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## Left ventricular reconstruction in ischemic cardiomyopathy

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# Chapter 2

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## Early and late outcome of left ventricular reconstruction surgery in ischemic heart disease

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## SUMMARY

A systematic review of the literature was performed to determine early and late mortality associated with left ventricular (LV) reconstruction surgery and to assess the influence of different surgical techniques, concomitant surgical procedures, clinical and hemodynamic parameters on mortality. The MEDLINE database (January 1980—January 2005) was searched and from the pooled data, hospital mortality and survival were calculated. Summary estimates of relative risks (RR) were calculated for the techniques that were used and for concomitant coronary artery bypass grafting (CABG) and mitral valve surgery. The risk-adjusted relationships between mortality and clinical and hemodynamic parameters were assessed by meta-regression. A total of 62 studies (12,331 patients) were identified. Weighted average early mortality was 6.9%. Cumulative 1-year, 5-year and 10-year survival were 88.5%, 71.5% and 53.9%, respectively. Endoventricular reconstruction (EVR) showed a reduced risk for both early (RR = 0.79,  $p < 0.005$ ) and late (RR = 0.67,  $p < 0.001$ ) mortality compared to the linear repair (early: RR = 1.38,  $p < 0.001$ ; late: RR = 1.83,  $p < 0.001$ ). Early and late mortality were mainly cardiac in origin, with as predominant cause heart failure in respectively 49.7% and 34.5% of the cases. Ventricular arrhythmias caused 16.6% of early deaths and 17.2% of late deaths. Concomitant CABG significantly decreased late mortality (RR = 0.28,  $p < 0.001$ ) without increasing early mortality (RR = 1.018,  $p = 0.858$ ). Concomitant mitral valve surgery showed both an increased risk for early (RR = 1.57,  $p = 0.001$ ) and late mortality (RR = 4.28,  $p < 0.001$ ). No clinical or hemodynamic parameters were found to influence mortality. It is noteworthy that only one third of patients included in the current analysis were operated for heart failure (14 studies, 4135 patients). In this group we noted an early mortality of 11.0% with a late mortality (3-year) of 15.2%. This analysis of pooled literature data showed that LV reconstruction surgery is performed with acceptable mortality and EVR may be the preferred technique with a reduced risk for early and late mortality. Concomitant CABG improved outcome, whereas the need for mitral valve surgery appeared an index of gravity. No clinical or hemodynamic parameters were found to influence mortality; specifically LV ejection fraction and LV volumes both did not predict outcome.

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Keywords: Left ventricular reconstruction surgery; Aneurysmectomy; Surgical ventricular restoration; Dor procedure; Ischemic heart disease; Heart failure

## 1. INTRODUCTION

The formation of scar tissue after myocardial infarction leads to changes in left ventricular (LV) shape and function (remodeling) [1]. The normally elliptical LV tends to sphericity and chamber dilatation, while the transmural extent of the myocardial scar determines whether or not a true LV aneurysm (dyskinetic segment) will develop [2]. Likoff and Bailey described the first aneurysmectomy in 1952 [3], subsequently followed by the first aneurysmectomy with linear repair using cardio-pulmonary bypass reported by Cooley in 1958 [4]. A number of different surgical techniques and modifications have since developed to restore LV shape and to improve LV function [4–9]. The most commonly used techniques are the endoventricular repair (EVR), with or without the use of an endoventricular patch, introduced by Dor in 1985 [4] and the aforementioned linear repair. Dor et al. demonstrated the feasibility of his procedure not only for the true LV aneurysms with a dyskinetic segment, but also for remodeled left ventricles with extensive akinesia [2]. Surgeons who advocate the different surgical techniques, all report on good short- and long-term results. Only a few reports are available that compare different surgical techniques, particularly in respect to long-term results [10–15,75]. The aims of this study were:

1. to compare early and late mortality in LV reconstruction surgery using different surgical techniques, based on pooled analysis of literature studies,
2. to evaluate the causes of early and late mortality in LV reconstruction surgery,
3. to evaluate the influence of factors including concomitant surgical procedures, clinical and hemodynamic parameters on early and late mortality.

LV reconstruction surgery is increasingly being employed as an alternative surgical therapy for patients with ischemic heart failure. In these patients the issues listed above are particularly important and therefore a sub-analysis was conducted for this category of patients.

## 2. METHODS

### 2.1. Review of published reports

The studies were identified by means of several combined search strategies: (1) A search of the MEDLINE database (January 1980–January 2005) was conducted using the following Keywords: ‘left ventricular aneurysm’, ‘left ventricular restoration’, ‘surgical ventricular restoration’, ‘left ventricular remodeling surgery’, ‘aneurysmectomy’, and ‘Dor procedure’. (2) A manual search of six cardiothoracic surgery and cardiology journals (*Annals of Thoracic Surgery*, *Journal of Thoracic and*

Cardiovascular Surgery, European Journal of Cardiothoracic Surgery, Thoracic and Cardiovascular Surgery, Circulation and Journal of the American College of Cardiology). (3) The reference lists of the reports obtained through these searches were screened for additional articles that may have been missed. Only articles in English were considered, and reviews, editorials, animal or in vitro experimental studies, abstracts and articles concerning LV reconstruction surgery for non-ischemic heart disease were disregarded. The most recent publication or the publication concerning the largest patient population was included for analysis if multiple publications were available from the same institute to avoid double counting.

## 2.2. Statistical analysis

The following parameters were extracted from each article and entered into the database: pooled, average and median rates of in-hospital mortality and survival, specified causes of death (whether cardiac, subdivided in heart failure, ventricular arrhythmias, acute myocardial infarction and other, non-cardiac or unknown), follow-up duration, mean age, gender, interval post myocardial infarction, patients with ischemic heart failure (defined as LV ejection fraction (EF)  $\leq 35\%$  and New York Heart Association (NYHA) class III or IV), surgical technique used, mortality and survival with concomitant CABG and mitral valve surgery, LVEF, LV end-diastolic volume index (LVEDVI), LV end-systolic volume index (LVESVI), LV end-diastolic dimension (LVEDD) and LV end-systolic dimension (LVESD). From the data, pooled, median and weighted-average early and late mortality were calculated. Cumulative survival was calculated from the pooled late mortality. Using comprehensive meta-analysis software (Borrestein M, Hedges L, Higgins J, Rothstein H. Comprehensive meta-analysis Version 2, Biotstat, Englewood, NJ (2005)), the summary estimates of relative risks (RR) were calculated for the different surgical techniques that were used and for concomitant CABG and mitral valve surgery. The relative risk (with 95% confidence intervals, CI) was calculated using a random effects model. The riskadjusted relationship between mean age, time from infarction, LVEF, LVEDVI, LVESVI, LVEDD and LVESD and hospital mortality and survival was assessed by meta-regression. A sub-analysis on survival in patients with heart failure was conducted. A Chi-square test from homogeneity was calculated and Fisher's exact test was used for comparing events. A  $p$  value  $< 0.05$  was considered significant.

## 3. RESULTS

Two hundred and eight citations were returned and the articles scrutinized. After excluding non-English articles, reviews, editorials, animal or in vitro experimental

studies, abstracts and articles concerning LVRS for non-ischemic heart disease, 121 articles were evaluated. After exclusion of all but the most recent publication from the same institute and those not reporting deaths, 62 articles [10–70] were entered into the pooled analysis.

### 3.1. Early and late mortality in LV reconstruction surgery

Pooling of all data from the 62 studies [10–70] (12,331 patients) showed a pooled early mortality (defined as in-hospital or 30-day mortality) of 6.8% and a median early mortality of 7.9%. Weighted average early mortality is 6.9%. Forty-seven studies also reported on long-term survival [11–53,71–74], following 8571 patients for a median of 49 months. Cumulative 1-, 5- and 10-year survival was 88.5%, 71.5% and 53.9%, respectively (Fig. 1).

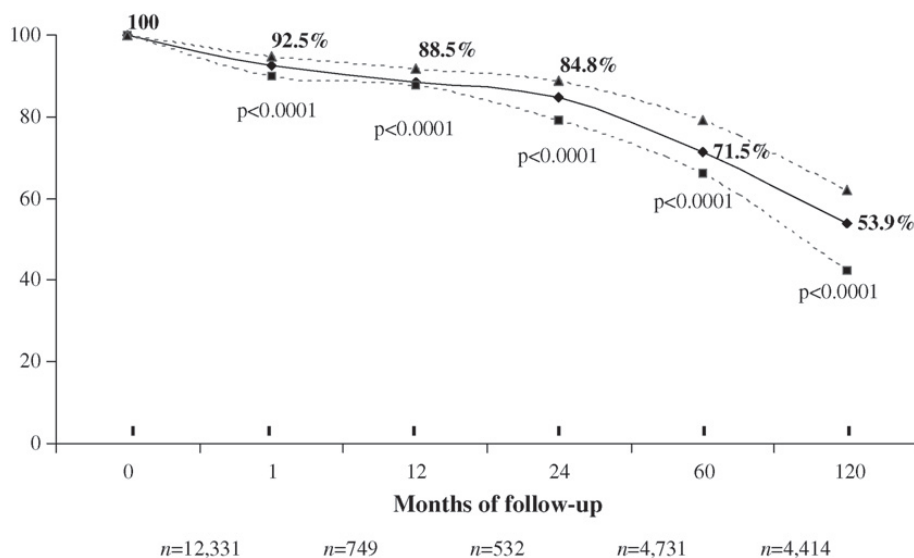


Fig. 1. Cumulative survival after LV reconstruction surgery calculated from 62 published reports ( $n = 12,331$  patients) that reported on early mortality and 47 published reports following 8571 patients for a median of 49 months (25th, 75th percentile = 23, 62 months). Cumulative 1-, 5- and 10-year survival were 88.5%, 71.5% and 53.9%, respectively. Straight line: weighted average cumulative survival; dotted lines: 95% confidence intervals.

### 3.2. Different surgical techniques versus early and late mortality

The different techniques for LV reconstruction surgery, reported between January 1980 and January 2005, can be grouped into five main types of surgery: (1) direct reconstruction of the LV wall using a circular patch, (2) endoventricular reconstruction of the LV with or without the use of an endoventricular patch (EVR) as described by Jatene and Dor [9,60], (3) linear repair, (4) linear repair with septoplasty as described by Mickleborough et al. [5] and (5) septo-exclusion technique as described

by Guilmet et al. [7] and Stoney et al. [6]. Fig. 2 shows the summary estimates of the relative risks for the different surgical techniques for early mortality. Comparing the two main techniques, EVR shows a reduced risk for early mortality (RR = 0.79,  $p = 0.002$ ) compared to the linear repair (RR = 1.38,  $p < 0.001$ ). In Fig. 3, the summary estimates of the relative risks for the different surgical techniques are shown for late mortality. Again, considering the two main techniques EVR shows a significantly reduced risk on late mortality (RR = 0.67,  $p < 0.001$ ) compared to linear repair (RR = 1.83,  $p < 0.001$ ).

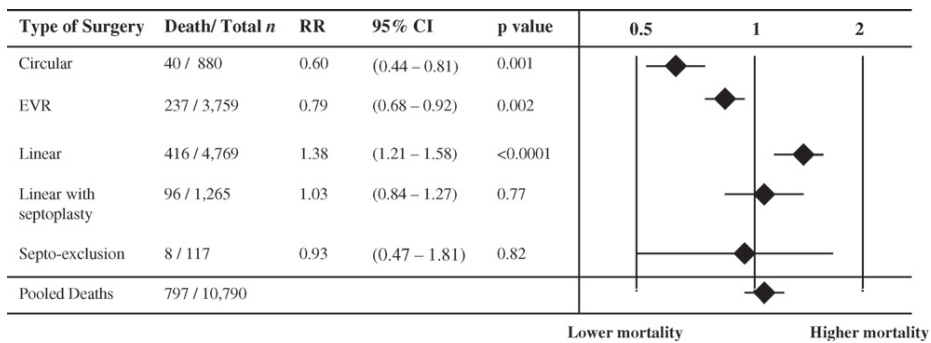


Fig. 2. Summary estimates of the relative risks for the different surgical techniques for early mortality. Comparing the two main techniques, EVR showed a reduced risk for early mortality (RR = 0.79,  $p = 0.002$ ) compared to the linear repair (RR = 1.38,  $p < 0.001$ ). LVRS: LV reconstruction surgery; Circular: direct reconstruction of LV wall using a circular patch; EVR: endoventricular reconstruction of the LV with or without a patch; linear: linear repair; linear with septoplasty: linear repair with a plasty of the interventricular septum; septo-exclusion: septo-exclusion technique.

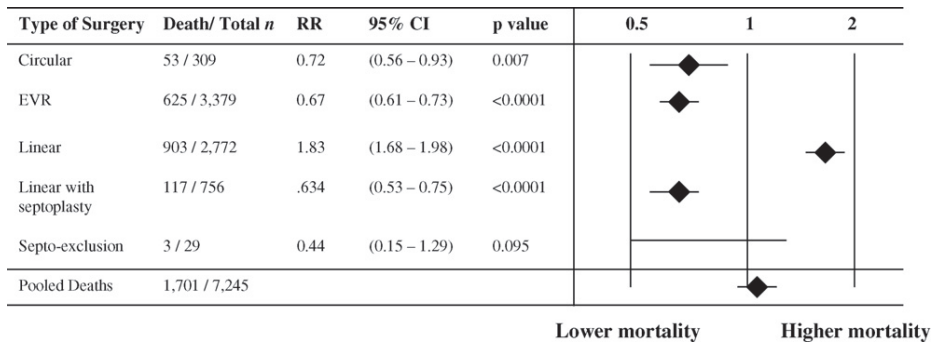


Fig. 3. Summary estimates of the relative risks for the different surgical techniques for late mortality. Comparing the two main techniques, EVR showed a significantly reduced risk on late mortality (RR = 0.67,  $p < 0.001$ ) compared to the linear repair (RR = 1.83,  $p < 0.001$ ). LVRS: LV reconstruction surgery; Circular: direct reconstruction of LV wall using a circular patch; EVR: endoventricular reconstruction of the LV with or without a patch; linear: linear repair; linear with septoplasty: linear repair with a plasty of the interventricular septum; septo-exclusion: septo-exclusion technique.

### 3.3. Causes of early and late mortality in LV reconstruction surgery

A total of 20 studies ( $n = 3729$  patients) were identified that specified causes of early mortality. In Table 1, the causes of early mortality are shown. Early mortality was mainly cardiac in origin (84.7%), with as predominant cause heart failure in 49.7% of the cases. Ventricular arrhythmias were responsible for 16.5% of early mortality.

**Table 1**  
Causes of early mortality after LVRS (20 studies,  $n = 3729$  patients)

Cause of death	No. of patients	% of cardiac early mortality	% of total early mortality
Cardiac early mortality	261		84.7
Heart failure/LCO	153	58.6	49.7
VT/VF	51	19.5	16.6
AMI	34	13.0	11.0
Other	23	8.8	7.5
Non-cardiac early mortality	47		15.3
Total early mortality	308		

Early mortality was mainly cardiac in origin (84.7%), with as predominant cause heart failure in 49.7% of the cases. Ventricular arrhythmias were responsible for 16.6% of early mortality.

LCO: low cardiac output; VT/VF: ventricular tachycardia/ventricular fibrillation; AMI: acute myocardial infarction.

A total of 13 studies ( $n = 2702$  patients) were identified that specified causes of late mortality. In Table 2, the causes of late mortality are summarized. Late mortality was also mainly cardiac in origin (70.2%). Heart failure constituted 34.5% and ventricular arrhythmias 17.2% of the late deaths. In 12.6% of late deaths, the cause was unknown.

**Table 2**  
Causes of late mortality after LVRS (13 studies,  $n = 2702$  patients)

Cause of death	No. of patients	% of cardiac late mortality	% of total late mortality
Cardiac late mortality	368		70.2
Heart failure/LCO	181	49.2	34.5
VT/VF	90	24.5	17.2
AMI	88	23.9	16.8
Other	9	2.5	1.7
Non-cardiac late mortality	90		17.2
Unknown	66		12.6
Total late mortality	524		

Late mortality was also mainly cardiac in origin (70.2%). Heart failure constituted 34.5% and ventricular arrhythmias 17.2% of the late death. In 12.6% of late deaths, the cause was unknown.

LCO: low Cardiac output; VT/VF: ventricular tachycardia/ventricular fibrillation; AMI: acute myocardial infarction.



### 3.4. Concomitant surgical procedures potentially influencing mortality

Seven studies (1525 patients) reported on concomitant CABG and early mortality in LV reconstruction surgery, and three studies (497 patients) reported on concomitant CABG and late mortality. Concerning concomitant mitral valve surgery (mitral valve repair or replacement): eight studies (524 patients) reported on early mortality in LV reconstruction surgery, two studies (84 patients) reported on late mortality. In Fig. 4, the summary estimates of the relative risks for concomitant CABG and mitral valve surgery for both early and late mortality are provided. Concomitant CABG was not associated with an increased risk for early mortality (RR = 1.018,  $p = 0.858$ ), but was associated with a significantly lower risk for late mortality (RR = 0.28,  $p < 0.001$ ). Concomitant mitral valve surgery was associated with both an increased risk for early (RR = 1.57,  $p = 0.001$ ) and late mortality (RR = 4.28,  $p < 0.001$ ).

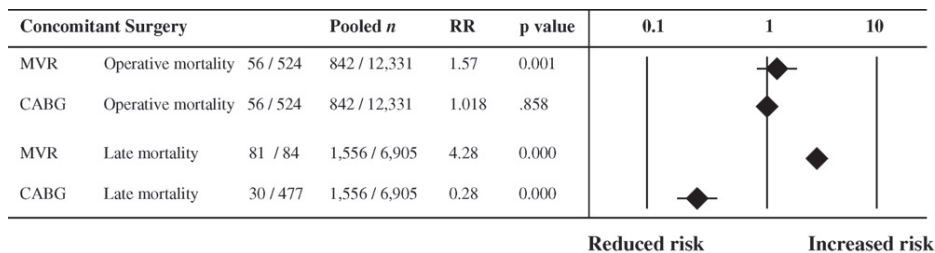


Fig. 4. Comparison of left ventricular reconstruction surgery with concomitant CABG or mitral valve surgery on early (in-hospital or 30-day mortality) and late (5-year) mortality. Concomitant CABG was not associated with an increased risk for early mortality (RR = 1.018,  $p = 0.858$ ), but was associated with a significantly lower risk for late mortality (RR = 0.28,  $p < 0.001$ ). Concomitant mitral valve surgery was associated with both an increased risk for early (RR = 1.57,  $p = 0.001$ ) and late mortality (RR = 4.28,  $p < 0.001$ ). MVR: mitral valve surgery (repair or replacement); CABG: coronary artery bypass grafting.

### 3.5. Factors potentially influencing mortality

The following parameters were evaluated: mean age, gender, interval post myocardial infarction, LVEF, LVEDVI, LVESVI, LVEDD and LVESD. None of the parameters were significantly related to early or late mortality. In particular, LVEF and indexed LV volumes were not related to early or late mortality.

### 3.6. Heart failure

Fourteen of the 62 (22.6%) reports included LV reconstruction surgery in patients with heart failure, with a total of 4135 patients. The pooled, median and average weighted early mortality patients with heart failure were 5.2%, 12.9% and 11.6%, respectively. Ten studies (802 patients) also reported on late mortality after LV reconstruction surgery showing a pooled, median and average weighted late mortal-

ity at 3-year follow-up of 15.7%, 14.7% and 15.7%, respectively (Fig. 5). Eight studies ( $n = 2376$  patients) reported on EVR and early mortality in ischemic heart failure patients, four studies (1045 patients) reported on linear repair and early mortality in ischemic heart failure patients. Comparison of these two techniques for the relative risk of early mortality, revealed a significantly reduced risk for early mortality with EVR ( $RR = 0.66, p = 0.004$ , Fig. 6). There were no statistical significant relationships for any of the parameters postulated to possibly influence early and late mortality.

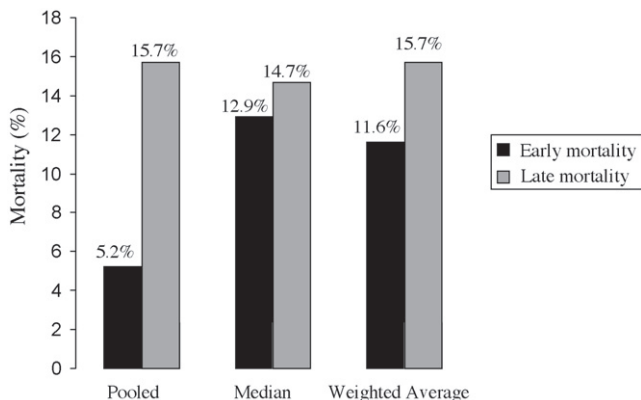


Fig. 5. Early (in-hospital or 30-day mortality) and late (3-year) mortality in patients with heart failure. The pooled, median and average weighted early mortality (14 studies,  $n = 4135$  patients) were 5.2%, 12.9% and 11.6%, respectively. The pooled, median and average weighted late mortality (10 studies,  $n = 802$  patients) were 15.7%, 14.7% and 15.7%, respectively.

EVR	Linear repair	RR	95% CI	p value	0.5	1	2
135 / 3,005	71 / 1,045	0.66	(0.50–0.87)	0.004			

Fig. 6. Summary estimates of the relative risk for EVR (8 studies,  $n = 2376$  patients) versus linear repair technique (4 studies,  $n = 1045$  patients) in patients with heart failure. EVR shows a significantly reduced risk for early mortality ( $RR = 0.66, p = 0.004$ ). EVR: endoventricular reconstruction of the LV with or without a patch; linear: linear repair.

#### 4. DISCUSSION

In this pooled analysis of available studies in the literature, we found that surgical treatment of a LV aneurysm has an acceptable early mortality of 6.9% and a good longterm outcome (10-year survival 53.9%). This compared favorably to the natural history of LV aneurysms with a reported 5-year survival of 12% to 47% [76,77]. Improved medical treatment of ischemic heart disease has since then undoubtedly improved survival and delayed hemodynamic decompensation, but

survival in patients with a LV aneurysm is still limited. Faxon et al. demonstrated in the Coronary Artery Surgery Study (CASS) that patients with a LV aneurysm and three-vessel coronary artery disease and patients with clinical heart failure have improved survival with surgical therapy [74]. To date there have been no results from prospective randomized controlled trials comparing modern medical and surgical treatment. Historically, only a few patients with heart failure were considered for cardiac surgery in the absence of a clear need for coronary revascularization or valve repair or replacement. Indications for LV reconstruction have evolved over time from aneurysmectomy for thromboembolic complications or progressively enlarging aneurysms to LV reconstruction for improvement of ventricular function in the treatment of heart failure. One third of patients included in the current analysis were operated for heart failure (14 studies, 4135 patients). In this group we noted an early mortality of 11.0% with a late mortality (3-year) of 15.2%. Tertiary referral centers for cardiovascular care with large experience in LV reconstruction surgery for heart failure, like the Centre Cardio-Thoracique in Monaco and the San Donato Hospital in Milan, reported an early mortality ranging between 10% and 13% with survival at 3 years ranging from 62.7% to 77.2% [28,39,89]. It is noteworthy in this respect that the ‘realworld’ application of LV reconstruction surgery, as reported by Hernandez et al. in their study from the data of the STS National Cardiac Database shows higher operative risks, especially in specific subgroups of patients [95].

#### 4.1. Surgical techniques and mortality

Comparing the two most used and reported techniques, endoventricular reconstruction of the LV with or without a patch (EVR) and linear repair, EVR shows a significantly reduced risk for early mortality (RR = 0.79,  $p = 0.002$ ). The linear repair technique cannot exclude the septal scar, and also carries the risk of creating a restrictive residual LV cavity, especially in large aneurysms, leading to diastolic dysfunction and LV failure [27,78,79]. Sizing of the residual LV cavity in EVR, either by an intracavitary balloon or a commercially available shaper device to a volume of 50–60 ml/m<sup>2</sup> BSA avoids creating a residual LV cavity that is restrictive [9,29,39]. Another explanation for EVR to show better results could be that EVCPP patients were operated in a more recent era with improved myocardial protection, anesthesiological techniques, and perioperative care. Because of the limited number of patients in the currently available reports, the relative risks for early mortality calculated for the linear repair with septoplasty, and the septo-exclusion techniques did not reach statistical significance. The reconstruction of the LV wall using a circular patch did however show a significantly reduced risk for early mortality (RR = 0.60,  $p = 0.001$ ), but again patient numbers for this technique are limited. In the meta-analysis by Parolari et al. concerning the early outcomes following

different LV reconstruction techniques, the authors also concluded that geometric reconstruction carries a reduced risk for early mortality compared to linear repair [90]. In contrast, in a sub-analysis comparing geometric and linear reconstruction techniques that were carried out in the same time lag, a difference in early mortality could not be demonstrated. Mukaddirov et al. recently published a study advocating a tailored approach (linear or patch plasty repair) in LVR depending on the specific anatomy of individual patients [99].

In the current pooled analysis, EVR also showed a significantly reduced risk for late mortality (RR = 0.67,  $p < 0.0001$ ). Possibly, the complete exclusion of the septal scar and the more anatomical reconstruction leading to a more efficient myocardial fiber orientation and systolic function contributed to this reduction in late mortality [9,80]. Also the fact that grafting the left anterior descending coronary artery is more feasible in the EVR technique and may play a role [11,81,78]. The linear repair with septoplasty and direct reconstruction of the LV wall using a circular patch also both showed a significantly reduced risk for late mortality (RR = 0.72,  $p = 0.007$  and RR = 0.63,  $p < 0.0001$ , respectively), but for both techniques available patient numbers are limited.

The factors that may have contributed to the reduced risk for mortality with the EVR technique in the pooled analysis of all patient categories may be even more important in patients with heart failure. Generally, these patients often have severely enlarged LV volumes, associated with depressed contractile function of the remote myocardium [88,89]. Indeed, we noted that in heart failure patients both early and late mortality were less with the EVCPP technique.

#### 4.2. Fatal-failure modes of LVR

It was noted that 50% of early deaths and 30% of late deaths were caused by heart failure. With respect to the technique of reconstructing the LV cavity, three possible explanations exist for early and late LV failure: first, the aforementioned problem of creating a restrictive residual LV cavity, leading to diastolic dysfunction and LV failure; second, leaving a too large residual LV cavity only partially reverses the remodeling process and may lead to redilatation of the left ventricle. Also a residual large akinetic area has been mentioned as possible cause for redilatation. Ueno et al. demonstrated redilatation and increasing sphericity after Dor- and SAVE-procedures at intermediate follow-up, resulting in increased wall tension with reduced compliance as possible causes for late heart failure [92]. Raman et al. associated the use of a stiff and relatively big patch in EVR as cause for some adverse long-term outcomes [94]. Patch size, shape and orientation may prove to be important in preventing

adverse ventricular remodeling over time, as Cirillo et al. have shown in a small group with an EVR technique using a small, obliquely oriented and oval-shaped patch [93]. Third, insufficient residual remote myocardium to survive the procedure and to translate the surgically induced morphological changes to functional improvement leads to LV failure. No data are available on preoperative assessment of the functional capacity of the remote myocardium and used as predictor of outcome after LV reconstruction surgery.

Early and late mortality due to ventricular arrhythmias in this study were 16.5% and 17.2%, respectively (of note, it is unknown whether these patients already had ventricular arrhythmias preoperatively). Early ventricular arrhythmias after LV reconstruction surgery can be ascribed to electrolyte abnormalities, tissue edema and inflammation. Late ventricular arrhythmias have been related to ventricular dilatation with high wall stress and stretch [96]. It has been postulated that LV reconstruction surgery due to volume reduction reduces arrhythmogenicity. Exclusion of the myocardial scar, concomitant complete revascularization and mechanical resynchronization further reduces the trigger for electrical instability and may render the need for an implantable cardioverter-defibrillator (ICD) unnecessary [96,97]. Some authors like Dor et al. [79] and Mickleborough et al. [5] advocate routine use of concomitant endocardectomy of the border zone of viable and non-viable myocardium and cryotherapy to further decrease the risk of ventricular arrhythmias. These authors have reported a low late incidence of ventricular arrhythmias with this strategy. The relatively high incidence of death due to ventricular arrhythmias observed in the present pooled analysis raises the question whether LV reshaping with volume reduction, scar exclusion and revascularization is sufficient antiarrhythmic to make adjunctive device therapy of little use. O'Neill et al. demonstrated a high incidence of ventricular arrhythmias after LV reconstruction surgery and advocate the use of pre-discharge electrophysiological studies and/or ICD implantation before hospital discharge [98]. More studies are needed to clarify the need for device therapy after LV reconstruction surgery.

### **4.3. Concomitant surgical procedures potentially influencing mortality**

We found that concomitant myocardial revascularization with LV reconstruction surgery improved late survival without increasing the risk for early mortality. Besides symptomatic relief of angina, revascularization of viable, remote myocardium in non-scarred segments may improve compensatory contractile function [82]. Also, revascularization of the proximal left anterior descending coronary artery to improve septal perfusion may contribute favorably [11]. Another contributing

factor could be that revascularization further reduced the risk for late ventricular arrhythmias. These factors probably outweigh the increase in operative and extracorporeal circulation time and thus did not result in higher early mortality. This finding underlines the importance of (complete) revascularization in these patients.

Concomitant mitral valve surgery, whether repair or replacement, shows an increased risk for early (RR = 1.57,  $p = 0.001$ ) and late mortality (RR = 4.28,  $p < 0.001$ ). In patients with previous anterior myocardial infarction, functional mitral regurgitation occurs mainly in the setting of LV dilatation, with tethering of the mitral valve leaflets, displacement of the subvalvular apparatus and dilatation of the mitral annulus causing secondary incompetence of the mitral valve. Functional mitral regurgitation therefore mainly reflects a more advanced stage of disease, and has been shown to be associated with an increased mortality, independent of the degree of underlying LV dysfunction [85–87]. The need for mitral valve surgery in LV reconstruction surgery is therefore an index of gravity. This is by no means an argument not to perform mitral valve surgery in these patients, since mitral regurgitation-related volume overload has been shown to promote further LV remodeling and progression of heart failure. Correcting mitral regurgitation improves clinical functional class and may prevent LV redilatation [39,72,91]. However, this analysis does not permit any conclusion on the benefits of mitral valve surgery, since no comparison between treated and non-treated patients was available in the literature.

#### 4.4. Factors potentially influencing mortality

Besides the surgical technique and concomitant procedures, a number of parameters have been traditionally identified that influence early and late mortality. A low LVEF has been reported in earlier reports to be a predictor of higher early and late mortality [12,49,51,80]. The observation that LV dilatation is more closely related to outcome than (decreased) LVEF was first described by White et al., showing the correlation between increased LV volumes after myocardial infarction with increased mortality [83]. This work was subsequently confirmed by DiDonato et al. and Dor et al. for ventricular restoration procedures [26].

These authors have published that mortality after EVR procedures increased with larger preoperative LV volumes, irrespective of baseline LVEF [82]. Interestingly, we could neither confirm the relationship of LVEF with mortality, nor that of LV volumes in the current pooled analysis. An important explanation for this phenomenon may be the heterogeneity in the functional capacity of the residual remote myocardium. Since stroke volume is relatively constant at rest, LVEF is mainly determined by

the LV enddiastolic volume. If the LV end-diastolic volume is large due to a localized (dyskinetic) scar tissue, the improvement in LVEF after a LVR procedure will parallel improvement in function. On the other hand, if the LV end-diastolic volume is large due to remodeling or cardiomyopathy, a reduction will not be accompanied by improvement in LV function. Therefore neither LVEF, nor LV volumes per se can predict improvement in LV function and outcome [84]. The failure of LVEF, LV volumes, age, gender and time interval post-myocardial infarction in predicting outcome, questions the use of these parameters in risk stratification for these patients. Newer models using advanced imaging techniques that can test for the functional capacity of the remote myocardium, like (contrast-enhanced) magnetic resonance imaging or (3D) echocardiographically derived wall motion score indexes, may prove useful for improved risk stratification.

## 5. LIMITATIONS

A pooled analysis, when well designed and appropriately performed, is a powerful tool to combine in a single conclusion the results of different studies conducted on the same topic. Random effect models were used to control for within-study and between-study variability (random effects modeling). In addition, meta-regression analysis was used to adjust for the influence of patient demographics and prognostic indicators that covaried with the dependent variable. Despite the advantages of a pooled analysis, such as increased statistical power of a comparison and improved estimation of the effect of a treatment, several limitations of the current analysis should be addressed. Publication bias may have influenced our results, since observational studies with a poor outcome may not have been published in fulllength papers. Second and most important, surgical techniques and approaches have improved over time, which affects the current results. Third, since to date no prospectively randomized controlled trials have been published concerning LV reconstruction surgery, all studies included in this analysis were observational reports.

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