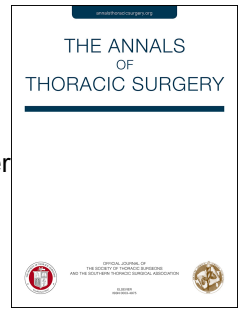
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Surgical Treatment of Post-Infarction Left Ventricular Free-Wall Rupture: a Multicenter Study

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PII: S0003-4975(20)32095-6

DOI: https://doi.org/10.1016/j.athoracsur.2020.11.019

Reference: ATS 34622

To appear in: *The Annals of Thoracic Surgery*

Received Date: 2 July 2020

Revised Date: 15 October 2020

Accepted Date: 2 November 2020

Please cite this article as: Matteucci M, Kowalewski M, De Bonis M, Formica F, Jiritano F, Fina D, Meani P, Folliguet T, Bonaros N, Sponga S, Suwalski P, De Martino A, Fischlein T, Troise G, Dato GA, Serraino FG, Shah SH, Scrofani R, Antona C, Fiore A, Kalisnik JM, D'Alessandro S, Villa E, Lodo V, Colli A, Aldobayyan I, Massimi G, Trumello C, Beghi C, Lorusso R, Surgical Treatment of Post-Infarction Left Ventricular Free-Wall Rupture: a Multicenter Study, *The Annals of Thoracic Surgery* (2021), doi: https://doi.org/10.1016/j.athoracsur.2020.11.019.

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Surgical Treatment of Post-Infarction Left Ventricular Free-Wall Rupture: a Multicenter Study

Running head: Left Ventricular Free-Wall Rupture

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Total Word Count: 4780

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Abstract

Background: Left ventricular free-wall rupture (LVFWR) is an uncommon but serious mechanical complication of acute myocardial infarction (AMI). Surgical repair, though challenging, is the only definitive treatment. However, given the rarity of this condition, results following surgery are still not well established. The aim of this study was to review a multicenter experience with the surgical management of post-infarction LVFWR and analyze the associated early outcomes.

Methods: Using the CAUTION study database, we identified 140 patients who were surgically treated for post-AMI LVFWR in 15 different centers from 2001 to 2018. The main outcome measured was operative mortality. Multivariate analysis was carried out by constructing a logistic regression model to identify predictors of postoperative mortality.

Results: The mean age of patients was 69.4 years. The oozing type of LVFWR was observed in 79 patients (56.4%), and the blowout type in 61 subjects (43.6%). Sutured repair was used in the 61.4% of cases. The operative mortality rate was 36.4%. Low cardiac output syndrome was the main cause of perioperative death. Myocardial re-rupture after surgery occurred in 10 patients (7.1%). Multivariable analysis revealed that preoperative left ventricular ejection fraction ($p < 0.001$), cardiac arrest at presentation ($p = 0.011$), female gender ($p = 0.044$), and the need for preoperative extracorporeal life support ($p = 0.003$) were independent predictors for operative mortality.

Conclusions: Surgical repair of post-infarction LVFWR carries a high operative mortality. Female gender, preoperative left ventricular ejection fraction, cardiac arrest, and extracorporeal life support, are predictors of early mortality.

Abbreviations

AMI = acute myocardial infarction

AKI = acute kidney injury

CABG = coronary artery bypass grafting

CPB = cardiopulmonary bypass

ECMO = extracorporeal membrane oxygenation

IABP = intra-aortic balloon pump

LCOS = low cardiac output syndrome

LVEF = left ventricular ejection fraction

LVFWR = left ventricular free-wall rupture

MCS = mechanical circulatory support

PCI = percutaneous coronary intervention

STEMI = ST-elevation myocardial infarction

ST = sutured repair

STL = sutureless repair

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Left ventricular free-wall rupture (LVFWR) is a life-threatening mechanical complication of acute myocardial infarction (AMI). With the advent of reperfusion strategies for AMI, including thrombolysis and percutaneous coronary intervention (PCI), LVFWR has become increasingly rare, with current literature reporting an incidence between 0.01% and 0.5% of AMI cases (1,2). Despite significant improvements over the last decades in the overall mortality for patients with AMI, the outcome of subjects who develop LVFWR remains dismal (2). LVFWR usually proves fatal, although some patients with acute or subacute rupture present a window of opportunity for intervention. Prompt diagnosis is key and prompt surgery, though challenging and associated with high mortality (3), is the treatment of choice. Because of the rarity of LVFWR, most published reports on this topic consist of single-center experiences with small sample size, and little is known about the clinical results of surgical LVFWR repair, particularly regarding in-hospital results. Thus, we conducted an international, multicentre, retrospective study to evaluate the early outcome, and investigate the prognostic factors of operative mortality in patients who underwent cardiac surgery for post-infarction LVFWR.

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Patients and Methods

Patient Population and Study Design

The study cohort consisted of 140 adult patients (aged > 18 years) who underwent surgical repair of post-AMI LVFWR between January 1, 2001 and December 31, 2018 in 15 different centers. The patients were recruited from the database of the CAUTION study ("Mechanical Complications of Acute Myocardial Infarction: an International Multicenter Cohort Study"). The CAUTION study (trial registration: Clinicaltrials.gov, NCT03848429) is a retrospective, multicenter, observational trial aimed at evaluating the postoperative outcome of subjects undergoing cardiac surgery for post-AMI mechanical complications. The study protocol was authorized by the local ethical committee of each center, and conducted in accordance with the guidelines of the Declaration of Helsinki for patient data use and evaluation. A unified patient dataset was used to record pertinent information,

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clinical history, and examination data from medical record. The "data collection form" used to collect data is presented in the Supplemental material.

Definitions and Outcome Measures

Cardiogenic shock was defined as persistent hypotension (systolic blood pressure < 90 mmHg) with reduction in cardiac index (< 1.8 L/min/m2) despite maximal treatment. The patterns of LVFWR were defined as blowout and oozing types: blowout type was defined as an abrupted rupture characterized by active bleeding and a macroscopic tear in the infarcted area, while oozing type was defined as an incomplete rupture characterized by epicardial extravasation or slow bleeding which may be temporarily sealed by clot or pericardial adhesion. Regarding the surgical technique used to repair the post-AMI LVFWR, a sutureless technique (STL) was considered when LVFWR repair was accomplished using a collagen sponge, or pericardium patch fixed on epicardium with glues, to cover the infarcted myocardium, while sutured technique (ST) was considered when the repair was performed using sutures to close the myocardial tear or to secure a patch on the epicardium as previously described.

The primary endpoint of this study was operative mortality, defined as death from any cause occurring within 30 days after surgery, or after 30 days during the same hospitalization related to the operation. The secondary outcome was identification of risk factors for early mortality after surgical repair of post-infarction LVFWR.

Statistical Analysis

Summary statistics for outcomes and baseline patient characteristics were expressed as mean ± standard deviation (SD) for continuous variables, and as frequency and percentage for categorical variables. Differences between groups were assessed using the Student's *t*-test for continuous variables and the Chi-square test or Fisher exact test for categorical variables. Subsequently, variables that achieved a *p*-value < 0.2 in the univariate analysis were examined using multivariable analysis by forward stepwise logistic regression in order to identify independent predictors of operative mortality. The above analyses were performed using the software package SPSS 25.0 for

Windows (IBM, Chicago, USA). A *p*-value < 0.05 was considered statistically significant.

Results

Clinical Characteristics

Preoperative patient characteristics are shown in Table 1. The mean age at admission was 69.4 years, and male gender was predominant. Pre-existing hypertension was the most common comorbidity, followed by dyslipidaemia. Initial evaluation revealed ST-elevation myocardial infarction (STEMI) in most patients: only 12 individuals (8.6%) suffered from non-ST-elevation myocardial infarction (NSTEMI) before the occurrence of LVFWR. The mean interval between the onset of AMI and the diagnosis of LVFWR was 50.6 ± 84.7 hours, and the interval between LVFWR and the operation was 4.7 ± 6 hours. Before surgery, 104 patients (74.3%) underwent coronary angiography: single-vessel disease was present in 40 patients and multi-vessels disease in 64 subjects. Pericardial tamponade was present in 100 patients (71.4%), and pericardiocentesis was performed in 30 subjects (21.4%). Forty-eight (34.3%) individuals required PCI before the operation, while only 10 patients (7.1%) received thrombolysis. The average left ventricular ejection fraction (LVEF) was 44 ± 4.7%. Most patients were in cardiogenic shock at the time of surgery, and 51 subjects (36.4%) had intra-aortic balloon pump (IABP) placed preoperatively. Among the 16 subjects requiring preoperative extracorporeal membrane oxygenation (ECMO) support, 11 patients experienced cardiac arrest at presentation.

Surgical Repair

Operative information is summarized in Table 2. In 56 patients (40%) LVFWR repair was performed on beating heart without cardiopulmonary bypass (CPB), whereas 84 individuals (60%) were operated using CPB. Mean duration of CPB was 104.4 ± 53.8 minutes and aortic cross-clamp time was 67.1 ± 35.7 minutes. Oozing rupture was the type of LVFWR most commonly encountered. The locations of the rupture site were as follows: the anterior wall in 47 patients (33.6%), the lateral wall in 52 patients (37.1%), the inferior wall in 23 (16.4%), and the posterior

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wall in 18 patients (12.9%). ST repair was used in 86 cases (61.4%), in the remaining patients a STL was applied to treat the rupture. No patient was managed with endocardial exclusion technique. Only 9 subjects (14.8%) with blowout rupture were treated with STL; on the other hand, most patients with oozing rupture underwent STL repair (Table 3). Concomitant coronary artery bypass grafting (CABG) was performed in 34 patients (24.3%), while ventricular septal rupture (VSR) closure or mitral valve surgery for papillary muscle rupture (PMR) were associated with LVFWR repair in 15 subjects (10.7%). Postoperatively, three quarters of patients required inotropic agents, whereas IABP was need in almost half of the cases. Only 11 patients (7.9%) were assisted by ECMO after the operation.

Postoperative Outcomes

Early outcomes are reported in Supplemental Table 1. Postoperative complications were common, including low cardiac output syndrome (LCOS) as the most frequent major adverse event in 29 subjects (20.7%), followed by acute kidney injury (AKI), stroke, and pneumonia. Re-exploration for mediastinal bleeding was also rather common. Ventricular re-rupture occurred in 6 patients after STL, and in 4 subjects after ST. Only 2 subjects with re-rupture who underwent reoperation were discharge alive. The details of patients with myocardial re-rupture are shown in Supplemental Table 2. In our cohort, no variables was identified as an independent predictor for ventricular re-rupture.

No significant differences were observed between ST and STL repair in terms of postoperative bleeding, ventricular re-rupture, and operative mortality (Figure 1). However, patients treated with ST had a trend towards higher rate of postoperative bleeding (16/86, 18.6% vs 7/54, 13%) and operative mortality (35/86, 40.7% vs 16/54, 29.6%), while myocardial re-rupture occurred more frequently in the STL group (6/54, 11.1% vs 4/86, 4.7%).

Overall, the operative mortality rate was 36.4% (51/140). Mortality rates for patients with blowout rupture and those with oozing rupture were 49.2% and 26.6%, respectively. Cause of operative death included: brain death (n = 8), septic shock (n = 1), LCOS with associated multiorgan failure (n = 22), AKI (n = 2), bowel ischemia (n = 1), re-rupture (n = 8), and huge, irreparable myocardial

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rupture (n = 9). The mean duration of hospitalization for the survivors was 17.1 ± 15.3 days. Pre-discharge echocardiography performed in survivors diagnosed a left ventricular (LV) pseudoaneurysm in 2 patients, both underwent surgical correction.

Univariable analysis identified the associations between operative mortality and sex (p = 0.037), preoperative ECMO support (p < 0.001), cardiogenic shock (p = 0.019), preoperative low LVEF (p < 0.001), cardiac arrest at presentation (p = <0.001), preoperative pericardiocentesis (p = 0.128), time from LVFWR to surgery (p = 0.130), type of rupture (p = 0.009), CPB time (p = 0.088), cross-clamp time (p = 0.029), and need for postoperative ECMO (p = 0.105). Multivariable analysis showed that female gender (odds ratio 4.195, 95% confidence interval 1.562-11.265, p = 0.044), preoperative LVEF (odds ratio 0.938, 95% confidence interval 0.902-0.976, p = <0.001), cardiac arrest at presentation (odds ratio 4.117, 95% confidence interval 1.389-12.199, p = 0.011), and preoperative ECMO (odds ratio 10.266, 95% confidence interval 2.194-48.035, p = 0.003) were independent predictors of operative mortality.

Comment

LVFWR complicating AMI is increasingly rare in the reperfusion era, but mortality remains high without appropriate and prompt intervention (1,4). Medical management of LVFWR is usually futile with rare exception (5); thus, definitive surgery is considered the standard of care, but remains a well-known challenging operation. In this 18-year observational study, we evaluated early outcomes and complications of the surgical management of post-infarction LVFWR. Our main findings were as follows: 1) the overall operative mortality rate was 36.4%; 2) female gender, preoperative LVEF, cardiac arrest, and ECMO support were independent predictors for early mortality; 3) no significant difference was observed with respect to the surgical (STL or ST) technique used to repair the myocardial rupture; 4) the use of mechanical circulatory support (MCS) was not associated with lower mortality. To the best of our knowledge, the present analysis is the largest to date evaluating outcomes in patients undergoing post-AMI LVFWR surgical repair.

In this study, we noted a male preponderance, contrary to the traditional view of higher female predisposition (6), old age (> 65 years) predilection, and association with pre-existing hypertension. Our findings are substantially in accordance with previous studies which have reported that the classical clinical manifestations of LVFWR, such as cardiogenic shock or electromechanical dissociation, are dependent on the rapidity of bleeding and pericardial tamponade formation, usually occurring within the first days after AMI (2). LVFWR may present as “blowout” or “oozing” pattern, where the former is characterized by active bleeding and a macroscopic tear in the epicardium, while the latter by localized small myocardial lesions with recurrent mild bleeding (7). We found that blowout type rupture was associated whit a higher operative mortality rate compared with oozing type because of massive hemopericardium accumulation and consequent acute course (49.2% vs 26.6%, respectively). Our observations are in accordance to Haddadin’s findings showing worse in-hospital survival in patients with blowout type of LVFWR (7).

Several different techniques have been developed over the time to repair the rupture of the ventricular wall (8), but all can be referred to two different categories: ST and STL, depending on the use of sutures to treat LVFWR. Initially, ST was the only method used. This repair, however, has the disadvantage of placing and tying sutures though friable necrotic muscle. More recently, the availability of tissue adhesive and surgical glues have allowed the wide diffusion of the STL. In this procedure, a collagen sponge or a glued prosthetic patch is placed without stiches over the area of rupture (9,10). To date, which surgical method is the most appropriate in the presence of this post-AMI mechanical complication is still controversial, particularly in terms of rupture recurrence and postoperative bleeding.

In a recent review, ST and STL repair for post-infarction LVFWR showed comparable in-hospital mortality (11). We did not find any statistical significant difference in terms of outcomes between the two surgical methods. Nevertheless, a trend towards higher rate of operative mortality and bleeding requiring rethoracotomy was detected in the ST group while myocardial re-rupture occurred more frequently in the STL group. We can postulate that the difference in mortality

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observed between ST and STL was affected by the hemodynamic status at presentation (cardiac arrest was more common in the ST group: 31.4% vs 27.8%, respectively) and the small number of patients with blowout ruptures underwent STL repair (14.8%). In light of this, the selection of the appropriate surgical repair is crucial in each patient with LVFWR. Although STL has also been successfully used for subjects with blowout rupture (9), this condition is probably best approached with ST: it is very unlikely that a simply glued patch can withstand the intraventricular pressure when there is a direct communication between the LV cavity and pericardial space. STL is a simple and fast option in the surgical treatment for LVFWR, but surgeons should be aware that it has a potential risk of re-rupture and its actual effectiveness in frank blowout rupture is a matter of controversy. Further and dedicated studies are required to provide additional and more consistence data, and to assess whether one technique is superior over the other.

Early mortality rates of surgical LVFWR repair have been reported to range from 17.1% to 34.3% (3, 12-14). The operative mortality in this series was 36.4%; such a result is probably reflective of the higher prevalence of blowout type rupture in our cohort, which represents a risk factor for a highly complicated course of such a myocardial illness.

Debate remains concerning the effect of concomitant CABG in the setting of post-AMI LVFWR repair. Although many surgeons do not revascularize the culprit vessel in the infarcted region associated with the myocardial rupture, other coronary lesions are often grafted at the time of LVFWR repair. Mantovani et al. demonstrated that concomitant CABG has a positive impact on survival and freedom of angina (15). We, like others investigators (3), did not find a beneficial effect of additive CABG on the short-term outcome. We speculate that the real effectiveness of the myocardial revascularization is underestimated by the low number of patients who had undergone CABG. In emergency situations, indeed, the execution of a coronary angiogram is not always possible due to the need to quickly proceed with surgery. Since the survival benefit of concomitant CABG is unclear, it is advisable to proceed with coronary angiography in stable patients as soon as LVFWR is suspected, and perform CABG at the time of the ventricular repair, when suitable (3,8).

ESC and ACC/AHA Guidelines for the management of patients with STEMI advocate the use of mechanical circularity support devices (MCS), such as IABP and ECMO, in patients with post-AMI mechanical complications and haemodynamic compromise, in order to achieve temporary circulatory stabilization on the way to surgery (16,17). In addition, IABP insertion, providing mechanical afterload reduction and augmentation of cardiac output, can prevent transition from the oozing to blowout rupture preoperatively, and limit or avoid the development of LCOS after surgery, the most common cause of death in these patients. The results of this study did not provide evidence to support any benefit of MCS on survival. Moreover, we observed that ECMO support represented an independent predictor of operative death. However, we should consider that most patients suffering from LVFWR have received ECMO support during cardiopulmonary resuscitation maneuvers, hence creating a subpopulation of subjects with a hospital mortality approaching to 100%. This extremely severe hemodynamic status might explain the apparently futility of ECMO in such clinical scenario. The rates of perioperative LCOS or multiorgan failure observed in our study and the low rate of aggressive MCS (below 10%) as opposed to less invasive IABP (almost 50%) might indicate a limited use of more effective circulatory assistance. Recent studies have shown an increase used of MCS in this context (18), suggesting that complicated LVFWR cases, particularly by enhancing LV unloading and peripheral organ perfusion, might benefit from this approach (19), although dedicated investigations will be warranted to confirm these hypotheses.

Limitations

There are several important limitations to this study. First, and most importantly, since this study was retrospective in nature both the presence of selection bias and unmeasured confounders cannot be excluded. Second, the number of subjects enrolled may still be considered relatively small despite the data coming from different centers, therefore our findings should be validated in a larger cohort size. Third, the multicenter design necessitated a data collection form with a limited number of variables to avoid missing data; thus, the possibility that non reported variables could have

influenced the results of the analysis cannot be completely ruled out. Fourth, we evaluated the effect of concomitant CABG on mortality, however we were unable to distinguish the target of CABG, culprit or non-culprit vessel. Finally, because this study is limited by the operative (surgical) outcomes, it does not provide information on the durability of surgical repair of post-AMI LVFWR, and data concerning patients managed conservatively or who died without surgery are lacking.

Conclusions

LVFWR remains a serious and challenging complication of AMI in the contemporary era. Surgical repair is feasible with acceptable early mortality (36.4%). Female gender, preoperative LVEF, cardiac arrest at presentation, and the need for preoperative ECMO are poor independent prognostic factors. Concomitant CABG during LVFWR repair do not confer a survival advantage. Further prospective studies are warranted to validate our findings.

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Table 1. Baseline and preoperative characteristics

Variables	**Patients** (n = 140)	**Survivors** (n = 89)	**Non-Survivors** (n = 51)	**p-value**
Age *(years)*	69.4 ± 10.2	69 ± 9.8	70 ± 10.9	*0.578*
Age > 70 years	71 (50.7%)	42 (47.2%)	29 (56.9%)	*0.353*
Gender *(female)*	49 (35%)	25 (28%)	24 (47.1%)	*0.037*
Hypertension	98 (70%)	62 (69.7%)	36 (70.6%)	*0.936*
Diabetes Mellitus	28 (20%)	19 (21.3%)	9 (17.6%)	*0.758*
Dyslipidaemia	55 (39.3%)	33 (37.1%)	22 (43.1%)	*0.603*
Smoker	49 (35%)	30 (33.7%)	19 (37.3%)	*0.806*
Chronic Renal Failure	14 (10%)	8 (9%)	6 (11.8%)	*0.811*
COPD	18 (12.9%)	11 (12.4%)	7 (13.7%)	*0.967*
Peripheral artery disease	17 (12.1%)	12 (13.5%)	5 (9.8%)	*0.707*
LVEF *(%)**	41.7 ± 13.5	45.2 ± 12.4	35.7 ± 13.3	*<0.001*
Haemodynamics at presentation				
Cardiogenic Shock	100 (71.4%)	57 (64.1%)	43 (84.3%)	*0.019*
Cardiac Arrest	42 (30%)	13 (14.6%)	29 (56.9%)	*<0.001*
Pericardial Tamponade	100 (71.4%)	61 (68.5%)	39 (76.5%)	*0.416*
IABP support	51 (36.4%)	32 (36%)	19 (37.3%)	*0.977*
ECMO support	16 (11.4%)	3 (3.4%)	13 (25.5%)	*<0.001*
Thrombolysis	10 (7.1%)	4 (4.5%)	6 (11.8%)	*0.203*
PCI	48 (34.3%)	31 (34.8%)	17 (33.3%)	*0.996*
Pericardiocentesis	30 (21.4%)	15 (16.9%)	15 (29.4%)	*0.128*
Interval from AMI to LVFWR *(h)*	50.6 ± 84.7	53.1 ± 96.6	48.5 ± 60.6	*0.759*
Interval from LVFWR to OR *(h)*	4.7 ± 6	5.2 ± 6.3	3.6 ± 5.4	*0.130*

Data are shown as mean ± standard deviation or n (%) as appropriate.
n = number; cm = centimeters; Kg = kilograms; COPD = chronic obstructive pulmonary disease; LVEF = left ventricular ejection fraction; CPR = cardiopulmonary resuscitation; IABP = intra-aortic balloon pump; ECMO = extracorporeal membrane oxygenation; PCI = percutaneous coronary intervention; AMI = acute myocardial infarction; LVFWR = left ventricular free-wall rupture; OR = operative room; h = hours; * = last value detected (following AMI) before surgery (missing data: < 5%).

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Table 2. Perioperative data

Variables	**Patients** (n = 140)	**Survivors** (n = 89)	**Non-Survivors** (n = 51)	**p-value**
Type of Rupture				
Blowout	61 (43.6%)	31 (34.8%)	30 (58.8%)	*0.009*
Oozing	79 (56.4%)	58 (65.2%)	21 (41.2%)	
Technique of LVFWR repair				
Sutured	86 (61.4%)	51 (57.3%)	35 (68.6%)	*0.254*
Sutureless	54 (38.6%)	38 (42.7%)	16 (31.4%)	
Mode of ECC				
CPB	84 (60%)	54 (60.7%)	30 (58.8%)	*0.967*
Off-pump	56 (40%)	35 (39.3%)	21 (41.2%)	
Concomitant CABG	34 (24.3%)	23 (25.8%)	11 (21.6%)	*0.724*
Concomitant PMR/VSR repair	15 (10.7%)	8 (9%)	7 (13.7%)	*0.561*
Cross-clamp Time *(min)*	67.1 ± 35.7	63 ± 36.6	76.6 ± 32.5	*0.029*
CPB Time *(min)*	104.4 ± 53.8	98.7 ± 49	114.9 ± 61.2	*0.088*
Postoperative Inotropes	106 (75.7%)	68 (76.4%)	38 (74.5%)	*0.962*
Postoperative IABP support	67 (47.9%)	43 (48.3%)	24 (47.1%)	*0.969*
Postoperative ECMO support	11 (7.9%)	4 (4.5%)	7 (13.7%)	*0.105*

Data are shown as mean ± standard deviation or n (%) as appropriate.

n = number; LVFWR = left ventricular free-wall rupture; ECC = extracorporeal circulation; CPB = cardiopulmonary bypass; CABG = coronary artery bypass grafting; min = minutes; IABP = intra-aortic balloon pump; ECMO = extracorporeal membrane oxygenation; PMR = papillary muscle rupture; VSR = ventricular septal rupture.

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Table 3. Main clinical characteristics and outcomes according to the type of rupture

Variables	Total (n = 140)	Oozing Type (n = 79)	Blowout Type (n = 61)
Cardiogenic Shock	100 (71.4%)	54 (68.3%)	46 (75.4%)
Cardiac Arrest	42 (30%)	19 (24%)	23 (37.7%)
Tamponade	100 (71.4%)	56 (70.9%)	44 (72.1%)
Sutured Repair	86 (61.4%)	34 (43%)	52 (85.2%)
Sutureless Repair	54 (38.6%)	45 (57%)	9 (14.8%)
CPB	84 (60%)	42 (53.2%)	42 (68.9%)
Off-pump	56 (40%)	37 (46.8%)	19 (31.1%)
Operative Mortality	51 (36.4%)	21 (26.6%)	30 (49.2%)
LVFW Re-rupture	10 (7.1%)	7 (8.9%)	3 (4.9%)

Data are shown as n (%).

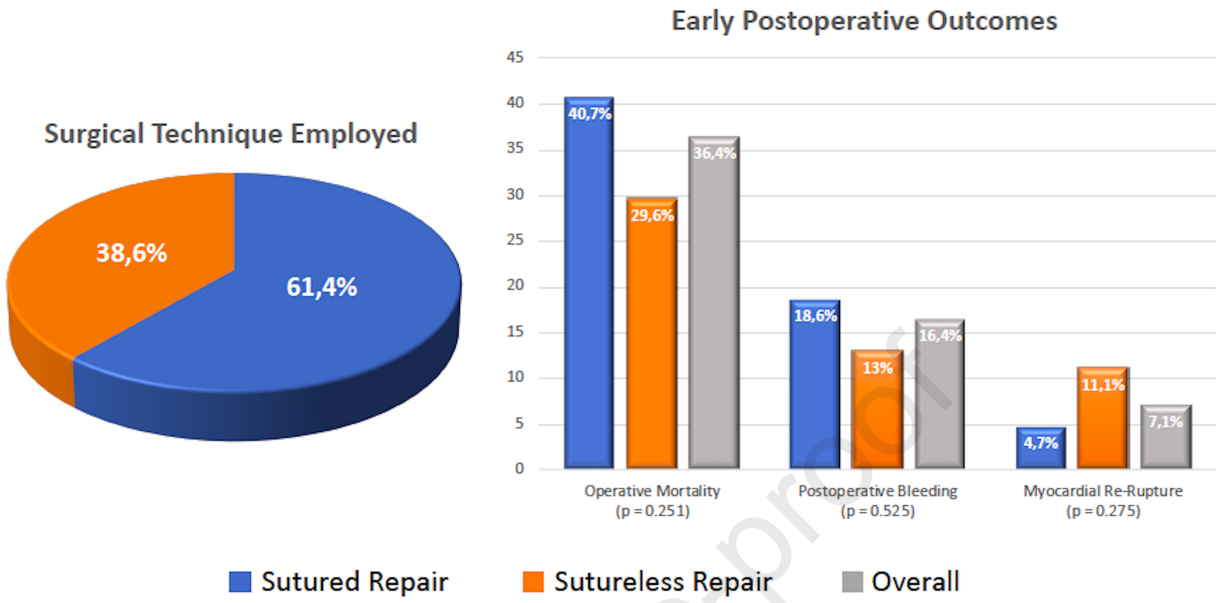
n = number; LVFW = left ventricular free-wall; CPB = cardiopulmonary bypass.

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Figure Legends

Figure 1. Main outcomes of operated patients according to the repair techniques (ST vs STL)

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