Risk Scores for Predicting Mortality After Surgical Ventricular Reconstruction for Ischemic Cardiomyopathy – Results of a Japanese Multicenter Study

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ABSTRACT (237 words)

Objective

Surgical ventricular reconstruction (SVR) has been believed to be beneficial for those with ischemic cardiomyopathy. However, the effectiveness of SVR was not proved by a large-scale trial and no report has clearly demonstrated the exact indications and limitations of SVR. The purpose of this study was to elucidate predictive factors of mortality after SVR and to develop a prognostic model by calculating risk scores.

Methods

The study subjects were 596 patients who underwent SVR for chronic ischemic heart failure in 11 Japanese cardiovascular hospitals between 2000 and 2010. Potential predictors of postoperative mortality were assessed using the Cox proportional hazards model and a risk score was calculated.

Results

Forty-one patients died before discharge and 81 died during a mean follow-up time of 2.9 years. Four independent predictors of mortality were identified: age, the INTERMACS profile, left ventricular ejection fraction, and severity of mitral regurgitation. Each variable was assigned a number of points proportional to its regression coefficient. A risk score was calculated using the point scores for each patient and three risk groups were developed: a low-risk group (0-4 points), intermediate-risk group (5-6 points), and high-risk group (7-12 points). Their 3-year survival rates were 93%, 81%, and 44%, respectively (log-rank $P<0.001$). Harrell's C-index of the predictive model was 0.69.

Conclusions

A simple prognostic model was developed to predict mortality after SVR. It can be useful in clinical practice to select treatment options for ischemic heart failure.

ULTRAMINI ABSTRACT

We assessed 596 patients who underwent surgical ventricular reconstruction for ischemic heart failure in 11 Japanese cardiovascular hospitals between 2000 and 2010. Four independent predictors for postoperative mortality were identified and a prognostic model was developed using a risk score calculated for each patient.

ABBREVIATIONS

CABG: coronary artery bypass grafting

INTERMACS: Interagency Registry for Mechanically Assisted Circulatory Support

LVDd: left ventricular end-diastolic diameter

LVEF: left ventricular ejection fraction

LVESVI: left ventricular end-systolic volume index

MR: mitral regurgitation

NYHA: New York Heart Association

SVR: surgical ventricular reconstruction

VAD: ventricular assist device

BACKGROUND

Indications for ischemic heart failure treatments vary depending on the severity of the patient's condition. Surgical ventricular reconstruction (SVR) has been believed to be beneficial for those with ischemic cardiomyopathy[1-3]. However, the Surgical Treatment for Ischemic Heart Failure (STICH) trial concluded that SVR plus coronary artery bypass grafting (CABG) had no further beneficial effect on survival compared with CABG alone[4]. However, the STICH results are controversial because this large-scale trial enrolled less severe patients than in the previous studies supporting the effectiveness of SVR[5]. In contrast, implantable ventricular assist devices (VADs) have become more common in the treatment of severe heart failure and are filling a gap between medical treatment and heart transplantation[6]. However, VAD therapy has inherent unresolved problems[7, 8] such as neurologic dysfunction, bleeding, device failure pump thrombosis, and lower cost-effectiveness, which may not be associated with SVR. Therefore, SVR could be more beneficial for appropriately selected patients compared with CABG alone or VAD therapy. We hypothesized that risk stratification for SVR could make it possible to identify the responders to this procedure and therefore help with appropriate patient selection, which in turn would contribute to more practical comparisons among different procedures for ischemic heart failure. Therefore, the purpose of this study was to develop a practical prognostic model to predict mortality after SVR for ischemic heart failure by calculating a risk score using a multivariate Cox proportional hazards model.

MATERIALS AND METHODS

Study Design

We conducted a retrospective multicenter study to investigate the outcomes of SVR.

Those who underwent SVR for ischemic heart failure from 2000 to 2010 in 11 Japanese cardiovascular hospitals were enrolled in this study. The indications for SVR were aneurysmal and akinetic left ventricle (LV) in 194 (31%) and 412 (69%) patients, respectively. Participating hospitals were selected based on the number of SVR procedures performed annually. Principally, the hospitals that performed 5 or more SVR procedures annually were selected (n=7). Although 4 hospitals did not have 5 cases per year on average during the study period, they were selected because they were leading cardiovascular centers in Japan that also perform heart transplantation (n=2) or considering their recent academic activities (n=2). The median number of SVR procedures in each hospital during the study period was 52 (range: 17 to 166) cases. All data were collected from medical records and examination reports retrospectively. Mortality was detected based on medical records or follow-up inquiries to the attending cardiologists that were made in each hospital. The study protocol was approved by the Institutional Review Boards in all of the participating hospitals.

Initially, 627 patients were enrolled in this study. Then those with acute myocardial ischemia, no LV incision, and no follow-up data were excluded. Finally, there were 596 study subjects. The LV sizes and functions were measured using multiple modalities within 2 weeks before surgery. Postoperative imaging studies were repeated before discharge at 0.8±1.8 months after surgery. Echocardiography was performed for all the patients. LV end-diastolic diameter (LVDd), LV end-systolic diameter, and the LV ejection fraction (LVEF) were acquired by B-mode echocardiography. The severity of mitral regurgitation (MR) was graded based on color Doppler images as follows: 1+ = mild, 2+ = moderate, 3+ = moderate-to-severe, and 4+ = severe.[9] The deceleration time was acquired from the transmitral flow analysis. Systolic pulmonary artery pressure data were obtained from the catheter data or estimated using echocardiographic data. The LV end-diastolic volume index, LV end-systolic volume index (LVESVI), and LVEF were collected from the results of left

ventriculograms, quantitative gated scintigrams, and magnetic resonance imaging in 288, 82, and 49 patients, respectively. For the patients with multimodality assessments, the modality that was available both preoperatively and postoperatively was selected to compare the values before and after surgery. Complete imaging data sets of preoperative and postoperative values from the same modality were acquired for LV diameters, LVEF, and LV volumes in 542 (91%), 515 (95%), and 299 (50%) patients, respectively.

Statistical analyses

Continuous variables were expressed as mean ± standard deviation and categorical variables as numbers and percentages. The percentage was calculated exclusive of those with missing values. Preoperative and postoperative data were compared using the Wilcoxon signed-rank test. Intergroup comparisons for categorical data were conducted using the chi-square test or Fisher's exact test, if appropriate. Postoperative mortality was estimated using the Kaplan–Meier method, and differences in mortality among groups were assessed by the log-rank test. Univariate and multivariate Cox proportional hazards models were used to determine the contributions of potential variables to the mortality. Variables for the multivariate model were selected considering the proportion of patients with missing data (<5%), the results of univariate analyses, their confounding, and clinical importance. Selection of variables in the multivariate analysis was performed using the backward elimination method ($P<0.10$). Finally, to develop a practical prognostic score, we assigned the independent predictors in the final Cox model weighted point scores proportional to the β regression coefficient values (multiplied by a constant and rounded to the nearest integer). A risk score was then calculated for each patient, and the population was divided into three categories: patients at low risk, patients at intermediate risk, and patients at high risk for postoperative mortality. The predictive accuracy of the scoring system was examined by

calculating Harrell's C-index[10]. A two-sided P value <0.05 was considered to indicate statistical significance in all the tests. All analyses were performed using IBM SPSS Statistics (version 20, IBM Corporation, Somers, NY, USA).

RESULTS

Patients' baseline characteristics

Table 1 shows the patients' baseline characteristics. Their mean age was 63±10 (range, 29-87) years and 372 (62%) were male. In addition to the New York Heart Association (NYHA) functional class, the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profile[11] at the time of surgery was used for the assessment of heart failure status. Those with NYHA functional class I/II were categorized into INTERMACS profile level 7 or more. Most of the patients (81%) presented with NYHA functional class III/IV. Seventy-nine (13%) patients required inotropic support preoperatively. Of them, 21 (4%) patients had INTERMACS profile 1.

Surgical procedures

Table 2 summarizes the operative procedures. There were 5 different SVR procedures performed: endventricular circular patch plasty[12], partial left ventriculectomy[13], septal anterior ventricular exclusion[14], overlapping left ventriculoplasty[15], and linear ventriculoplasty. Each procedure was selected based on surgeons' preferences in each hospital. However, in common, an LV incision was placed at the myocardial scar lesion that was determined according to the findings of MRI, echocardiography, or scintigraphy. A procedure using a patch was performed in 442 (74%) patients. Concomitant mitral valve procedures were performed in 259 (42%) patients, most of whom underwent annuloplasty.

CABG was performed concomitantly in 513 (86%) patients who had untreated coronary artery lesions.

Cardiac sizes and functions

Table 3 summarizes perioperative cardiac sizes and functions. LV sizes decreased and LVEF increased significantly after surgery (P<0.001 for each parameter). Mitral regurgitation (MR) improved postoperatively. Preoperatively, MR ≥3+ was observed in 137 (24%) patients, while 485 (93%) patients had MR ≤1+ after surgery. In the analysis of the 299 patients with both preoperative and postoperative LV volume data from the same modality, the mean LVESVI reduction rates were 18%, 30%, and 37% for those with baseline LVESVI ≤60ml/m^2, 60-90 ml/m^2, and >90 ml/m^2, respectively. A reduction of 30% or more was achieved for 44%, 55%, and 69% of them, respectively. The LVEF increased significantly for each group (LVESVI ≤60ml/m^2: 40% to 45%, P=0.001; LVESVI 60-90 ml/m^2: 30% to 38%, P=0.003; LVESVI >90 ml/m^2: 22% to 30%, P<0.001).

Postoperative mortality

During the follow-up period of 2.9±2.5 years, 122 (21%) patients died. Among them, 12 (2%) and 41 (7%) patients died within 30 days after surgery and before discharge from the hospital, respectively. Cardiac-related death was observed in 60 (10%) patients, 22 of whom died before discharge. Readmission and reoperation were required for 110 (19%) and 15 (3%) patients, respectively. Reoperation for mitral regurgitation was performed in 6 patients, including 2 replacements. Among them, 5 had previous mitral valve repair concomitant with SVR. Four patients required an LV assist device and 2 patients underwent heart transplantation.

Assessment of potential predictors of mortality

Potential predictors of mortality were assessed using univariate and multivariate Cox proportional hazards models (Tables E1 and 4). Variables that were entered into the multivariate Cox model were as follows: age, sex, the INTERMACS profile, LVDd, LVEF, MR grade, SVR procedure, concomitant CABG, and concomitant mitral valve procedures. Because data for some variables were missing for some patients, the final sample used in the multivariate analysis consisted of 570 patients, 113 of whom died.

Four independent predictors were identified in the final multivariate Cox model: age, the INTERMACS profile, LVEF, and MR grade (Table 4). Harrell's C-index of the model was 0.690. Figure E1 shows Kaplan-Meier survival curves for each predictor.

Development of risk categories for postoperative mortality

Each independent predictor of mortality was assigned a weighted score in points as shown in Table 4, and a risk score was calculated for each patient by summing the scores for the predictors. As a result, the risk score ranged from 0 to 12. Then 3 risk groups were developed according to the risk scores: low risk (0-4 points), intermediate risk (5-6 points), and high risk (7-12 points). The 30-day mortality rates were 0.3%, 0.7%, and 5% in the low-risk, intermediate-risk, and high-risk groups, respectively (P=0.004). Hospital mortality percentages were 2%, 4%, and 22% for the groups, respectively (P<0.001).

Figure 1 shows Kaplan-Meier curves for all-cause survival and readmission-free survival. Both survival rates were significantly different among the 3 different risk groups (P<0.001 for each). The 3-year all-cause survival rates were 93%, 81%, and 44% in the low-risk, intermediate-risk, and high-risk groups, respectively. The 3-year readmission-free survival rates were 78%, 65%, and 37% for the low-risk, intermediate-risk, and high-risk groups, respectively.

NYHA functional classes at different time points were compared among 3 risk groups (Figure E2). Those in the high-risk group presented with a significantly worse NYHA functional class than the others at every time point ($P<0.001$ for each). Approximately 90% of the low-risk patients and 80% of the intermediate-risk ones had NYHA functional class of II or less even at the latest follow-up.

DISCUSSION

In this study, we identified four independent predictors of mortality after SVR for ischemic heart disease: age, the INTERMACS profile, LVEF, and the MR grade. We developed a prognostic model by calculating weighted risk scores assigned to those predictors. Then three risk categories were developed to predict the prognosis according to the risk scores.

Several treatment options can be selected for ischemic heart failure depending on the patient's condition: medication, revascularization, SVR, VAD, and heart transplantation. Because medication alone[16] or CABG alone[17] was not associated with satisfactory results in those with severe LV dilatation, acute reverse remodeling by SVR was expected to benefit such patients by reducing LV volume[18] and restoring LV shape[19]. Although a retrospective study with a relatively small sample size showed favorable results for SVR[20], a large-scale trial (STICH) found there was no beneficial effect on survival in SVR plus CABG compared with CABG alone[4]. However, the validity of the STICH results is controversial[5, 21]. STICH seemed to enroll a CABG-preferable population, considering the reported risk factors related to CABG alone such as an extensively dilated LV and increased number of non-viable segments,[22] as well as severe LV systolic dysfunction[3]. CABG alone or SVR plus CABG may be appropriate for different populations with a small overlap between them. Therefore,

they cannot be compared directly. Such a comparison, if the conditions are matched as in the STICH trial, can exclude a number of patients who are eligible for each procedure. Thus, it may result in an inappropriate conclusion that does not reflect the real world. Indeed, favorable results of SVR for those excluded from STICH were reported[23, 24].

However, despite the criticism, that first large-scale trial had enough power to make physicians and surgeons hesitate to select SVR. Although the efficacy of SVR was denied for patients without severe deterioration, the application of SVR for more severe patients has also been considered negatively. Instead, VAD therapy has become spotlighted in this field. Recently, VAD has become the more common treatment for severe heart failure, with progressive improvement of survival[6]. It has advantages in terms of full functional recovery of systemic circulation, though there are unresolved complications such as stroke, hemorrhage, and device failure[7]. The cost has also been a problem in VAD therapy[8]. SVR does not increase the risk of such complications, though it can achieve partial functional recovery of the heart because it utilizes the patient's own diseased myocardium. Therefore, it is natural that all patients cannot benefit sufficiently from SVR, though it is more cost-effective if performed for appropriately selected patients[25].

Thus, a comprehensive approach for ischemic heart failure should be developed, including medication, catheter interventions, CABG, SVR, VAD, and heart transplantation. However, the conditions of the patients who are eligible for them may be different. Thus studies considering the strata of different risk levels for each therapeutic option may be required for more practical comparisons among them and to find the optimal one for each patient. For this purpose, risk stratification for SVR would be a meaningful process to identify the responders to this procedure. We therefore conducted this multicenter study to establish a prognostic model to predict mortality after SVR. We believe our results will

contribute to the practical decision-making process in the treatment of those with ischemic heart failure.

INTERMACS profile

An advanced NYHA functional class was reported to be an independent predictor of adverse outcomes after SVR[1, 2, 26]. In our previous study, NYHA functional class IV was also proved to be one of the strongest predictors of mortality (unpublished data). In clinical practice, however, NYHA functional class IV is not always associated with adverse outcomes. Indeed, Williams et al. reported that NYHA functional class IV was not a significant predictor of mortality[27]. Inotropic dependence is a condition included in NYHA functional class IV and may be a stronger predictor of mortality. SVR for those with a maximum dose of inotropes due to cardiogenic shock was associated with high mortality[28]. In contrast, there was a report that concluded that inotrope use was not a predictor of mortality after SVR for end-stage ischemic cardiomyopathy[29]. These various results indicate that severe heart failure is a complicated and relatively broad-spectrum condition.

Recently, the status of severe heart failure was finely categorized in the INTERMACS profile for VAD therapy[11]. It is a detailed classification in terms of grading severe heart failure considering inotropic support, organ failure, and cardiogenic shock. As far as we know, no study has evaluated the outcomes of SVR using the INTERMACS profile. We selected the INTERMACS profile as an integrated variable including the NYHA functional class, inotropic dependence, hypotension, and renal failure. Moreover, analysis including the INTERMACS profile can make it possible to compare the results and indications for SVR with those of VAD therapy. The indication for SVR should be considered as one treatment option in the comprehensive treatment strategy for severe heart failure.

Left ventricular size

There is a contradiction about the indication for SVR in that an extremely dilated LV is a risk for SVR[1], though a dilated LV is an indication for the procedure[20]. Recently, subanalysis of the STICH trial concluded that SVR was worse for those with a large LV[30]. However, LV size is a variable that has great potential for confounding (e.g., the severity of heart failure, MR grade, and LVEF), though most previous studies did not conduct multivariate analysis of survival time to assess the contribution of baseline LV size to postoperative mortality[1, 2]. In contrast, recent studies focused on the postoperative LV volume (<60-70ml/m^2) with sufficient volume reduction as an important predictor of adverse outcomes[26, 31]. However, such studies can exclude those whose condition is too severely deteriorated to undergo postoperative LV assessment studies. Of course, in terms of the quality of SVR, sufficient volume reduction and postoperative LV volume may be important benchmarks. If the concern is who is eligible for SVR, however, those in severely deteriorated condition should not be excluded from the analysis. Therefore, we assessed only the preoperative value in terms of LV size using a multivariate Cox proportional hazards model with a relatively large sample size. As a result, preoperative LV diameter itself was not identified as a predictor of mortality after SVR. It was also true that LV volume (LVESVI) did not predict the mortality in the multivariate analysis including this variable (n=406, data were not shown). Therefore, our results suggested that the patient's condition (heart failure status) and MR severity were more important predictors than LV size. Even for patients with an extremely large LV, SVR can be indicated if heart failure is well controlled and MR is not severe.

Mitral regurgitation and mitral procedures

In this study, preoperative MR of 4+ was identified as the strongest predictor of mortality, though all of those with it underwent mitral valve surgery. This was consistent with previous reports that preoperative MR ≥3+ predicted mortality in those who underwent SVR with mitral valve procedures[29,32]. Recently, the STICH trial suggested that additional mitral valve repair for moderate to severe ischemic MR might improve survival compared with CABG alone or medical treatment alone[33]. In this study, however, a concomitant mitral valve procedure was not identified as a predictor of survival. O'Neill et al. reported the outcomes of 220 consecutive patients who underwent SVR[34]. Mitral valve surgery was performed for 49% of them but was not proved to affect survival. It was difficult to assess the efficacy of a concomitant mitral valve procedure because this was an observational study and all of the patients with significant MR underwent the mitral valve procedure. Further study will be required to elucidate the efficacy of mitral procedures.

SVR procedures

The appropriate selection of SVR procedures may also be important. Suma et al. reported that site selection of the LV incision according to the location of the scar lesion resulted in improvement of the survival after SVR for nonischemic dilated cardiomyopathy[35]. Various SVR procedures were performed in our cohort but the differences of the procedures did not affect the outcomes. Although the surgeons in each participating hospital selected SVR procedures based on their preferences, they agreed in considering the regional myocardial viability in selecting the location of the LV incision. Thus, the difference of the procedures (e.g., patch usage, and shape) may not be the predominant issue if the location of the LV incision is appropriately selected. It is considered that 30% or more reduction of LVESVI is required for an acceptable SVR procedure[5]. In our cohort, LVESVI reduction ≥30% was achieved in 44%, 55%, and 69% of those with baseline LVESVI ≤60ml/m^2, 60-90

ml/m^2, and >90 ml/m^2, respectively. These rates were higher than those for the STICH trial (26%, 36%, and 45%, respectively)[31]. However, changes in LVEF were comparable.

Limitations

There were several limitations that should be mentioned. First, the number of procedures performed in each participating hospital was relatively small. However, the results were similar among the participating hospitals (log-rank P=0.11). Second, the relatively short length of the follow-up period could reduce the statistical power of our prognostic model. Third, some variables that may be important (e.g., diastolic function) could not be entered into the multivariate analysis due to missing values. Fourth, because only half of the patients had paired data for LV volume from the same modality, it could not be evaluated sufficiently whether SVR in our cohort was performed adequately. Fifth, we did not evaluate the generalizability of our prognostic model using an external validation set. Finally, this is a retrospective and non-comparative study. Although we conducted risk prediction analysis regarding SVR, this scoring system itself cannot indicate the benefit of SVR compared with other treatments (e.g., CABG alone, medication, and VAD). Thus a prospective study that compares different treatment sets considering the risk stratification for each treatment and examines our prognostic model is required.

CONCLUSIONS

We developed a prognostic model to predict mortality after SVR for those with ischemic heart failure. It can be useful in clinical practice to consider the indication for SVR in a comprehensive treatment strategy including medication, catheter interventions, CABG,

SVR, VAD, and heart transplantation. Moreover, risk stratification of SVR will contribute to future studies comparing it with other treatment options.

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DISCLOSURES

None.

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Table 1 Patients' baseline characteristics

N	596
Age, years (range)	63±10 (29-87)
Male sex, n (%)	372 (62%)
No. of diseased coronary arteries, n (%)	
None	12 (2%)
One	112 (19%)
Two	151 (25%)
Three	321 (54%)
Coronary artery lesion, n (%)	
Left main	76 (13%)
Anterior descending	545 (91%)
Circumflex	343 (58%)
Right	341 (57%)
LV shape, n (%)	
Aneurysmal	184 (31%)
Akinetic	412 (69%)
Renal failure, n (%)	97 (16%)
Dialysis, n (%)	26 (4%)
Atrial fibrillation, n (%)	49 (8%)
Beta-blocker usage, n (%)	224 (38%)
NYHA functional class, n (%)	
I	22 (4%)
II	150 (25%)
III	267 (45%)

IV	156 (26%)
INTERMACS profile	
Level 1	21 (3%)
Level 2	12 (2%)
Level 3	46 (8%)
Level 4	77 (13%)
Level 5-6	267 (45%)
Level ≥7	172 (29%)
Inotropic support, n (%)	79 (13%)
IABP, n (%)	73 (12%)
PCPS, n (%)	3 (0.5%)

LV = left ventricle, NYHA = New York Heart Association, INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support, IABP = intraaortic balloon pumping, PCPS = percutaneous cardiopulmonary support

Table 2. Operative procedures

SVR procedures, n (%)	
EVCPP	258 (43%)
PLV	14 (2%)
SAVE	184 (31%)
Overlapping	62 (11%)
Linear	78 (13%)
Patch/non-patch	442 (74%) / 154 (26%)
Mitral valve procedures, n (%)	259 (43%)
Plasty/replacement	251 (42%) / 8 (1%)
Submitral procedures, n (%)	99 (17%)
Papillary muscle approximation	91 (15%)
Papillary muscle suspension	26 (4%)
CABG, n (%)	513 (86%)
No. of distal anastomoses	2.6±1.6
Tricuspid annuloplasty, n (%)	75 (13%)
Aortic valve replacement, n (%)	24 (4%)
Maze procedure, n (%)	22 (4%)
Surgical ablation for ventricular tachyarrhythmia, n (%)	61 (10%)
ICD implant, n (%)	44 (7%)
Cardiopulmonary bypass time, min	181±70
Cross-clamp time, min	101±54

EVCPP = endoventricular circular patch plasty, PLV = partial left ventriculectomy, SAVE = septal anterior ventricular exclusion, CABG = coronary artery bypass grafting, ICD = implantable cardiac defibrillator

Table 3. Perioperative cardiac sizes and functions

	Preoperative	Postoperative	P Value
LVDd, mm (range)	62±10 (37-90)	57±10 (33-82)	<0.001
LVDs, mm (range)	50±10 (13-83)	46±11 (20-74)	<0.001
LVEDVI, ml/m^2 (range)*	144±51 (45-358)	103±36 (40-308)	<0.001
LVESVI, ml/m^2 (range)*	107±47 (29-286)	70±33 (22-236)	<0.001
LVEF, % (range)	27±10 (5-78)	35±12 (4-65)	<0.001
DT, msec (range)*	190±73 (20-494)	183±61 (74-420)	0.15
SPAP, mmHg (range)*	36±17 (7-86)	34±18 (4-120)	0.08
MR grade	1.6±1.1	0.6±0.6	<0.001

LV = left ventricle, LVDd = LV end-diastolic diameter, LVDs = LV end-systolic diameter, LVEDVI = LV end-diastolic volume index, LVESVI = LV end-systolic volume index, LVEF = LV ejection fraction, DT = deceleration time, SPAP = systolic pulmonary artery pressure, MR = Mitral regurgitation

*Proportion of those with missing values ≥30%

Table 4. Multivariate Cox proportional hazards analysis and scoring system

	P Value	Hazard Ratio (95%CI)	β Regression Coefficient	Points
Age, years	0.001			
<65		1		0
>=65		1.91 (1.29-2.85)	0.649	2
INTERMACS profile	<0.001			
Level 1		4.54 (2.19-9.43)	1.513	4
Level 2		4.16 (1.79-9.67)	1.425	3
Level 3		2.71 (1.54-4.76)	0.995	2
Level 4		1.53 (0.90-2.60)	0.425	1
Level ≥5		1		0
LV ejection fraction, %	0.007			
<20		3.63 (1.49-8.82)	1.289	3
20-40		2.26 (0.97-5.27)	0.816	2
>=40		1		0
Mitral regurgitation	<0.001			
≤1+		1		0
2+		2.09 (1.25-3.50)	0.738	2
3+		2.08 (1.20-3.62)	0.734	2
4+		5.09 (2.91-8.92)	1.628	4

CI = confidence interval, INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support, LV = left ventricle

Table E1. Assessment of potential predictors of mortality using univariate Cox proportional hazards model

	N	P Value	Hazard Ratio (95% CI)
Age, years		0.06	
<65	306		1
≥65	290		1.40 (0.98-2.01)
Sex		0.65	
Female	224		1
Male	372		0.92 (0.64-1.33)
NYHA functional class		<0.001	
I	22		1
II	150		1.51 (0.36-6.44)
III	267		1.61 (0.39-6.66)
IV	156		4.46 (1.09-18.27)
Inotropic support		<0.001	
No	513		1
Yes	79		3.79 (2.56-5.63)
INTERMACS profile		<0.001	
Level 1	21		5.19 (2.48-10.89)
Level 2	12		7.74 (3.30-18.17)
Level 3	46		3.82 (2.09-6.99)
Level 4	77		1.99 (1.12-3.56)
Level 5-6	267		1.11 (0.67-1.84)
Level ≥7	172		1

LV shape*		0.07	
Aneurysmal	184		0.68 (0.45-1.03)
Non-aneurysmal	379		1
LV end-diastolic diameter, mm		<0.001	
≤55	142		1
55-60	118		1.56 (0.78-3.13)
60-70	206		2.28 (1.26-4.10)
>70	108		4.08 (2.25-7.40)
LV end-systolic volume index, ml/min^2*		0.003	
≤80	119		1
80-100	93		2.12 (0.88-5.12)
100-140	117		3.36 (1.53-7.40)
>140	89		4.13 (1.86-9.16)
LV ejection fraction, %		<0.001	
≤20	135		4.60 (1.97-11.0)
20-40	354		2.66 (1.16-6.13)
>40	80		1
Mitral regurgitation		<0.001	
None	110		1
1+	207		1.02 (0.51-2.04)
2+	116		2.52 (1.30-4.92)
3+	84		3.02 (1.51-6.04)
4+	53		6.36 (3.13-12.91)
SVR procedure (patch usage)		0.68	
No patch	154		1

Patch	442		1.10 (0.72-1.68)
SVR procedure (type)		0.39	
EVCPP	258		1
PLV	14		0.69 (0.10-5.00)
SAVE	184		1.32 (0.87-2.00)
Overlapping	62		1.61 (0.92-2.82)
Linear	78		0.96 (0.50-1.85)
CABG		0.001	
Not performed	83		1
Performed	513		0.49 (0.32-0.76)
Mitral valve procedure		<0.001	
Not performed	345		1
Performed	251		2.66 (1.85-3.83)

CI = confidence interval, NYHA = New York Heart Association, INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support, LV = left ventricle, SVR = surgical ventricular reconstruction, EVCPP = endoventricular circular patch plasty, PLV = partial left ventriculectomy, SAVE = septal anterior ventricular exclusion, CABG = coronary artery bypass grafting

*Proportion of those with missing values ≥5%

FIGURE LEGENDS

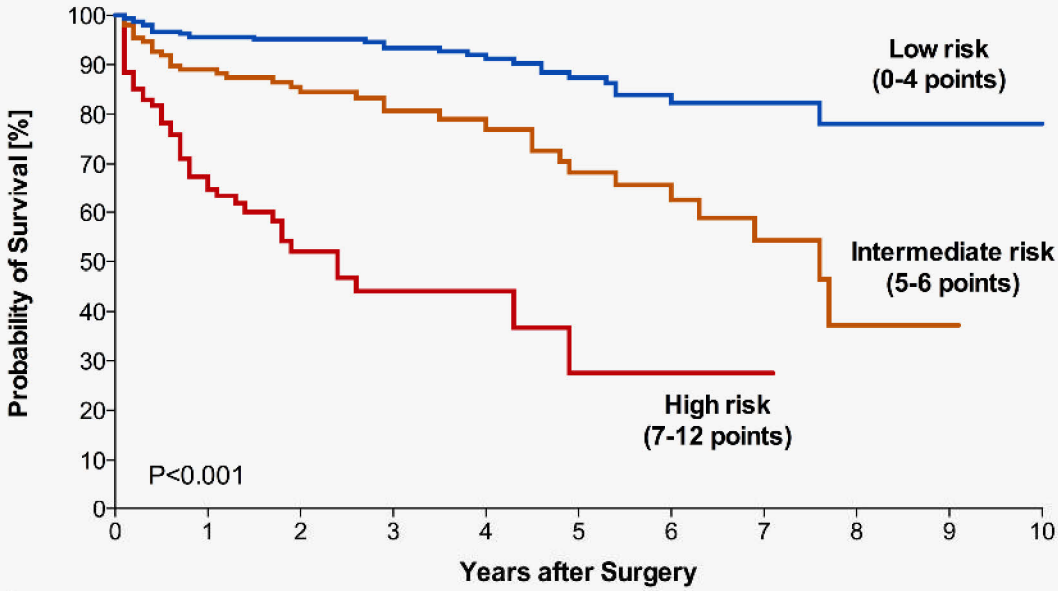
Figure 1. Comparisons of Kaplan-Meier survival curves of each risk group according to all-cause mortality (A) and readmission-free survival (B).

Figure E1. Comparisons of Kaplan-Meier survival curves in terms of INTERMACS profiles (A), LV ejection fraction (B), mitral regurgitation (C), and age (D).

LV = left ventricle, MR = mitral regurgitation

Figure E2. Comparisons of New York Heart Association functional classes among risk groups at different time points.

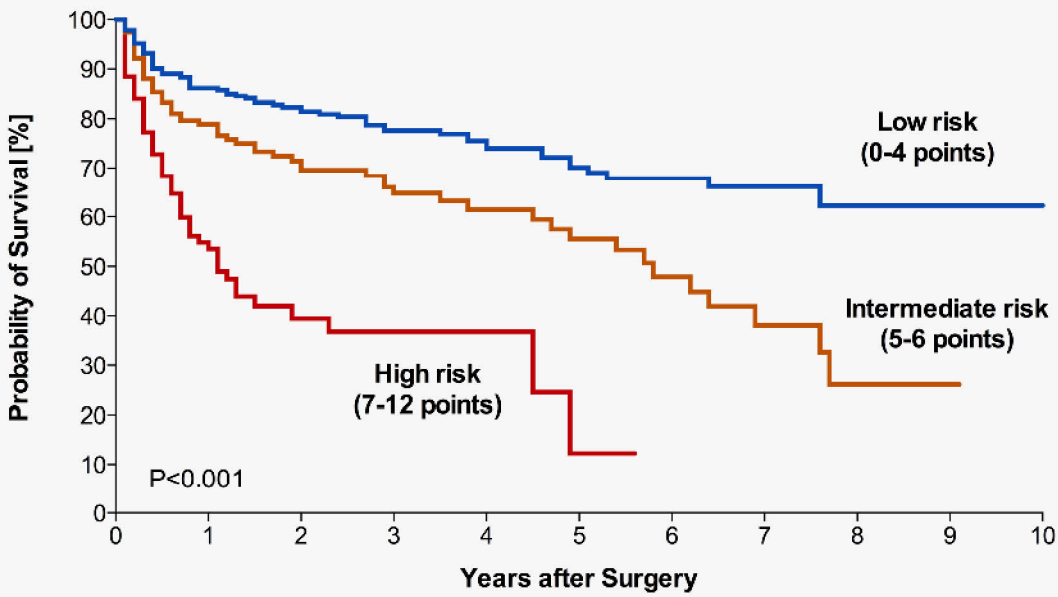
A. All-cause Mortality



No. at Risk

Low risk	317	254	201	153	117	83	53	31	18	11
Intermediate risk	156	118	83	63	39	31	20	12	5	2
High risk	95	52	24	15	8	4	2	2		

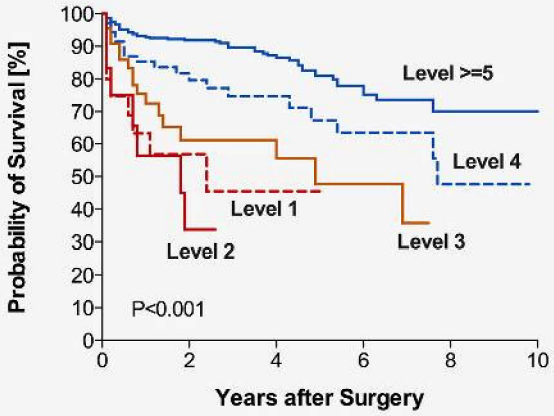
B. Readmission and All-cause Mortality



No. at Risk

Low-risk	317	230	177	131	100	68	46	26	15	10
Intermediate-risk	156	107	74	55	34	28	18	10	5	2
High-risk	95	41	17	11	5	2				

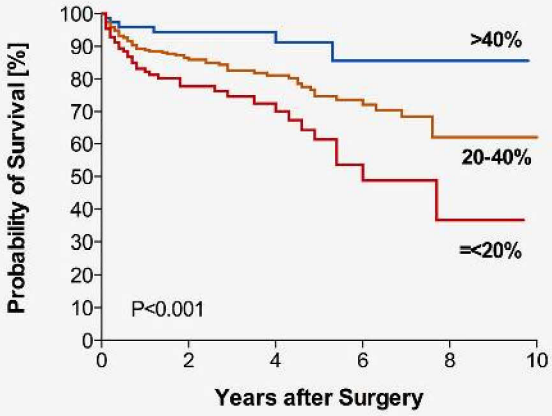
A. INTERMACS profile



No. at Risk

Level 1	20	7	4		
Level 2	12	3			
Level 3	44	16	11	6	
Level 4	72	39	22	13	7
Level >=5	409	247	129	58	18

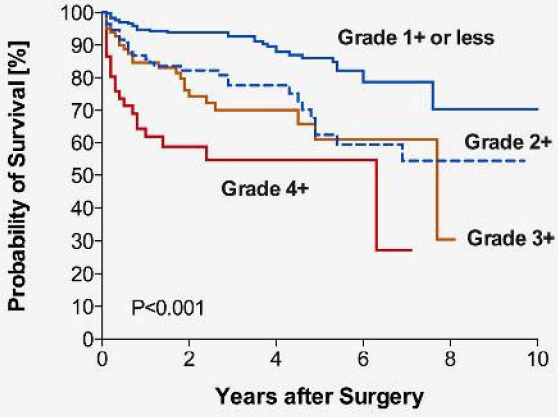
B. LV ejection fraction



No. at Risk

>40%	76	53	30	13	2
20-40%	341	190	101	50	18
=<20%	129	58	30	11	4

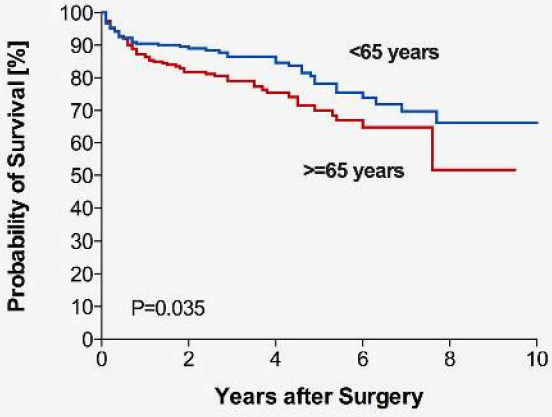
C. Mitral regurgitation



No. at Risk

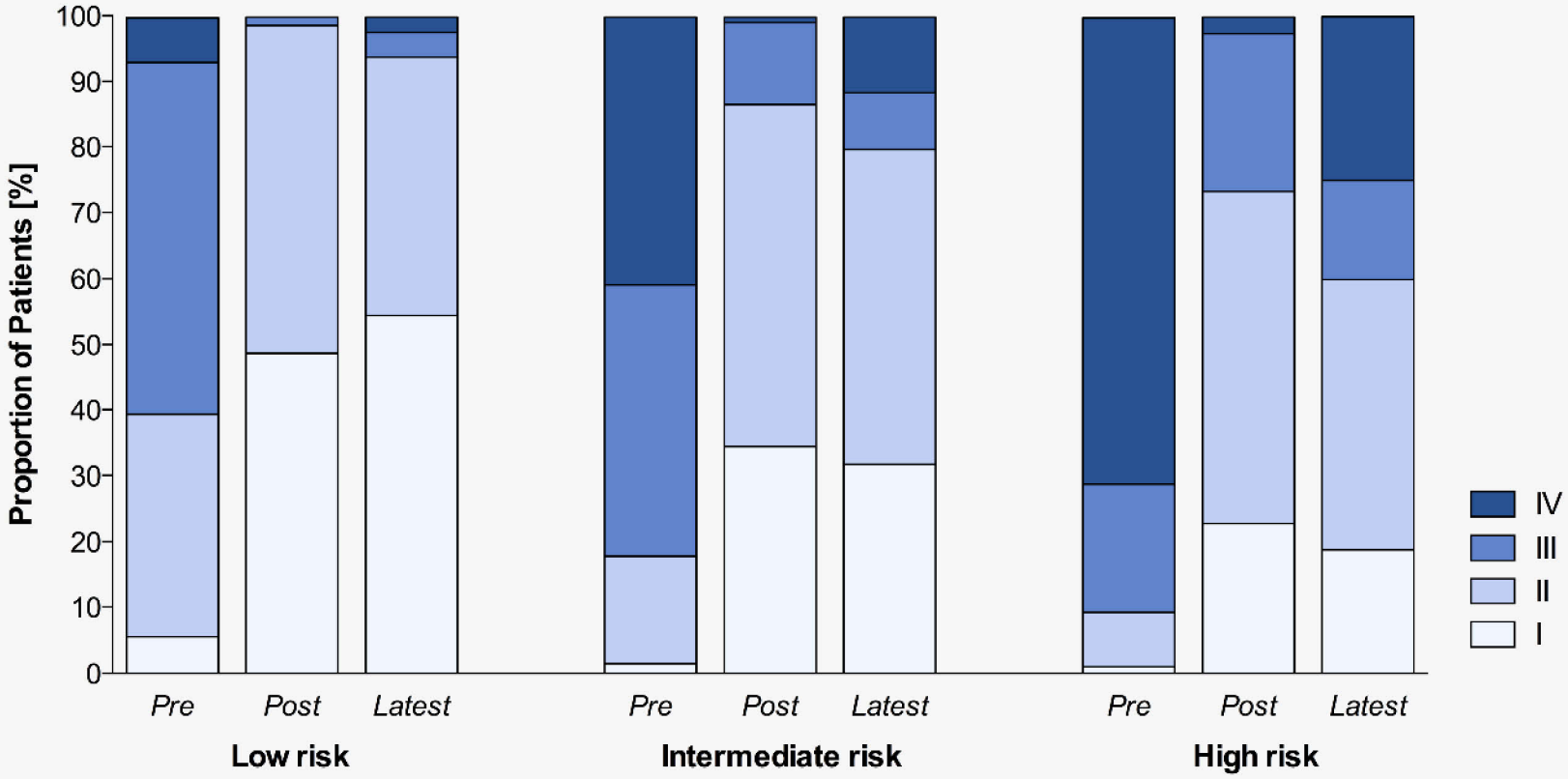
Grade 1+ or less	310	188	106	47	17
Grade 2+	112	62	39	16	7
Grade 3+	83	43	18	11	2
Grade 4+	52	17	5	3	

D. Age



No. at Risk

<65 years	283	165	95	45	17
>=65 years	274	145	69	30	7


Proportion of Patients [%]
100
90
80
70
60
50
40
30
20
10
0
Pre
Post
Latest
Low risk
Intermediate risk
High risk
IV
III
II
I