | .245    |
| Diabetes                                      | 22 (28.6)              | 9 (11.7)             | 13 (16.9)         | 1.000   |
| Dialysis                                      | 3 (3.9)                | 0 (0)                | 3 (3.9)           | .256    |
| Hypertension                                  | 62 (80.5)              | 24 (31.2)            | 38 (49.4)         | .156    |
| Nicotine abuse                                | 19 (24.7)              | 3 (3.9)              | 16 (20.8)         | .007    |
| Chronic obstructive pulmonary disease         | 2 (2.6)                | 0 (0)                | 2 (2.6)           | .504    |
| Hyperlipidemia                                | 36 (36.8)              | 11 (14.3)            | 25 (32.5)         | .064    |
| Peripheral vascular disease                   | 9 (11.7)               | 4 (5.2)              | 5 (6.5)           | 1.000   |
| Pulmonary artery pressure >60 mmHg            | 8 (10.4)               | 2 (2.6)              | 6 (7.8)           | .454    |
| Left ventricular ejection fraction <35%        | 9 (11.7)               | 3 (3.9)              | 6 (7.8)           | .725    |
| Sinus rhythm                                  | 53 (68.8)              | 21 (27.3)            | 32 (41.6)         | .460    |
| Cardiopulmonary resuscitation                 | 5 (6.5)                | 2 (2.6)              | 3 (3.9)           | 1.000   |
| Ventilation                                   | 4 (5.2)                | 0 (0)                | 4 (5.2)           | .131    |
| Cerebrovascular accident                      | 3 (3.9)                | 1 (1.3)              | 2 (2.6)           | 1.000   |
| Prior cardiac surgery                         | 3 (3.9)                | 1 (1.3)              | 2 (2.6)           | 1.000   |
| Shunt location                                |                        |                      |                   | .642    |
| Anterior                                      | 45 (58.4)              | 18 (23.4)            | 27 (35.1)         |         |
| Posterior                                     | 32 (41.6)              | 15 (19.5)            | 17 (22.1)         |         |
| Time of AMI occurrence to surgery <7 d        | 26 (33.8)              | 20 (26.0)            | 6 (7.8)           | <.001   |
| Cardiogenic shock                             | 53 (68.8)              | 30 (39.0)            | 23 (29.9)         | <.001   |
| Preoperative MCS                              | 40 (51.9)              | 21 (27.3)            | 19 (24.7)         | .104    |
| Emergency surgery                             | 38 (49.4)              | 24 (31.2)            | 14 (18.2)         | .001    |
| Medication                                    |                        |                      |                   |         |
| Acetylsalicylic acid                          | 52 (67.5)              | 19 (24.7)            | 33 (42.9)         | .141    |
| Clopidogrel                                   | 15 (19.5)              | 6 (7.8)              | 9 (11.7)          | 1.000   |
| Beta-blockers                                 | 37 (48.1)              | 11 (14.3)            | 26 (33.8)         | .038    |
| Angiotensin-converting enzyme inhibitors       | 41 (43.2)              | 11 (14.3)            | 30 (39.0)         | .003    |
| Diuretics                                     | 49 (63.6)              | 12 (15.6)            | 37 (48.1)         | <.001   |

* Categorical variables are presented as n (%) and continuous parameters as mean ± SD. P values are for comparison of survivors and nonsurvivors (30-day mortality).
The cumulative 1-, 5-, and 10-year survival rates were 57.1%, 57.1%, and 31.2%, respectively (Figure 1A). The follow-up period for the entire cohort was 3.2 ± 3.9 years. Patients who survived >30 days were followed for 5.6 ± 4.9 years.

Multiple logistic regression analysis revealed that a duration between AMI and surgery of <7 days (odds ratio [OR] 5.229; \( P = .011 \)), preoperative absence of diuretics (OR 6.913; \( P = .005 \)), and preoperative CS (OR 3.558; \( P = .040 \)) were independent predictors of 30-day mortality (Table 4). The only independent predictor of overall mortality was cardiopulmonary bypass time (hazard ratio 1.013, confidence interval [CI] 1.004 to 1.021; \( P = .002 \)), as determined by Cox regression analysis.

**Table 2. Periprocedural Details***

| Variable                              | Entire Cohort (n = 77) | Nonsurvivor (n = 33) | Survivor (n = 44) | \( P \) Value |
|---------------------------------------|------------------------|----------------------|------------------|--------------|
| Total procedural time (min)           | 192.7 ± 73.3           | 209.5 ± 69.9         | 181.1 ± 74.2     | .109         |
| Cardiopulmonary bypass time (min)     | 113.2 ± 52.3           | 128.4 ± 52.6         | 101.6 ± 49.6     | .028         |
| Cross-clamp time (min)                | 65.1 ± 33.8            | 63.5 ± 35.8          | 66.4 ± 32.6      | .742         |
| Cardioplegia (mL)                     | 2082.2 ± 1000.4        | 2109.7 ± 1177.2      | 2061.6 ± 871.1   | .880         |
| Minimal temperature (°C)              | 32.3 ± 2.3             | 31.8 ± 2.8           | 32.7 ± 1.7       | .089         |
| Number of bypass grafts/patient       | 1.6 ± 0.9              | 1.5 ± 0.6            | 1.8 ± 1.1        | .288         |
| Technique                             |                        |                      |                  |              |
| Buttressed mattress suture without patch | 9 (11.7)              | 2 (2.6)              | 7 (9.1)          | .286         |
| Simple single patch                   | 34 (44.2)              | 13 (16.9)            | 21 (27.3)        | .496         |
| Simple double patch                   | 2 (2.6)                | 2 (2.6)              | 0 (0)            | .181         |
| Sandwich double patch                 | 1 (1.3)                | 1 (1.3)              | 0 (0)            | .429         |
| Infarct exclusion by David et al [1995] | 31 (40.3)             | 15 (19.5)            | 16 (20.8)        | .485         |
| Patch material                        |                        |                      |                  |              |
| No patch used                         | 8 (10.4)               | 1 (1.3)              | 7 (9.1)          | .068         |
| Bovine pericardium                    | 18 (23.4)              | 8 (10.4)             | 10 (13.0)        | 1.000        |
| Dacron                                | 22 (28.6)              | 10 (13.0)            | 12 (15.6)        | .803         |
| Polytetrafluoroethylene               | 2 (2.6)                | 0 (0)                | 2 (2.6)          | .504         |
| Felt                                  | 1 (1.3)                | 1 (1.3)              | 0 (0)            | .429         |
| Combination of materials              | 1 (1.3)                | 1 (1.3)              | 0 (0)            | .429         |
| Unknown                               | 10 (13.0)              | 4 (5.2)              | 6 (7.8)          | 1.000        |
| Use of surgical glue                  | 28 (36.4)              | 15 (19.5)            | 13 (16.9)        | .162         |
| Surgical access to the pVSD           |                        |                      |                  |              |
| Apex                                  | 10 (13.0)              | 4 (5.2)              | 6 (7.8)          | 1.000        |
| Right atrium                          | 5 (6.5)                | 2 (2.6)              | 3 (3.9)          | 1.000        |
| Right ventricle                       | 6 (7.8)                | 3 (3.9)              | 3 (3.9)          | 1.000        |
| Left atrium                           | 2 (2.6)                | 1 (1.3)              | 1 (1.3)          | 1.000        |
| Left ventricle                        | 44 (57.1)              | 18 (23.4)            | 26 (33.8)        | .817         |
| Unknown                               | 10 (13.0)              | 5 (6.5)              | 5 (6.5)          | .737         |
| Concomitant non-CABG surgery          | 51 (66.2)              | 21 (27.3)            | 30 (39.0)        | .808         |
| Concomitant CABG surgery              | 35 (45.5)              | 15 (19.2)            | 20 (26.0)        | 1.000        |
| Incomplete revascularization          | 31 (40.3)              | 17 (22.1)            | 14 (18.2)        | .103         |
| Concomitant aneurysm repair           | 25 (32.5)              | 7 (9.1)              | 18 (23.4)        | .087         |
| Date of surgery before 2005           | 53 (68.8)              | 24 (31.2)            | 29 (37.7)        | .622         |

* Categorical variables are presented as n (%), and continuous parameters as mean ± SD. \( P \) values are for comparison of survivors and nonsurvivors (30-day mortality). CABG indicates coronary artery bypass graft surgery.
Table 3. Postoperative Outcomes*

| Variable                     | Entire Cohort (n = 77) | Nonsurvivor (n = 33) | Survivor (n = 44) | P Value |
|------------------------------|------------------------|----------------------|------------------|---------|
| Total ventilation time (h)   | 154.9 ± 254.0          | 78.5 ± 83.4          | 203.6 ± 312.5    | .087    |
| Total length of stay after surgery (d) | 16.4 ± 14.6          | 9.9 ± 9.4            | 21.3 ± 16.0      | <.001   |
| Total length of stay ICU (h) | 203.4 ± 263.7          | 132.4 ± 141.6        | 242.6 ± 307.8    | .184    |
| Total length of stay IMCU (h) | 64.7 ± 101.9          | 17.8 ± 59.0          | 90.5 ± 112.2     | .056    |
| New MCS                      | 20 (26.0)              | 16 (20.8)            | 4 (5.2)          | <.001   |
| Low cardiac output           | 38 (49.4)              | 20 (26.0)            | 18 (23.4)        | .109    |
| Myocardial infarction        | 7 (9.1)                | 6 (7.8)              | 1 (1.3)          | .038    |
| Cardiopulmonary resuscitation| 8 (10.7)               | 8 (10.7)             | 0 (0)            | .001    |
| Cardiac arrhythmia           | 29 (37.7)              | 14 (20.9)            | 15 (22.4)        | .485    |
| New pacemaker                | 1 (1.3)                | 0 (0)                | 1 (1.3)          | 1.000   |
| Redo surgery during same stay| 7 (9.1)                | 4 (5.2)              | 3 (3.9)          | .454    |
| Re-exploration for bleeding  | 5 (6.5)                | 4 (5.2)              | 1 (1.3)          | .158    |

Residual shunt
- After surgery
  | Entire Cohort (n = 77) | Nonsurvivor (n = 33) | Survivor (n = 44) | P Value |
  | 6 (7.8)               | 3 (3.9)              | 3 (3.9)           | 1.000   |
- At discharge
  | Entire Cohort (n = 77) | Nonsurvivor (n = 33) | Survivor (n = 44) | P Value |
  | 13 (16.9)             | 6 (7.8)              | 7 (9.1)           | 1.000   |
- Postoperative cognitive distress syndrome
  | Entire Cohort (n = 77) | Nonsurvivor (n = 33) | Survivor (n = 44) | P Value |
  | 5 (9.1)               | 0 (0)                | 5 (7.6)           | .150    |
- Cerebrovascular accident
  | Entire Cohort (n = 77) | Nonsurvivor (n = 33) | Survivor (n = 44) | P Value |
  | 1 (1.3)               | 1 (1.3)              | 0 (0)             | .400    |
- Deep sternal wound infection
  | Entire Cohort (n = 77) | Nonsurvivor (n = 33) | Survivor (n = 44) | P Value |
  | 0 (0)                 | 0 (0)                | 0 (0)             | 1.000   |
- Sepsis
  | Entire Cohort (n = 77) | Nonsurvivor (n = 33) | Survivor (n = 44) | P Value |
  | 6 (7.8)               | 3 (3.9)              | 3 (3.9)           | 1.000   |
- Gastrointestinal complications
  | Entire Cohort (n = 77) | Nonsurvivor (n = 33) | Survivor (n = 44) | P Value |
  | 7 (9.1)               | 1 (1.3)              | 6 (7.8)           | .228    |
- Dialysis
  | Entire Cohort (n = 77) | Nonsurvivor (n = 33) | Survivor (n = 44) | P Value |
  | 23 (29.9)             | 15 (19.5)            | 8 (10.4)          | .013    |
- Respiratory failure
  | Entire Cohort (n = 77) | Nonsurvivor (n = 33) | Survivor (n = 44) | P Value |
  | 22 (28.6)             | 8 (10.4)             | 14 (18.2)         | .611    |
- Tracheostomy
  | Entire Cohort (n = 77) | Nonsurvivor (n = 33) | Survivor (n = 44) | P Value |
  | 5 (6.5)               | 0 (0)                | 5 (6.5)           | .067    |
- Reintubation
  | Entire Cohort (n = 77) | Nonsurvivor (n = 33) | Survivor (n = 44) | P Value |
  | 3 (3.9)               | 2 (2.6)              | 1 (1.3)           | .547    |

*Categorical variables are presented as n (%) and continuous parameters as mean ± SD. P values are for comparison of survivors and nonsurvivors (30-day mortality). ICU indicates intensive care unit; IMCU, intermediate care unit.

Figure 1. Kaplan–Meier survival curves for all-cause mortality of the entire cohort (A) and comparison between patients with and without CS (B).
DISCUSSION

In this study, we investigated the risk factors for all-cause 30-day and overall mortality in patients with pVSD who underwent primary surgical repair via various techniques at our institution. The 30-day mortality rate of these patients was 42.8%; independent predictors were duration between AMI and surgery <7 days, preoperative absence of diuretics, and preoperative CS. Our detailed investigation of the surgical technique of pVSD closure and of concomitant surgeries revealed no variable that significantly influenced mortality. Longer cardiopulmonary bypass time proved to be an independent risk factor for overall all-cause mortality.

Perioperative Mortality and Risk Factors

Our cohort’s 42.8% 30-day mortality rate is relatively high, but is comparable to outcomes of the 2 benchmark studies on this issue. The Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries (GUSTO) trial’s operative mortality rate was 47% [Crenshaw 2000], and it was 42.9% in the study by Arnaoutakis et al [2012], which used the Society of Thoracic Surgeons National Database and was published a little over a decade after the GUSTO trial. In recent studies with smaller cohorts, however, perioperative mortality ranges from at least 4.3% [Kim 2015] to a maximum of 65.0% [Cinq-Mars 2016], with the majority of studies ranging between 20% and 40% [Lundblad 2014; Okamoto 2016; Papadopoulos 2009; Takahashi 2015; Yam 2013].

In patients with pVSD, preoperative CS appears to be the most important variable among risk factors for in-hospital mortality, and numerous authors have substantiated this link over the years [Arnaoutakis 2012; Cinq-Mars 2016; Coskun 2009; Pang 2013; Papadopoulos 2009]. CS was also an independent variable for 30-day mortality in our patient population. Note that the various studies applied no uniform definition of CS, and CS was sometimes not defined at all. However, it seems logical that forced emergency or ultima ratio surgery would be associated with a poor outcome because of failing hemodynamics. In this context, the risk factor present at the time of pVSD surgery is always reported. A brief interval between AMI and surgery usually results in poor in-hospital/30-day mortality rates [Cinq-Mars 2016; Lundblad 2014; Papadopoulos 2009; Takahashi 2015], which is consistent with our finding that an interval of <7 days between AMI and surgery is an independent risk factor for 30-day mortality. In our opinion, patients need to be hemodynamically stabilized before undergoing surgery, as several authors have shown or recommended [Arnaoutakis 2012; Cinq-Mars 2016; Takahashi 2015; Trivedi 2015], so that the infarct-damaged tissue can scar as much as possible before surgery. Hemodynamic stabilization should be attempted via ECLS if necessary, and the culprit lesion should be immediately revascularized percutaneously. In this context, bridging therapy with a percutaneous septal occluder device should also be considered until the patient has been stabilized hemodynamically and can be admitted for surgery.

Interestingly, the absence of diuretic use upon hospital admission was also an independent predictor of 30-day mortality. Almost 70% of our patients were in CS before surgery; therefore, we consider it logical that they were no longer on beta-blockers or angiotensin-converting enzyme inhibitors, as they were usually catecholamine dependent. However, it seems equally plausible that optimal diuretic therapy could play a decisive role in patients’ short-term outcomes. By optimizing the preload, pulmonary and local edema can be reduced or prevented, and an additional volume load on the right ventricle can be minimized. In addition, congestion of the liver and thus potential liver cell death can be prevented. There is little data available about the influence of preoperative medication in pVSD patients undergoing cardiac surgery. A study by Arnaoutakis et al [2012] investigated only beta-blockers and fat-lowering drugs: with about 50% of the patients in CS, significantly more patients who survived the first 30 days had been taking a beta-blocker. In a study by Thiele et al [2009], there was no difference in survival for those on beta-blockers. In this interventionally treated group, 55% of patients were in CS. We are not aware of any other data regarding preoperative diuretic therapy in patients with pVSD and subsequent surgical occlusion.

Impact of Surgical Repair Technique on Perioperative Mortality

The surgical technique for closing a pVSD has evolved over the past half-century, and perioperative outcomes have improved as a result of several milestones, from the first description of the technique by Cooley et al [1957] to a further iteration by Daggett et al [1977] to the infarct exclusion technique according to David et al [1995]. Although there are no randomized, controlled studies available that compare the different methods, the David infarct exclusion technique is still regarded as the preferred technique. In a metadata study by Lundblad and Abdelnoor [2014], a 30-day mortality rate of 16.7% was demonstrated with infarct exclusion in 42 patients. Thus, this pVSD closure technique was superior to that of Daggett et al [1977] for both early (30 days) and late survival.

Table 4. Results of the Logistic Regression Analysis for Independent Predictors of 30-Day Mortality

| Variable                          | OR    | 95% CI         | P Value |
|-----------------------------------|-------|----------------|---------|
| Time of AMI occurrence to surgery <7 d | 5.229 | 1.451 to 18.847 | .011    |
| Preoperative CS                   | 3.558 | 1.058 to 11.967 | .040    |
| Preoperative absence of diuretics | 6.913 | 1.808 to 26.490 | .005    |
| Posterior pVSD                    | 2.755 | 0.759 to 9.996  | .123    |

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It should be noted that the 2 groups in this study fall into different periods, as mentioned by Lundblad and Abdelnoor [2014]: the study covers 30 years, with the method of Daggett et al [1977] mainly used in the first half and the technique of David et al [1995] in the second half. In this study, the improvement of general perioperative management may also play a role that should not be underestimated. In addition, it is mentioned that the same surgeons who were initially trained with the method of Daggett et al [1977] in the first half of the study also used the technique of David et al [1995] later, after achieving a certain level of expertise, and then preferred it to the Daggett method. In the collective data first described by David et al [1995], a perioperative mortality rate of 13.6% was reported; this was similar to the 30-day mortality rate of 16.7% reported by Lafci et al [2006] for patients treated with the David infarct exclusion technique. Unfortunately, these values were not upheld in our collective: the 41 patients treated by the infarct exclusion technique had a 30-day mortality rate of 36.6%. However, our results are similar to those described in the work of Papadopoulos et al [2009]. In their group of 32 patients who underwent consecutive pVSD surgery using the infarct exclusion technique, the 30-day mortality rate was 31.5%.

Several groups have explored modifications of the technique of David et al [1995]. A recent paper by Kim et al [2015] presented results of the use of a slight but not uniformly modified infarct exclusion technique. They operated on 17 of their 23 patients with the modified technique. The defect was excluded using either a double patch with a conically shaped patch or a triple patch without a conically shaped patch. The remaining ventricular cavities excluded from the patch were then filled with a sealant of purified bovine serum albumin and glutaraldehyde. The 30-day mortality rate of these patients was 4.3%. Another modification of the infarct exclusion is the triple-patch technique, according to Okamoto et al [2016], in which the remaining spaces between the patches are also filled with surgical glue. In that study, a 30-day mortality rate of 23.8% was reported for a cohort of 21 consecutive patients. In addition to patch configurations, most new or modified infarction exclusion techniques explicitly emphasize using surgical adhesive to fill the ventricular cavities remaining after patch application [Isoda 2012; Kim 2015; Okamoto 2016]. We also applied surgical adhesive to just over a third of our patients, but its use did not affect 30-day mortality. However, in both the Kim et al [2015] and Okamoto et al [2016] studies, >80% of the patients had an anterior defect. It is described in the literature that patients with a posterior pVSD have a worse outcome [Coskun 2009; Cummings 1988; Sibal 2010]. In our cohort, with an approximately balanced distribution of the respective groups (anterior pVSD 58.4% versus posterior pVSD 41.6%), we did not observe any survival disadvantage for patients with posterior pVSD.

**Interventional pVSD Closure and Potential Hybrid Concepts**

It is also possible to close a pVSD using catheter-based intervention. Since its introduction by Lock et al [1988], this procedure, as with surgical pVSD closure, has been developed further so that the all-cause 30-day mortality rate has fallen to 14% to 66% [Holzer 2004; Maltais 2009; Thiele 2009; Zhu 2013]. However, there are still some limitations to the use of percutaneous pVSD closure due to patient anatomy and the configuration and size of the available occluders [Holzer 2004; Schlotter 2016; Thiele 2009; Zhu 2013]. In our opinion, a hybrid concept for the closure of a pVSD may offer an opportunity to reduce mortality rates further. Different kinds of hybrid approaches have been described [Gulkarov 2010; Jorge 2012; Vondran 2016]. The largest known case series contains 6 successful hybrid treatments. These patients had acute heart failure or CS and had a sizeable residual left-to-right shunt. The patients were hemodynamically stabilized before surgery, and only 1 patient (17%) died after reoperation due to occluder dislocation caused by endocarditis [Vondran 2016].

In the acute phase of pVSD therapy shortly after AMI, the focus should be on hemodynamic stabilization and shunt reduction. All currently available data suggest that CS is the critical variable for short-term survival [Arnaoutakis 2012; Cinq-Mars 2016; Coskun 2009; Pang 2013; Papadopoulos 2009]. The time between AMI and the associated fragility of the myocardium are also essential factors. If the patient has survived the acute phase, they have excellent chances of surviving in the long term [Arnaoutakis 2012; Cinq-Mars 2016; Takahashi 2015]. We think a small, residual shunt may play a subordinate role in in-hospital mortality, but data supporting this suggestion are lacking. Patients without CS should ideally wait until scarring of the pVSD has occurred before undergoing the final surgery. Depending on the character of the pVSD, implantation of a percutaneous occluder could be attempted beforehand for shunt reduction to counteract hemodynamic deterioration. A residual shunt should always be reinterpreted in a symptom-free interval before hemodynamic deterioration. For this reason, we recommend that the modern interventional heart surgeon also learn this technique to be able to offer the best possible therapy.

**Limitations**

Our study has all the limitations of a single-center retrospective study. Because of the rarity of pVSD, the number of patients in our cohort is small, and only small subgroups could be established to calculate independent predictors of all-cause 30-day and overall mortality.

**Conclusions**

In pVSD, the all-cause 30-day mortality rate remains high, and preoperative CS still influences mortality significantly. In our study, the outcome was not significantly influenced by surgical technique or the material applied. However, a preoperatively implanted MCS as a bridge to definitive surgical therapy may improve the outcome in patients with CS. A good cooperation between interventional cardiologists and cardiac surgeons in the heart team should be strived for to optimally treat patients with pVSD using a hybrid approach. Further studies are needed to explore this proposed approach.
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