Left ventricular reconstruction in ischemic cardiomyopathy

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Chapter 5

10-Year Outcomes After Left Ventricular Reconstruction: Rethinking the Impact of Mitral Regurgitation

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ABSTRACT

Background. Heart failure with reduced ejection fraction due to a post-infarction anteroseptal aneurysm carries a poor prognosis. Patients with refractory heart failure may be considered for advanced surgery, including left ventricular assist device implantation, heart transplantation and left ventricular reconstruction. The aim of this study was to evaluate outcomes after an integrated approach of left ventricular reconstruction with concomitant procedures (mitral/tricuspid valve repair, coronary revascularization), and assess risk factors for event-free survival, focusing on left ventricular geometry/ function and presence of functional mitral regurgitation (MR).

Methods. A total of 159 consecutive heart failure patients who underwent left ventricular reconstruction between 2002 and 2011 were included. Mid-term echocardiographic and long-term clinical outcomes were evaluated. Preoperative risk factors were correlated to event-free survival (freedom from mortality, left ventricular assist device implantation, and heart transplantation).

Results. Mid-term echocardiography demonstrated decreased indexed left ventricular end-systolic volumes (89 ± 42 mL/m^2 preoperatively; 51 ± 18 at mid-term, $p <$ 0.001), and absence of MR ≥ grade 2. Event-free survival was 83% ± 3% at 1-year, 68% ± 4% at 5-year, and 46% ± 4% at 10-year follow-up. Preoperative wall motion score index (WMSI; hazard ratio [HR] 3.1, 95% confidence interval [CI] 1.7–5.8, p < 0.001) and presence of MR ≥ grade 2 (HR 1.9, 95% CI 1.1–3.1, p = 0.014) were independently associated with adverse event-free survival.

Conclusions. Event-free survival is favorable in patients with WMSI < 2.5 and significantly worse when WMSI is ≥ 2.5. In both groups, the presence of preoperative MR ≥ grade 2 negatively affects event-free survival, despite successful correction of MR. Risk stratification by preoperative WMSI and MR grade supports the Heart team in choosing the optimal surgical strategy for patients with refractory heart failure.

INTRODUCTION

Ischemic heart disease is the most common cause of death worldwide [1, 2]. Although advances in treatment and secondary prevention have resulted in decreased mortality after myocardial infarction over the past decades, this decrease is paralleled by an increase in heart failure prevalence [1–4].

Optimal guideline-directed medical and device therapy constitute the cornerstone in the treatment of patients with heart failure with reduced ejection fraction (HFrEF) in the setting of ischemic heart disease [5–7]. When heart failure symptoms persist, advanced surgical treatment options—tailored to the specific pathology involved— may be considered by a dedicated multidisciplinary Heart team. These options include left ventricular assist device (LVAD) implantation, heart transplantation (HTx) and reconstructive surgery [6–9].

In refractory HFrEF due to a postinfarction anteroseptal aneurysm, left ventricular reconstruction (LVR) with concomitant procedures (mitral and tricuspid valve reconstruction, coronary revascularization, and arrhythmia surgery) may be considered. In a previous report, we demonstrated favorable clinical and echocardiographic outcomes up to 36 months after an integrated approach of LVR surgery with concomitant procedures [10]. Beneficial results after LVR surgery have also been reported by others [11–13]. Nevertheless, not all patients benefit from such extensive surgery, and very few studies have evaluated long-term results. Better patient selection by preoperative risk stratification may potentially reduce mortality and improve long-term outcomes after LVR procedures.

The aim of the present study was to evaluate 10-year clinical outcomes after an integrated approach of LVR with concomitant procedures (based on well-defined indications by the Heart team), and to assess preoperative risk factors for long-term clinical outcomes, focusing on left ventricular (LV) geometry, LV function, and the presence of functional mitral regurgitation.

PATIENTS AND METHODS

Study Population and Study Design

Consecutive patients with refractory HFrEF (LV ejection fraction (LVEF) ≤ 35% and New York Heart Association [NYHA] class III/IV) due to a postinfarction anteroseptal

LV aneurysm, who underwent LVR between April 2002 and April 2011, were included. Patients with concomitant aortic valve disease were excluded.

Baseline and surgical characteristics, echocardiographic data—preoperatively, at discharge, and at midterm follow-up—and clinical outcomes were evaluated for all patients. The institutional medical ethics committee approved the protocol and written informed consent was obtained from all patients.

Indications for LVR and Concomitant Procedures

The surgical strategy for each patient was determined by the Heart team, consisting of heart-failure cardiologists, interventional cardiologists, and cardiothoracic surgeons. The indication for LVR was presence of a postinfarction anteroseptal LV aneurysm and refractory HFrEF. Concomitant mitral valve repair was performed in patients with mitral regurgitation (MR) ≥ grade 2 on preoperative echocardiography, and in patients with an increase of MR to ≥ grade 2 on intraoperative transesophageal echocardiography (TEE) directly after LVR. Tricuspid annuloplasty was conducted in patients with tricuspid regurgitation ≥ grade 2 or a tricuspid annular diameter > 40 mm (or > 21 mm/m^2 body surface area [BSA]). Revascularization of remote (ie, non-infarcted) myocardium was performed in presence of ≥ 70% angiographic diameter reduction of a coronary artery. Patients with preoperative ventricular arrhythmias underwent cryoablation.

Surgical Technique

All procedures were performed using cardiopulmonary bypass, aortic cross-clamping, and intermittent warm blood cardioplegia. LVR was performed following the technique described by Dor and associates [14], using a shaping Fontan-stitch at the transitional zone between macroscopically viable and scarred myocardium. Sizing and shaping of the residual ventricular cavity was done using a balloon or, from late 2006 onwards, a commercially available shaping device (TRISVR, Chase Medical, Richardson, TX) filled to a volume of 55 mL/m^2 BSA. A remaining defect was closed with an endoventricular patch. Mitral valve repair was conducted using a downsized semi-rigid annuloplasty ring (Carpentier Edwards Physio Ring, Edwards Lifesciences, Irvine, CA) and was considered successful in case of no/mild MR and a leaflet coaptation height ≥ 8 mm on intraoperative TEE. Tricuspid annuloplasty was performed using a tricuspid annuloplasty ring (MC3 ring, Edwards Lifesciences). Epicardial and endocardial cryoablation was performed at the border zone between scar and viable myocardium.

Echocardiography

Two-dimensional and Doppler transthoracic echocardiograms were performed preoperatively, before discharge, and at mid-term follow-up, using a commercially available system (Vingmed Vivid 7, General Electric-Vingmed, Milwaukee, WI). All images were stored and analyzed by 2 independent investigators.

Severity of mitral and tricuspid regurgitation was graded semiquantitatively from color-flow Doppler in parasternal long-axis and apical 2-, 3- and 4-chamber images [15]. LV volumes were measured in apical 2- and 4-chamber images and indexed to BSA. LVEF was calculated by the modified biplane Simpson's method [16]. Systolic pulmonary artery pressure (sPAP) was assessed using the modified Bernoulli equation on the transtricuspid continuous-wave signal, adding the estimated right atrial pressure [17]. Preoperative LV systolic function was evaluated by the wall motion score index (WMSI). A 16-segment model was used for LV segmentation and each segment was analyzed in multiple views. Segments were scored as: 1 = normal or hyperkinetic, 2 = hypokinetic, 3 = akinetic, or 4 = dyskinetic. WMSI was calculated as the average score of all visualized segments; a higher WMSI indicates a more severely comprised LV function [16]. Right ventricular (RV) function was determined by calculating tricuspid annular plane systolic excursion (TAPSE) on M-mode recordings of the lateral tricuspid annulus in the RV apical view.

Study Endpoints

Information on clinical events was obtained from patients' medical records and direct patient interview. Primary endpoint was event-free survival, defined as freedom from LVAD implantation, HTx, and all-cause mortality up to 10 years after surgery. Secondary endpoints were severity of MR, LV volumes, LVEF, sPAP, and NYHA functional class at mid-term follow-up, and mitral valve reintervention and hospital readmissions for congestive heart failure (hospitalization with administration of parenteral diuretics or inotropes) up to 10 years after surgery.

Statistical Analysis

Continuous data are expressed as mean ± SD or median with interquartile range (IQR) and compared using the paired and unpaired Student's t test when appropriate. Categorical variables are described as frequencies and percentages and compared using the χ^2 test or Fisher's exact test. The Kaplan-Meier method was used to estimate cumulative incidence. Univariable Cox proportional hazards regression analysis was performed to assess preoperative variables associated with event-free survival; variables with $p < 0.05$ were entered in a multivariable model. For all tests

a p value of < 0.05 was considered significant. Statistical analysis was performed using SPSS statistical software version 20.0 (IBM Corp, Armonk, NY).

RESULTS

Study Population

The study population consisted of 159 patients who underwent LVR surgery for refractory HFrEF due to a postinfarction anteroseptal LV aneurysm. Baseline patient characteristics are summarized in Table 1. Mean age was 62 ± 10 years and 130 patients (82%) were men. The majority of patients were in NYHA class III (67%) or IV (15%), despite optimal medical and device therapy. Preoperative echocardiography demonstrated advanced LV remodeling with mean indexed LV end-systolic volume (LVESVI) 87 ± 39 mL/m^2 and LVEF 26% ± 7%. WMSI could be determined in 156 patients. Mean WMSI was 2.3 ± 0.4 and WMSI was ≥ 2.5 in 49 patients (31%). MR ≥ grade 2 was present in 70 patients (44%).

LVR was electively performed in all patients. Concomitant mitral valve repair was performed in 68 of 70 patients with preoperative MR ≥ grade 2. Mitral valve repair was not performed in 2 patients because of a completely calcified posterior mitral annulus. Preoperative MR ≥ grade 2 was absent in 89 patients. Nonetheless, intraoperative TEE showed an increase in MR to ≥ grade 2 immediately after LVR in 24 patients. These patients underwent additional mitral valve repair during a second period of aortic cross-clamping. Intraoperative echocardiography after mitral valve repair showed no more than mild MR in any of the patients and a leaflet coaptation height of 8 ± 1 mm. Tricuspid annuloplasty was performed in 38 patients (24%). Revascularization was conducted in 100 patients (63%). Surgical data are summarized in Table 2. In-hospital mortality was 11.9% (19 patients). Echocardiography before discharge demonstrated no or mild MR in all patients.

Mid-Term Echocardiographic and Clinical Outcomes

Mid-term echocardiographic assessment (median 21 [IQR 13 to 25] months after surgery) was available in 116 of 131 surviving patients (89%) and demonstrated a decrease in LVESVI (89 ± 42 to 51 ± 18 mL/m^2, p < 0.001), with improved LVEF (26% ± 7% to 35% ± 9%, p < 0.001). Furthermore, MR grade was significantly reduced (1.6 ± 1.1 to 0.7 ± 0.5, p < 0.001), with recurrent MR grade 2 in only 5 patients (4%). Comparison of preoperative and mid-term echocardiography is shown in Table 3. NYHA functional class had significantly improved after surgery (3.0 ± 0.6 preoperatively to 1.8 ± 0.7 at mid-term followup, p < 0.001).

Table 1. Baseline Patient Characteristics

Baseline Characteristics	Total Study Population (N = 159)	Survivors (n = 78)	Deaths (n = 81)	*p* Value
Preoperative clinical data				
Age, years	62 ± 10	59 ± 10	65 ± 8	<0.001
Male	130 (82)	62 (80)	68 (84)	0.531
Interval in years of infarction to surgery (median [IQR])	7 [1–14]	3 [1–10]	10 [1–18]	0.008
No. of coronary vessels with stenosis > 70%				
1	62 (39)	33 (42)	29 (36)	
2	43 (27)	20 (26)	23 (28)	
3	46 (29)	21 (27)	25 (31)	
Previous cardiac surgery	16 (10)	2 (3)	14 (17)	0.002
Renal insufficiency	9 (6)	2 (3)	7 (9)	0.168
Severe PH (sPAP > 60 mm Hg)	16 (10)	6 (8)	10 (12)	0.330
Logistic EuroSCORE I	8 ± 10	5 ± 6	10 ± 12	0.003
NYHA class	3.0 ± 0.6	2.8 ± 0.6	3.1 ± 0.5	0.002
III	107 (67)	50 (64)	57 (70)	
IV	23 (15)	7 (9)	16 (20)	
Clinical VT	35 (22)	9 (12)	26 (32)	0.002
Preoperative ICD	40 (25)	15 (19)	25 (31)	0.091
Preoperative echocardiographic data				
MR grade	1.6 ± 1.0	1.3 ± 1.0	1.8 ± 1.1	0.003
LVEF, %	26 ± 7	27 ± 7	25 ± 6	0.050
LVEDV, mL	228 ± 86	227 ± 87	228 ± 86	0.932
LVESV, mL	171 ± 78	168 ± 81	173 ± 76	0.678
LVEDVI, mL/m^2	116 ± 43	116 ± 44	116 ± 41	0.975
LVESVI, mL/m^2	87 ± 39	86 ± 42	88 ± 37	0.768
WMSI[a]	2.3 ± 0.4	2.2 ± 0.4	2.4 ± 0.5	0.002
sPAP, mm Hg[b]	37 ± 15	34 ± 15	40 ± 15	0.060
TAPSE	18 ± 4	18 ± 3	17 ± 4	0.003

[a] Wall motion score index (WMSI) was available in 156 patients. [b] Systolic pulmonary artery pressure (sPAP) was available in 92 patients, due to absence of tricuspid regurgitation in 67 patients.
Values are mean ± SD or n (%) unless otherwise indicated.
EuroSCORE = European System for Cardiac Operative Risk Evaluation; ICD = implantable cardioverter defibrillator; IQR = interquartile range; LVEDV = left ventricular end-diastolic volume; LVEDVI = LVEDV indexed to body surface area; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; LVESVI = LVESV indexed to body surface area; MR = mitral regurgitation; No. = number; NYHA = New York Heart Association; PH = pulmonary hypertension; TAPSE = tricuspid annular plane systolic excursion; VT = ventricular tachyarrhythmia.

Table 2. Surgical Data

Surgical Characteristics	Total Study Population (N = 159)	Survivors (n = 78)	Deaths (n = 81)	*p* Value
LVR with patch	153 (96)	75 (96)	78 (96)	0.962
Patch size, cm^2	13 ± 7	13 ± 7	14 ± 7	0.808
Balloon/shaper size, mL	108 ± 12	108 ± 12	109 ± 11	0.527
CABG	100 (63)	47 (60)	53 (65)	0.499
No. of distal anastomoses/patient	2.3 ± 1.2	2.3 ± 1.1	2.4 ± 1.2	0.548
Use of bypass grafts				
LIMA only	26 (26)	17 (36)	9 (17)	
RIMA only	5 (5)	1 (2)	4 (8)	
BIMA	19 (19)	13 (28)	6 (11)	
LIMA+vein	29 (29)	11 (23)	18 (34)	
Vein only	21 (21)	5 (11)	16 (30)	
Mitral valve repair	92 (58)	43 (55)	49 (61)	0.493
Median ring size [IQR]	28 [26–28]	28 [26–28]	26 [24–28]	
Tricuspid annuloplasty	38 (24)	12 (15)	26 (32)	0.013
Median ring size [IQR]	30 [28–32]	30 [28–32]	32 [28–32]	
Cryoablation	53 (33)	24 (31)	29 (36)	0.501
LV lead	76 (48)	33 (42)	43 (53)	0.174
IABP	38 (24)	11 (14)	27 (33)	0.004
ECC time, minutes	208 ± 63	196 ± 56	217 ± 68	0.100
Aortic cross-clamp time, minutes	142 ± 43	138 ± 40	145 ± 45	0.393

Values are n (%) or mean ± SD unless otherwise indicated.
BIMA = bilateral internal mammary artery; CABG = coronary artery bypass grafting; ECC = extracorporeal circulation; IABP = intraaortic balloon pump; IQR = interquartile range; LIMA = left internal mammary artery; LV = left ventricular; LVR = LV reconstruction; No. = number; RIMA = right internal mammary artery.

Long-Term Clinical Outcomes

Clinical follow-up was complete for all patients and median follow-up duration was 8.7 years (IQR, 3.9 to 10 years). During follow-up, 4 patients underwent LVAD implantation (all between 5.5 and 7.5 years after LVR surgery) and 2 patients underwent HTx (both 2.5 years after surgery), all for progressive heart failure. In addition to the 19 in-hospital deaths, 62 patients died. Cause of death was cardiac in 69% (heart failure, arrhythmias, and death from unknown causes). Overall cumulative eventfree survival rate was 83% ± 3% at 1-year, 68% ± 4% at 5-year, and 46% ± 4% at 10-year follow-up (Fig 1).

Mitral valve replacement was performed in 2 patients because of endocarditis with partial mitral ring dehiscence. Thirty-seven patients (23%) were readmitted for congestive heart failure; in total these patients experienced 105 readmissions (9.8 per 100 patient-years).

Table 3. Preoperative and Mid-Term Echocardiographic Data (n = 116)

Echocardiographic Characteristics	Preoperative	Mid-Term Follow-Up	*p* Value
MR grade	1.6 ± 1.1	0.7 ± 0.5	<0.001
Grade 0	13 (11)	44 (38)	
Grade I	54 (47)	67 (58)	
Grade II	22 (19)	5 (4)	
Grade III	18 (16)	0	
Grade IV	9 (8)	0	
LVEF, %	26 ± 7	35 ± 9	<0.001
LVEDV, mL	234 ± 94	156 ± 52	<0.001
LVESV, mL	176 ± 87	101 ± 39	<0.001
LVEDVI, mL/m^2	119 ± 46	79 ± 23	<0.001
LVESVI, mL/m^2	89 ± 42	51 ± 18	<0.001
sPAP, mm Hg[a]	35 ± 15	36 ± 16	0.903

[a] Systolic pulmonary artery pressure (sPAP) was available in 64 patients.
Values are mean ± SD or n (%) unless otherwise indicated.
LVEDV = left ventricular end-diastolic volume; LVEDVI = LVEDV indexed to body surface area; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; LVESVI = LVESV indexed to body surface area; MR = mitral regurgitation.

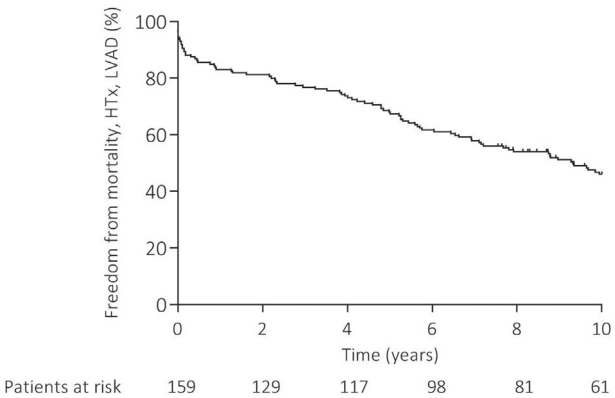

Fig 1. Overall event-free survival after surgery (n = 159). (HTx = heart transplantation; LVAD = left ventricular assist device.)

Preoperative Risk Factors for Event-Free Survival

Potential preoperative risk factors for event-free survival after surgery were assessed using univariable Cox regression analysis (Table 4). Six risk factors for adverse event-free survival were identified: increased age, preoperative renal insufficiency, higher preoperative WMSI, presence of preoperative MR (≥ grade 2), lower TAPSE, and a longer interval between myocardial infarction and surgery. Note that preoperative LV volumes were not associated with event-free survival. In a multivariable analysis, age (hazard ratio [HR] 1.03, 95% confidence interval [CI] 1.01–1.06, p = 0.016),

preoperative WMSI (HR 3.14, 95% CI 1.72–5.75, $p < 0.001$), presence of preoperative MR (HR 1.89, 95% CI 1.14–3.14, $p = 0.014$), and a longer interval between myocardial infarction and surgery (HR 1.05, 95% CI 1.02–1.08, $p = 0.001$) were independently associated with adverse event-free survival.

Table 4. Preoperative Risk Factors for Event-Free Survival

Variable	Univariable Analysis		Multivariable Analysis	
	Hazard Ratio [95% CI]	*p* Value	Hazard Ratio [95% CI]	*p* Value
Age	1.04 [1.02–1.07]	<0.001	1.03 [1.01–1.06]	0.016
Gender	0.75 [0.42–1.35]	0.750		
Renal insufficiency	2.77 [1.27–6.03]	0.010	2.24 [0.87–5.74]	0.093
Severe PH (sPAP > 60 mm Hg)	1.40 [0.70–2.68]	0.343		
NYHA class IV	1.53 [0.88–2.50]	0.135		
Interval in years of infarction to surgery	1.04 [1.02–1.07]	0.001	1.05 [1.02–1.08]	0.001
LVEF	0.97 [0.94–1.00]	0.066		
LVEDVI	1.00 [1.00–1.01]	0.910		
LVESVI	1.00 [1.00–1.01]	0.837		
WMSI	2.86 [1.75–4.68]	<0.001	3.14 [1.72–5.75]	<0.001
MR ≥ grade 2	2.00 [1.30–3.08]	0.002	1.89 [1.14–3.14]	0.014
TAPSE	1.10 [1.04-1.18]	0.002	1.06 [0.99–1.15]	0.105

CI = confidence interval; LVEDVI = left ventricular end-diastolic volume indexed to body surface area; LVEF = left ventricular ejection fraction; LVESVI = left ventricular end-systolic volume indexed to body surface area; MR = mitral regurgitation; NYHA = New York Heart Association; PH = pulmonary hypertension; sPAP = systolic pulmonary artery pressure; TAPSE = tricuspid annular plane systolic excursion; WMSI = wall motion score index.

Combined Effect of Preoperative WMSI and Preoperative MR

The combined effect of preoperative WMSI and preoperative MR ≥ grade 2 on the primary endpoint can be appreciated in Figure 2, where patients are divided into 4 groups: (1) patients with WMSI < 2.5 without MR (n = 64), used as reference; (2) patients with WMSI < 2.5 with MR (n = 43); (3) patients with WMSI ≥ 2.5 without MR (n = 24); and (4) patients with WMSI ≥ 2.5 with MR (n = 25). In patients with WMSI < 2.5, the presence of MR negatively affected event-free survival (HR 2.33, 95% CI 1.30–4.17, $p = 0.005$). Event-free survival was even worse in patients with WMSI ≥ 2.5 without MR (HR 3.11, 95% CI 1.61–6.01, $p = 0.001$), and extremely poor for patients with WMSI ≥ 2.5 with MR (HR 4.74, 95% CI 2.54–8.85, $p < 0.001$).

Heart failure readmissions were observed in 13% of patients with WMSI < 2.5 without MR (4 readmissions per 100 patient-years), in 26% of patients withWMSI<2.5 with MR (13 readmissions per 100 patient-years), in 42% of patients withWMSI ≥

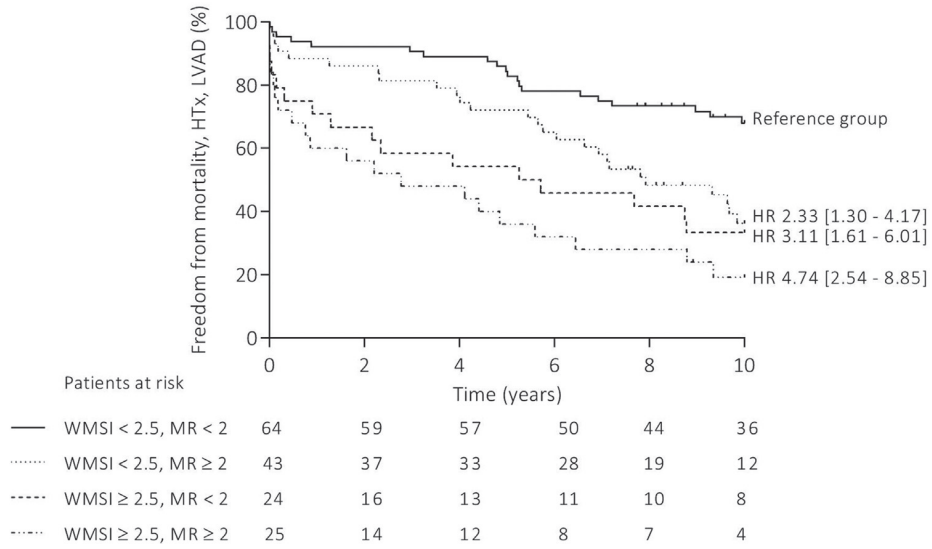

Fig 2. Event-free survival for patients with wall motion score index (WMSI) < 2.5 and ≥ 2.5, and mitral regurgitation (MR) < and ≥ grade 2. (HR = hazard ratio; HTx = heart transplantation; LVAD = left ventricular assist device.)

2.5 without MR (22 readmissions per 100 patient-years), and in 32% of patients with WMSI ≥ 2.5 with MR (14 readmissions per 100 patient-years).

COMMENT

In the present study, mid-term echocardiographic and long-term clinical outcomes were evaluated in patients who underwent an integrated surgical treatment, consisting of LVR with concomitant procedures (mitral valve repair, tricuspid valve repair, revascularization, and arrhythmia surgery) for refractory HFrEF due to a postinfarction anteroseptal LV aneurysm. This integrated approach resulted in LV reverse remodeling and absence of MR ≥ grade 2 at mid-term follow-up, and 46% event-free survival 10 years after surgery. Increased age, higher preoperative WMSI, preoperative presence of MR ≥ grade 2 and a longer time interval after myocardial infarction were associated with worse eventfree survival after surgery. Event-free survival is favorable in patients with WMSI < 2.5 and significantly worse when WMSI is ≥ 2.5. In both groups, the presence of preoperative MR grade ≥ 2 negatively affects event-free survival, despite successful correction of MR.

Surgery for Refractory HFrEF: Echocardiographic and Clinical Outcomes

Heart failure is the most common complication due to myocardial infarction and is associated with adverse clinical outcomes [3, 4, 18]. Optimal medical and device therapy improve outcomes in these patients. However, when heart failure symptoms persist, surgical treatment options—implantation of an LVAD, HTx, and reconstructive surgery (targeting the left ventricle as well as concomitant functional valve regurgitation)—should be carefully considered by a dedicated Heart team [6–9].

In the present study, all patients underwent a personalized surgical approach with LVR as the mainstay, combined with concomitant procedures based on welldefined indications. Structured outpatient follow-up and optimal medical therapy were continued after surgery in all patients. This integrated medicosurgical approach resulted in LV reverse remodeling (LVESVI –36%), improved LVEF (+46%), and absence of MR ≥ grade 2 at mid-term follow-up. Others have reported similar echocardiographic results after LVR surgery [11–13]. To the best of our knowledge, the current study is the first to extend clinical follow-up to 10 years after surgery. Eventfree survival in this study (83% ± 3% at 1-year, 68% ± 4% at 5-year, and 46% ± 4% at 10-year follow-up) is better than the overall 5-year survival of patients with heart failure after myocardial infarction (approximately 50%) [4], and comparable to the 5-year survival after LVR surgery reported by others [11, 12].

Risk Factors for Event-Free Survival

Risk stratification and careful preoperative patient selection are crucial to optimize outcomes after LVR surgery. In the present study, 4 preoperative risk factors for adverse event-free survival were identified: increased age, higher WMSI, presence of MR ≥ grade 2 and a longer interval between myocardial infarction and surgery.

WMSI is an echocardiographic measure of LV systolic function. In a previous study, we demonstrated that WMSI at a cutoff value of ≥ 2.5 is associated with poor outcomes 1 year after LVR surgery (a combined endpoint of mortality and NYHA class ≥ III) [19]. In the present study, WMSI ≥ 2.5 proved to be an independent risk factor for event-free survival up to 10 years after surgery as well. This finding indicates that the extent and function of the remote myocardium plays a key role in translating surgically induced LV changes into beneficial long-term outcomes.

Functional MR is a common phenomenon in patients with ischemic heart failure, resulting from a combination of papillary muscle displacement, systolic leaflet tethering, annular dilatation, and reduced closing forces due to LV remodeling [20].

Functional MR is associated with poor survival [21, 22], but its management at the time of LVR surgery remains controversial [13]. In the present study, mitral valve repair was performed in all patients with MR ≥ grade 2. The presence of preoperative MR negatively affected event-free survival in both patients with WMSI < 2.5 and WMSI ≥ 2.5 despite successful mitral valve repair. Consequently, the presence of preoperative MR could be interpreted as a marker of LV remodeling. Advanced LV systolic dysfunction and presence of functional MR provide a fatal combination.

Finally, a longer interval between myocardial infarction and LVR surgery was independently associated with adverse event-free survival. The compensatory LV volume increase seen in remodeling after myocardial infarction results in increased LV wall pressure with hypoperfusion of the remote myocardium [23]. Because LV remodeling is a progressive process, myocardial fibrosis will be more severe in patients with a longer interval between myocardial infarction and surgery, which might explain its association with adverse clinical outcomes.

Interestingly, preoperative LV volumes were not associated with adverse outcomes in the present study, in contrast to previous reports [11, 12, 24]. However, the extent and function of the remote myocardium—and consequently the ability to recover after LVR surgery— may differ between patients with equally increased LV volumes. This heterogeneity in remote myocardium may explain why global ventricular measures such as LV volumes may not accurately predict event-free survival after LVR surgery.

Although RV function, as determined by TAPSE, was not independently associated with event-free survival, this does not imply that RV function should be disregarded. Other studies have shown reduced 30-day and long-term survival after LVR in patients with RV dysfunction, but these studies did not take into account the degree of LV systolic dysfunction or MR severity [25, 26]. The interaction between LV and RV dysfunction remains complex; in the current study LV dysfunction as reflected by WMSI and MR grade proved to be the strongest predictor of long-term event-free survival.

Clinical Implications

The optimal treatment strategy for patients with refractory HFrEF due to a postinfarction anteroseptal LV aneurysm remains a subject of debate. LVAD implantation and HTx may be considered for these patients [5]. Although survival after LVAD implantation as destination therapy has improved (1-year survival of approximately 50%), LVADs still have their limitations—namely, thromboembolic events,

anticoagulation-related hemorrhage, and infection [27]. Heart transplantation is limited by donor shortage and strict selection criteria, and has a 5-year survival rate of approximately 70%. An integrated approach consisting of LVR with concomitant procedures, as described in this study, is a viable alternative for these patients.

In the present study, we identified risk factors that can easily be determined and may help the Heart team to decide on which intervention to choose for patients with refractory HFrEF. LVR with concomitant procedures is favorable for patients with a preoperative WMSI < 2.5— both with and without functional MR, provided that the mitral valve is successfully repaired. In patients with WMSI ≥ 2.5 without MR, LVR may still be considered a viable option, however with slightly worse outcomes at longer follow-up. For patients with WMSI ≥ 2.5 and presence of MR, event-free survival is extremely poor despite durable correction of MR. For these patients, the Heart team might first consider alternatives such as LVAD implantation or HTx. LVR might still have a place in patients with contraindications for these alternatives, and in those for whom it might be warranted to defer LVAD implantation or HTx. Given that a longer interval between myocardial infarction and surgery was associated with adverse event-free survival, LVR surgery should preferably be considered in an early stage if patients develop symptoms of heart failure.

Study Limitations

The present study is a single-center observational study, with a limited study population. However, 10-year followup was complete for all patients and the study population was very homogeneous, only including patients with refractory HFrEF (LVEF ≤ 35% and NYHA class III/IV) due to a postinfarction anteroseptal aneurysm. Higher preoperative WMSI and preoperative presence of MR ≥ grade 2 were found to be independently associated with adverse event-free survival. These findings should be confirmed in other, larger studies. Because of the retrospective nature of this study and the study period (starting in 2002), data regarding preoperative viability were not available for the majority of patients and quality of echocardiographic images was insufficient for assessment of more-advanced RV function parameters (such as RV fractional area change or RV longitudinal peak systolic strain).

CONCLUSION

In the present study, an integrated approach of LVR with concomitant procedures for patients with HFrEF due to a postinfarction anteroseptal aneurysm resulted in LV reverse remodeling and absence of functional MR at midterm follow-up. Event-free

survival is favorable in patients with WMSI < 2.5 and significantly worse when WMSI is ≥ 2.5. In both groups, the presence of preoperative MR grade ≥ 2 negatively affects event-free survival, despite successful correction of MR. These findings indicate that preoperative echocardiographic assessment, specifically focused on preoperative WMSI and presence of MR, is useful for the decision-making process on which intervention to choose for patients with refractory HFrEF.

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