The impact of preoperative left ventricular ejection fraction on short and mid-term outcomes in ischaemic mitral valve repair

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Abstract

Background: It has been well established that reduced left ventriclular ejection fraction (LVEF) has adverse impact on the outcome of patients undergoing ischaemic mitral valve repair. However, the exact value of LVEF which should be used for risk stratification, has not been well established.

Aim: To asses which preoperative LVEF (pLVEF) value has the best predictive value in patients undergoing ischaemic mitral valve repair.

Methods: A retrospective analysis of 105 patients with ischaemic mitral regurgitation (IMR) treated between January 2003 and June 2009 was conducted. Patients were divided into two groups according to their pLVEF value. The primary endpoints were early in-hospital and late follow-up deaths.

Results: The pLVEF cut-off value was determined based on univariate analysis of parameters for primary end-points. The investigated parameters were: age, pLVEF, postoperative NYHA, postoperative mitral regurgitation and postoperative LVEF. The Cox proportional hazard regression analysis identified pLVEF (HR 1.5; 95% CI 1.4–5.0; p < 0.008) as the only independent predictor of the primary end-point. The pLVEF cut-off value of 40% was found to have the highest sensitivity of 76% and specificity of 70% in predicting death. Patients were divided into two groups using the cut-off value of pLVEF of 40%. The compromised group (pLVEF < 40%) of 34 patients and the uncompromised group (pLVEF > 40%) of 71 patients had inhospital death rates of three (9%) vs two (3%) (NS) and five year mortality of 18 (54%), eight (11%) (p < 0.001), respectively.

Conclusions: In IMR surgery, a pLVEF value of 40% is an important prognostic marker for mid-term survival.

Key words: mitral valve, ischaemic mitral valve repair, ischaemic mitral regurgitation

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INTRODUCTION

Ischaemic mitral regurgitation (IMR) is caused by coronary artery disease (CAD) and is mainly a ventricular disease [1]. Previous myocardial infarction (MI) causes left ventricular (LV) dysfunction and annular and subvalvular apparatus geometry changes in the LV. Annular dilation and lateral displacement of the subvalvular apparatus is frequently seen in IMR. While

ventricular function is compromised after MI, progressive dilation of the LV gives rise to MR. These morphological changes in the LV are the source of dilatation of the mitral annulus and these changes eventually lead to valvular insufficiency. In patients with IMR, the valve leaflets and chordae appear normal [2, 3]. The IMR confers a definite risk for higher mortality, especially in patients with poor LV functions. Extensive rese-

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arch on the mechanism of IMR has been conducted. In these studies [4, 5] left ventricular ejection fraction (LVEF) has been closely studied. However, the optimal cut-off LVEF value for risk stratification has not been well established.

The purpose of the current study was to investigate the parameters that may influence the outcome of patients with IMR undergoing surgical mitral valve repair, and to find out whether preoperative LVEF (pLVEF) levels are valuable in predicting the prognosis.

METHODS Patients

A total of 105 patients (64 males, mean age 62 \pm 12 years) with IMR were included in the study, which was approved by the Institutional Ethics Committee. We retrospectively reviewed the charts of patients with IMR that had resulted from MI during the period between January 2003 and June 2009. Exclusion criteria were: patients without a history of CAD; acute IMR; regurgitation caused by rheumatic heart disease; myxomatous degeneration, or other conditions. In patients with ischaemic cardiomyopathy with 3+ or 4+ MR, a preoperative viability test was done to assess the need for coronary artery bypass grafting (CABG).

Myocardial infarction was defined as a chest pain syndrome associated with either ST segment elevation in ECG or

elevated plasma cardiac enzymes two to three times above the upper limit values. A prior MI was assumed if an akinetic segment was observed on the echocardiogram, with or without associated Q waves in ECG.

Preoperatively, all patients had transthoracic (TTE) and transoesophageal (TEE) echocardiographic evaluations. The pLVEF value was obtained before surgery by an echocardiographic evaluation. Patients were divided into two groups according to their pLVEF cut-off value: an uncompromised (UC) group with pLVEF > 40% and a compromised (C) group with pLVEF \leq 40%. The other collected data included baseline clinical, echocardiographic, and laboratory parameters. The primary end-points were early in-hospital and late follow-up deaths.

Preoperative characteristics of all patients and concomitant valvular pathologies are shown in Tables 1 and 2.

Echocardiographic evaluation

Standard TTE was performed in the preoperative period using a Vivid Five System (GE, Vingmed Ultrasound, Horten, Norway). The severity of MR is graded on a scale of 1 to 4 according to colour jet area, pulsed wave Doppler of the pulmonary veins, and proximal isovelocity surface area according to the American Society of Electrocardiography guidelines [5]. In addition to the severity of MR, LVEF, regional LV function,

Table 1. Preoperative characteristics of all patients

	Compromised group	Uncompromised group	Р	
	n = 34	n = 71		
Age [years]	63	62	0.73	
Gender (male/female)	21/13	43/28	0.91	
Preoperative sPAP [mm Hg]	50 ± 11	47 ± 11	0.12	
Preoperative LVEF [%]	35 ± 5	53 ± 7	< 0.001	
Prior coronary artery bypass grafting	3 (9%)	6 (8%)	0.95	
Mitral pathologies:				
Anterior leaflet prolapsus	9 (26%)	16 (23%)	0.26	
Posterior leaflet prolapsus	2 (6%)	4 (6%)	0.26	
Anterolateral chordal elongation	6 (18%)	4 (6%)	0.26	
Posteriomedial chordal elongation	5 (15%)	6 (8%)	0.26	
Rupture in anterolateral chordae	4 (12%)	7 (10%)	0.26	
Rupture in posteriomedial chordae	3 (9%)	6 (8%)	0.26	
Annular dilatation	17 (50%)	45 (63%)	0.26	
Preoperative NYHA class:				
II	3 (8%)	8 (11%)	0.8	
III	20 (58%)	41 (57%)	0.8	
IV	11 (32%)	22 (31%)	0.8	
Preoperative mitral regurgitation:				
Grade 1–2	_	1 (1%)	0.9	
Grade 3–4	34 (100%)	70 (99%)	0.9	

 $sPAP -- systolic \ pulmonary \ artery \ pressure; \ LVEF -- left \ ventricular \ ejection \ fraction; \ NYHA -- New \ York \ Heart \ Association$

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Table 2. Reconstruction procedures

	Compromised group	Uncompromised group	Р
	n = 34	n = 71	
Mitral procedures:			
Anterior leaflet repair	3 (9%)	11 (15%)	0.35
Posterior leaflet repair	12 (35%)	29 (41%)	0.59
Alfieri repair	0	3 (4%)	0.23
Ring annuloplasty	26 (76%)	60 (85%)	0.46
Subvalvular reconstruction:			
Chordal shortening	7 (21%)	11 (15%)	0.52
Neo-chordal creation	1 (3%)	5 (7%)	0.19
Aortic procedures: aortic valve replacement	0	4 (6%)	0.16
Tricuspid procedures: TDVA (with ring)	2 (6%)	3 (4%)	0.27
Coronary artery bypass grafting:			0.84
1 vessel	6 (9%)	22 (31%)	
2 vessel	11 (31%)	24 (23%)	
3 vessel	10 (29%)	8 (6%)	

TDVA — tricuspid DeVega annuloplasty

LV end-diastolic and end-systolic dimensions, left atrial diameter, systolic pulmonary artery pressure, and associated valvular lesions were all evaluated. Transoesophageal echocardiography was performed if TTE yielded poor quality images. Preoperatively, TEE was performed in 27 (25%) patients. Transoesophageal echocardiography was also performed in the operating room after the repair procedures.

Surgical technique

All operations were performed on cardiopulmonary bypass with moderate haemodilution and moderate hypothermia (32°C). Continuous retrograde blood cardioplegia was used for myocardial protection. A careful analysis of the anatomic and functional valvular lesions was completed to ensure for decision to repair. If functional IMR was present, only annuloplasty was done. Undersised annuloplasty rings was performed to increase leaflet coaptation [2]. Other mitral valvuloplasty techniques included restriction of increased mitral valve mobility by quadrangular resection of posterior leaflet and shortening of elongated chordae or chordaplasty. Occasionally, papillary muscle shortening was employed. Elongated chordae tendinae were buried into the tip of the papillary muscles with a pledgeted suture [3]. Artificial chorda was formed by 5–0 polytetrafluoroethylene sutures. Concomitant tricuspid valve surgery was required in patients with tricuspid insufficiency. Aortic valve replacement was used in selected cases. The reconstructive procedures are shown in Table 2. The influencing factors which changed the intention to conduct valvuloplasty were: severe leaflet and chordae tendinae rupture and severe posterior leaflet retraction.

The distal coronary artery anastomosis was done first and followed by mitral valve repair, and then, if necessary, the tricuspid valve repair or aortic valve replacement was performed. Finally, the proximal anastomosis was completed.

Follow-up

The results of immediate postoperative TTE or TEE evaluations were assessed for the presence and severity of early residual MR within the first postoperative week. In our institution, an echocardiographic examination is performed before discharge, three and six months after discharge, and then every other year.

Follow-up was performed in our outpatient clinic and via telephone interviews. During the follow-up, valve-related complications, reoperation and New York Heart Association (NYHA) class were evaluated. Accurate valve analysis was achieved by TTE in all patients.

Statistical analysis

Data was analysed using SPSS for Windows (version 15.0, SPSS Inc, Chicago, Illinois, USA). Continuous variables are expressed as mean \pm SD. Comparisons were made using Student's t test, Mann-Whitney U test, Fisher's exact test, or χ^2 test, as appropriate. Spearman's correlation coefficient was used to test associations between mortality and pLVEF and clinical parameters. Univariate and multivariate Cox regression analysis (with backwards elimination model) were used

Table 3. Postoperative parameters

	Compromised group n = 34	Uncompromised group n = 71	Р
Postoperative ejection fraction	42	54	0.001
Postoperative mitral regurgitation:			0.73
None or mild	30 (88%)	62 (87%)	
Grade 3/4	4 (12%)	9 (13%)	
NYHA class I–II	13 (38%)	56 (79%)	< 0.001
NYHA class III–IV	21 (62%)	15 (21%)	0.80
Morbidity	8 (24%)	15 (22%)	0.78
Hospital mortality	3 (9%)	2 (3%)	0.33
Five-year mortality	18 (54%)	8 (11%)	< 0.001
Reoperation (mitral valve)	8 (24%)	5 (7%)	0.02
Readmission	10 (29%)	5 (7%)	0.01
Reoperation for bleeding	2 (6%)	5 (7%)	0.71

NYHA — New York Heart Association

to evaluate the prognostic value of variables. Receiver operating characteristic analysis was performed to determine the optimal cut-off level for pLVEF with respect to prognosis. The survival curve for pLVEF was derived using the Kaplan-Meier method. For all analyses, a p value < 0.05 was considered significant.

RESULTS

The pLVEF in the study group of 105 patients ranged from 25 to 65% (median 45%, mean \pm SD: 47 \pm 10%). Ninety-four (90%) patients were in NYHA class III or IV preoperatively. Preoperative MR was over 3+ in 99% and the mean pulmonary artery pressure was 48 \pm 11. The most commonly seen underlying condition related to IMR in groups C and UC was annular dilatation (17 [50%] patients in C vs 45 [43%] patients in UC). Clinical findings of all 105 patients are shown in Table 1.

Coronary artery bypass grafting was performed in 69 (67%) patients at the time of mitral valve repair. Among the other 36 patients, 21 had already undergone stent implantation by percutaneous coronary intervention (PCI), and nine had CABG during a prior procedure (Table 2). The remaining six did not require CABG due to either patent or chronically occluded vessels. Other interventions are presented in Table 2.

Postoperative complications included: MI in three patients, intraaortic balloon pump in seven patients, reoperation for bleeding in four patients, acute renal failure and temporary dialysis in three patients, and temporary transient ischaemic attack in two patients. In five patients, severe MR was seen during the first six months after surgery. In eight patients, recurrence of MR was seen during the five year follow-up period. Postoperative parameters are presented in Table 3.

Thirteen (12%) patients required reoperation, and all of these patients received mitral valve replacement with mechanical prostheses. Reoperation for bleeding was required in two (6%) patients in group C and in five (7%) patients in group UC (NS). The interval between initial operation and reoperation ranged from five to 49 months.

Predictors of outcome

The average duration of follow-up was 5.2 ± 2.4 years. Overall in-hospital mortality was not significantly different: in group C three (9%) vs in group UC two (3%) patients died (p = 0.33). Five year mortality was 54% (n = 18) and 11% (n = 8) in groups C and UC, respectively (p < 0.001). The cumulative survival rate at five years was 56% in group C and 89% in group UC (p = 0.006). Figure 1 shows Kaplan-Meier curves of the two groups.

Univariate analysis revealed that age, pLVEF, postoperative NYHA, postoperative MR and postoperative LVEF were associated with increased risk of reaching the primary endpoint. Cox proportional hazard regression analysis identified pLVEF (hazard ratio: 1.5; 95% confidence interval: 1.4–5.0; p < 0.008) as the only independent predictor of the primary end-point.

The pLVEF significantly correlated with mortality (p = 0.008, R = -0.45). Sensitivity and specificity values for different pLVEF are given in Table 4. Readmission rate also correlated with pLVEF (p = 0.02, R = -0.2) and postoperative LVEF (p < 0.001, R = 0.99). For readmission to the hospital, pLVEF $\leq 40\%$ was associated with increased risk. The ROC curves for pLVEF in predicting long-term mortality are shown in Figure 2. The cut-off value of 40% yielded optimal sensitivity and specificity values for predicting mortality.

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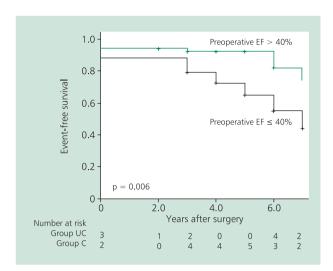


Figure 1. Kaplan-Meier survival curves for patients with pLVEF \leq 40% (group C) and pLVEF > 40% (group UC)

Table 4. ROC analysis: sensitivity and specificity values for different pLVEF cut-off values

LVEF [%]	Sensitivity	1-specificity
24.0000	1.000	1.000
27.5000	0.988	0.913
32.5000	0.976	0.696
37.5000	0.890	0.522
40.0000	0.766	0.302
42.5000	0.768	0.348
47.5000	0.524	0.130
52.5000	0.476	0.000
57.5000	0.244	0.000
62.5000	0.122	0.000
66.0000	0.000	0.000

DISCUSSION

Our results confirmed that pLVEF is a valuable echocardiographic parameter that allows risk stratification of patients with IMR undergoing valve repair. We also observed that the pLVEF cut-off value that provides optimal sensitivity and specificity for predicting the early in-hospital and late follow-up deaths was 40%. In recent studies, it has been demonstrated that surgical correction has improved survival rates and quality of life. Long-term survival in patients with IMR was poor in past decades. After surgical correction, the survival rates of surgically treated patients was found to be considerably better than those in medically treated patients [6, 7].

Hospital mortality in patients with IMR who undergo valve replacement or repair in combination with CABG is 9% to 15% [2]. The exact cause of limited survival after valve surge-

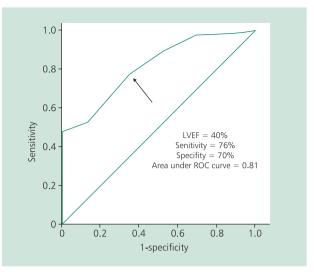


Figure 2. ROC curve for different pLVEF values. A 40% cut-off value had sensitivity of 76% and specificity of 70%; the area under the curve was 81%

ry is controversial, but recent studies suggested that the poor outcome was related to worse baseline characteristics [8]. Predictors of early mortality have been reported as: low LVEF (less than 30% to 35%), previous anterior infarction, extensive CAD, and advanced age [9]. Thirty-day mortality in the study of Grossi et al. [4] was 10% for mitral reconstruction and 20% for prosthetic replacement. They found that the short-term mortality was higher in patients in NYHA functional class IV than in those in classes I to III [4].

In IMR, pLVEF is an important predictor of event-free survival. Our results are similar to previous studies and underline the importance of pLVEF [2, 9]. There are only a few relevant studies that demonstrated the significance of pLVEF. It has been demonstrated that annular dilatation was an important surrogate variable for the poor ventricular function that decreased late survival (five-year survival for reconstruction of annular dilation was 43%) [10]. In the study by Grossi et al. [4], only NYHA functional class and the presence of annular dilatation were significant in multivariable analyses. In our study, the annular dilatation in the compromised study group was 50% and the mortality rate in this group rose to 54% in five years of follow-up, whereas in the uncompromised group it was 11%.

In the study by Onorati et al. [11], ischaemic cardiomy-opathy with chronic MR recurrence correlated with worsened NYHA class (p = 0.0001) and LVEF (p = 0.02). Hospital mortality was found to be 4.9% [10]. In our study, the NYHA class was poor at the beginning of the study and improved after the surgical procedure. We were not able to show a correlation between recurrence of MR and worsening of NYHA class. However, we were able to show a correlation with the pLVEF.

On the other hand, most surgeons agree that trace to mild (1+) MR should be left alone. The optimal management of mild to moderate (2+) MR remains controversial. Those who advocate the conservative approach of revascularisation alone point out that revascularisation will improve regional wall motion abnormality and potentially correct IMR [12]. In the study by Calafiore et al. [13], the mild–moderate MR group was compared with a no IMR group undergoing isolated CABG. They showed the negative impact of mild to moderate IMR in patients with LVEF of 31% to 40%. We generally perform the isolated CABG in patients with mild or moderate IMR as a clinical policy. Whether or not to repair IMR in patients with mild or moderate IMR undergoing isolated CABG should be clarified in further studies.

In our study, the recurrence of MR was 27% in the whole study group, whereas it was much higher and gradually increased in the compromised group up to 64%. This suggests that the LV function deteriorates and the LV restorations are insufficient to establish reverse remodelling of the LV [14]. Also in our study, the readmission rate was higher in the group C compared to the group UC.

Bax et al. [14] reported a significant reduction in left atrial and LV dimensions after surgery. This suggests the LV reverse remodelling. In their series, preoperative LVEF was 31 \pm 8%. After the operation of combined mitral ring annuloplasty and CABG, the preoperative grade 3 and 4 regurgitation improved to grade 1 to 2 and NYHA class improved from III to I (p < 0.01). This is similar to our findings, as we saw an improvement of MR and NYHA class.

Glower et al. [15] showed that advanced age and the number of preoperative comorbidities were independent predictors of survival. Gillinov et al. [16] compared the surgical results of IMR to the degenerative mitral valve repair and demonstrated that five-year survival rate was almost the same (degenerative 65% vs ischaemic 66%; p>0.9). In patients with IMR there are multiple comorbidities and they affect outcomes. In the study by Gazoni et al. [17] the five-year survival in patients with IMR was significantly lower compared to those with degenerative MR (ischaemic 84% vs degenerative 94%; p<0.01). In our study, the survival rate in group UC was better than group C after surgery.

Limitations of the study

This study has a number of limitations such as lack of randomisation and a relatively small sample size. The strength of our study, however, is the uniformity of surgical techniques and perioperative care performed in a single centre.

CONCLUSIONS

In ischaemic mitral valve surgery, a pLVEF of 40% shows an optimal cut-off value for predicting mid-term survival.

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Wpływ przedoperacyjnej wartości frakcji wyrzutowej lewej komory na wczesne i średnioterminowe wyniki operacji naprawczej u pacjentów z niedokrwienną niedomykalnością mitralną

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Streszczenie

Wstęp i cel: Celem niniejszego badania była ocena, czy przedoperacyjna wartość frakcji wyrzutowej lewej komory (LVEF) wpływa na rokowanie i wyniki leczenia chorych z niedokrwienną niedomykalnością zastawki mitralnej poddawanych operacji naprawczej.

Metody: Przeprowadzono retrospektywną analizę danych 105 pacjentów z niedokrwienną niedomykalnością mitralną z okresu od stycznia 2003 do czerwca 2009 roku. Pacjentów podzielono na dwie grupy zależnie od przedoperacyjnej funkcji lewej komory (pLVEF): z zachowaną (UC) oraz upośledzoną (C) funkcją lewej komory, z uwzględnieniem wartości granicznej pLVEF. Głównymi punktami końcowymi były wczesna śmiertelność wewnątrzszpitalna i odległa śmiertelność w okresie obserwacji.

Wyniki: Wartość graniczna pLVEF została określona na podstawie jednoczynnikowej analizy zmiennych dla głównych punktów końcowych. Do ocenianych parametrów należały: wiek, pLVEF, klasa NYHA po zabiegu, pooperacyjna niedomykalność mitralna i pooperacyjna LVEF. Analiza regresji na podstawie modelu proporcjonalnego hazardu Coxa wykazała, że jedynym niezależnym czynnikiem predykcyjnym głównego punktu końcowego była pLVEF (współczynnik narażenia — *hazard ratio*: 1,5; 95% przedział ufności 1,4–5,0; p < 0,008). Wartość odcięcia pLVEF równa 40% charakteryzowała się najwyższą czułością (76%) oraz specyficznością (70%). Podziału na grupy dokonano zależnie od pLVEF, za graniczną przyjmując wartość 40%. W grupie C (pLVEF < 40%) liczącej 34 pacjentów i w grupie UC (pLVEF > 40%) liczącej 71 pacjentów zanotowano odpowiednio 3 (9%) i 2 (3%) przypadki zgonów wewnątrzszpitalnych, natomiast po 5 latach liczba zgonów w tych grupach wynosiła odpowiednio 18 (54%) i 8 (11%).

Wnioski: U chorych operowanych z powodu niedokrwiennej niedomykalności mitralnej wartość pLVEF równa 40% stanowi ważny czynnik prognostyczny śmiertelności wewnątrzszpitalnej i średnioterminowej.

Słowa kluczowe: zastawka mitralna, zabieg naprawczy w niedokrwiennej niedomykalności mitralnej, niedokrwienna niedomykalność mitralna

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