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Results of mitral valve surgery for secondary regurgitation with poor left ventricular function

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Abstract

Background and aim: Surgical repair of secondary mitral regurgitation is still controversial especially when the cardiac function is reduced. The purpose of this study was to retrospectively investigate the operative and long-term results of mitral valve surgery for secondary mitral valve regurgitation with poor cardiac function. Risk factors for long-term mortality were also investigated. Methods Patients with preoperative echocardiographic left ventricular ejection fraction [?]30% who underwent mitral valve surgery due to secondary mitral regurgitation comprised the study group. Cardiac function and valve regurgitation was assessed with echocardiogram using modifiled Simpson's method and color-flow Doppler. Peri-operative results and long-term survival were investigated. Results Sixty-nine patients (mean age 65.5 years, 58 males) with secondary mitral regurgitation and poor left ventricular function comprised the study group, and their early results were investigated; long-term results were evaluated in 66 cases. There were no operative/in-hospital deaths. Postoperative echocardiograms showed significantly improved mitral regurgitation, from moderate to severe to less than trivial ($p<0.001$), although poor left ventricular function remained. Actual 1-, 3-, and 5-year survival rates were 90.5%, 76.5%, and 63.4%, respectively. The 1-, 3-, and 5-year re-admission-free rates due to heart failure were 74.6%, 61.6%, and 55.3%, respectively. Patients with clinical frailty scale scores [?]4 had a worse prognosis than patients with clinical frailty scale scores <4 (log-rank $p=0.046$). Conclusions Open mitral valve surgery could be appropriate for secondary mitral valve regurgitation with poor cardiac function, however, operative indications should be considered carefully in patients with high clinical frailty scale scores.

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Abstract

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Methods Patients with preoperative echocardiographic left ventricular ejection fraction [?]30% who underwent mitral valve surgery due to secondary mitral regurgitation comprised the study group. Cardiac function and valve regurgitation was assessed with echocardiogram using modifiled Simpson's method and color-flow Doppler. Peri-operative results and long-term survival were investigated.

Results Sixty-nine patients (mean age 65.5 years, 58 males) with secondary mitral regurgitation and poor left ventricular function comprised the study group, and their early results were investigated; long-term results were evaluated in 66 cases. There were no operative/in-hospital deaths. Postoperative echocardiograms showed significantly improved mitral regurgitation, from moderate to severe to less than trivial ($p<0.001$), although poor left ventricular function remained. Actual 1-, 3-, and 5-year survival rates were 90.5%, 76.5%, and 63.4%, respectively. The 1-, 3-, and 5-year re-admission-free rates due to heart failure were 74.6%, 61.6%, and 55.3%, respectively. Patients with clinical frailty scale scores [?]4 had a worse prognosis than patients with clinical frailty scale scores <4 (log-rank $p=0.046$).

Conclusions Open mitral valve surgery could be appropriate for secondary mitral valve regurgitation with poor cardiac function, however, operative indications should be considered carefully in patients with high clinical frailty scale scores.

Introduction

Since the emergence of percutaneous transcatheter mitral valve edge-to-edge repair, there have been more and more concerns about and understanding of mitral valve regurgitation.[1,2]According to the guideline for valve disease, there is consensus for surgical correction of the valve with primary mitral valve regurgitation because mechanical valve dysfunction can be fixed only by a mechanical solution.[3,4] On the other hand, secondary mitral regurgitation is referred to as left ventricular disease, not valve leaflet disease. Regurgitation itself is regarded as only one component in this situation, and restoration of mitral valve competence is not curative.[4,5] However, the presence of even moderate mitral regurgitation is associated with a worsened prognosis in ischemic mitral valve regurgitation, which is a form of secondary mitral valve regurgitation.[6,7] Correction of secondary mitral regurgitation seems to be beneficial.

The Mitra Clip (Abbott Vascular, Menlo Park, CA) has been proven to improve survival and hospitalization for a certain subset of secondary mitral valve regurgitation patients.[2,8] The Mitra Clip is less invasive than cardiac surgery, but it does not seem to offer superior control of mitral regurgitation compared to the surgery.[9] Mitral valve surgery can provide greater benefits in the postoperative course over the long-term if accomplished without increasing perioperative mortality or morbidity.

Clarification of early and long-term results of surgical correction for secondary mitral valve regurgitation is very important, especially in patients with poor left ventricular function, because high surgical mortality and morbidity rates are anticipated in this situation.

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The purpose of this study was to retrospectively investigate the operative and long-term results of mitral valve surgery for secondary mitral regurgitation with poor left ventricular function defined as left ventricular ejection fraction (LVEF) [?]30%. As a sub-analysis, risk factors for long-term mortality were also investigated.

Materials and Methods

Between November 2008 and April 2021, all cases of cardiac surgery performed at Nagoya Heart Center were screened, and patients with preoperative echocardiographic LVEF [?]30% were identified. Of these, cases that underwent mitral valve surgery due to secondary mitral valve regurgitation comprised the study group. Cases with concomitant aortic valve surgery were excluded.

On echocardiographic evaluations, cardiac chamber size was measured using the standard M-mode method, and LVEF was calculated using the modified Simpson's method. Valve regurgitation was assessed using color-flow Doppler as "trivial", "mild", "moderate", or "severe". Postoperative transthoracic echocardiographic evaluation was performed on each patient before discharge, usually on postoperative day 7.

Chronic obstructive pulmonary disease was defined as percentage predicted forced expiratory volume in 1.0 s <75%, partial pressure of oxygen in arterial blood <60 mmHg, or provision of medical therapy. The definition of liver dysfunction was total bilirubin [?]1.5 mg/dl or liver enzymes (aspartate aminotransferase or alanine aminotransaminase) [?]100 U/l. Clinical data were gathered from medical records, operative records, and the in-hospital surgical database.

Long-term results were assessed by direct contact with the patients or telephone interviews with the patients, their families, or their local doctors. Survival was assessed between January and April 2021.

The primary endpoints for the early results were peri-operative mortality and morbidity, and those for the long-term results were mortality and hospitalization due to heart failure. As the secondary endpoints, risk factors for mortality in the long-term were examined. Patients were divided into two groups, and their long-term results were compared. The groups were stratified as follows: sex, ischemic etiology, ejection fraction <20%, clinical frailty scale score [?]4, presence of hypertension, diabetes mellitus, hyperlipidemia, preoperative atrial fibrillation, peripheral artery disease, hemodialysis, history of smoking, percutaneous coronary intervention, myocardial infarction, main procedural type (mitral valve replacement or plasty), and concomitant procedures, including coronary artery bypass grafting, tricuspid valve plasty, Maze procedure, and left ventricular restoration surgery.

Data were analyzed using SPSS version 22 statistical software (SPSS, Chicago, IL). Results are expressed as means ± standard deviation. Continuous data were analyzed using the Mann-Whitney U test or *t*- test as appropriate. Categorical data were analyzed using the χ^2 test. Survival analysis was performed using the Kaplan-Meier method and the log-rank test. Results with values of $p<0.05$ were considered significant.

Operative procedures and strategy

We previously reported our standard operative procedure and strategy for mitral valve surgery with reduced left ventricular function[10]. Briefly, the procedures were performed through the median sternotomy approach, and cardiopulmonary bypass was established with ascending aortic and bicaval cannulations. In the re-do cases, cardiopulmonary bypass was established with peripheral cannulations as needed. Concomitant coronary artery bypass grafting was performed in an on-pump beating fashion where possible with the aim of reducing cross-clamp time. Other procedures were performed under cardiac arrest with antegrade, intermittent, cold-blood cardioplegia.

Our strategy for selecting repair or replacement was changed at the beginning of 2014, based on the results of a randomized, controlled study and the good results obtained with chordal-sparing mitral valve replacement.[11,12]Before 2014, our first choice of mitral procedure was mitral plasty even in cases with reduced cardiac function. Mitral valve replacement was chosen when left ventricular diastolic diameter was >70 mm, in re-do cases or in hemodialysis cases for which reverse remodeling was not expected. Since 2014, we have selected chordal-sparing mitral valve replacement as the first-line procedure in secondary mitral

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regurgitation with reduced cardiac function. Mitral plasty was performed for younger patients (early 60s or younger), and when left ventricular diastolic diameter was <60 mm.

Apart from this strategy, we have chosen mitral valve replacement for patients for whom a poor prognosis was anticipated, as in patients with advanced age, high frailty, or other critical conditions.

In mitral valve plasty, an undersized annuloplasty ring was used, and whether the mitral sub-valvular apparatus procedure was performed was determined by the surgeon based on the echocardiographic findings, including tethering height >10 mm[13] or the location of papillary muscles. Our sub-apparatus procedures consist of papillary muscle re-suspension to the mitral anterior annulus with CV3 or CV4. When papillary muscle heads were separated, the anterior and posterior heads were combined together with the re-suspension stitch, then re-suspended toward the saddle horn, as previously reported.[14]

In mitral valve replacement, valve leaflets were tucked in the annulus with stitches securing the prosthetic valve, sparing all chordae.

This study was approved (Approval No: NHC2021-0330-11) by the institutional ethics committee on March 30th, 2021, and the need to obtain written consent from patients was waived because of the retrospective study design.

Results

During the observation period, 3,012 cases of cardiac surgery were performed in our institution. Of these, 238 cases (7.9%) were identified as having poor left ventricular function (LVEF [?]30%), and 75 cases underwent mitral valve surgery without an aortic valve procedure. Three cases of congenitally corrected transposition of the great arteries were excluded from the analysis. Another 3 cases were also excluded because they did not have secondary mitral regurgitation. Three patients underwent mitral valve surgery twice during the observation period. Their first and second surgeries were included for early result analysis, and their second surgeries were excluded from the long-term result analysis. Thus, 69 cases of secondary mitral regurgitation with poor left ventricular function comprised the study group, and their early results were investigated; long-term results were investigated in 66 cases.

The preoperative characteristics of the 69 patients are shown in Table 1. Their mean age was 65.5 years, and 58 patients (84.1%) were male. Preoperative echocardiograms showed poor left ventricular function with a mean LVEF of 21.2% (26 cases <20%), and dilated left ventricular diameters in diastole/systole of 65.1/58.6 mm, respectively.

Peri-operative results are shown in Table 2. In all but one case, which underwent surgery through a right thoracotomy under hypothermic ventricular fibrillation because severe adhesions were anticipated due to previous cardiac surgery, the procedures were performed through a median sternotomy. Mitral valve replacement was performed in 33 cases, and mitral valve plasty was performed in 36 cases. Among the cases of mitral valve plasty, 23 cases underwent subvalvular apparatus procedures. Common concomitant procedures were coronary artery bypass grafting and tricuspid valve plasty (42.0% and 40.6%, respectively). The Maze procedure was performed in 26.1% of cases. Mean operation time was 289.5 min, and mean aortic cross-clamp time was 88.5 min. Transfusion was performed in 50 cases (72.5%).

Two patients required prolonged postoperative ventilation (>72 h), but postoperative morbidity rates were relatively low, except for atrial fibrillation (42%). There were no cases of operative/in-hospital death, and mean duration of hospitalization from operation to discharge was 23.6 days.

Postoperative echocardiograms showed significantly improved mitral regurgitation, from 3.4 (moderate to severe) to 0.75 (less than trivial, $p<0.001$), although poor left ventricular function remained.

The rate of successful collection of follow-up data was 98.5%, with a mean follow-up of 1,605 days (range, 6–4,525 days). Figure 1 shows the survival curve for all-cause death. Actual 1-, 3-, and 5-year survival rates were 90.5%, 76.5%, and 63.4%, respectively. Figure 2 shows the rate of freedom from re-admission due to heart failure; the 1-, 3-, and 5-year re-admission-free rates were 74.6%, 61.6%, and 55.3%, respectively.

Table 3 shows the results of the risk factor analysis for long-term survival. Patients with clinical frailty scale scores [?]4 had a worse prognosis than patients with clinical frailty scale scores <4 (Figure 3, log-rank p=0.046). The other factors including mitral valve procedure type and etiology did not affect long-term survival significantly in the present study.

Comment

This was a single-center, retrospective report of the early and long-term results of consecutive cases of mitral valve surgery for secondary mitral valve regurgitation with poor left ventricular function.

The early results of this study were good in terms of surgical mortality and morbidity. Our operative strategy was devised to reduce aortic cross-clamp time in poor left ventricular function. Concomitant coronary bypass was performed in on-pump beating fashion as much as possible, and mitral valve replacement was chosen for critically ill patients.[10] With these modifications, more patients could tolerate open heart surgery than we expected even with reduced cardiac function.

Since the results seem to imply that poor left ventricular function itself might not be a contraindication for open cardiac surgery, operative indications should be considered very carefully. In the present study, 26 cases (37.7%) had LVEF [?]20%, but no patient had LVEF <10%. Preoperative mean left ventricular diameter was not extremely large, being 65.1/58.6 mm in diastole/systole. The cases with extremely dilated or more reduced cardiac function may not be able to tolerate open heart mitral valve surgery. For such patients, a left ventricular assist device or heart transplantation may be indicated.

Since surgical stress or trauma is much greater than that of a catheter procedure, we should carefully choose which modality to use to restore secondary mitral regurgitation with poor left ventricular function, especially in very ill patients. For critical patients with poor left ventricular function, percutaneous treatment might be a better option even if it is less effective than surgical treatment[1].

Although there was no postoperative mortality, and the morbidity rate was low, except for paroxysmal atrial fibrillation, postoperative hospitalization was long, more than 3 weeks. This is probably because patients with poor cardiac function have a slow recovery and require a longer time to optimize their medication regimens that include angiotensin-converting enzyme inhibitors, angiotensin receptor/neprilysin inhibitors, mineralocorticoid receptor antagonists, beta-blockers, or sodium-glucose co-transporter 2 inhibitors[15].

Long-term survival in the present study was acceptable compared to the previous reports, in which the long-term results for secondary mitral valve regurgitation were dismal when only pharmacotherapy was provided.[16,17] However, re-admission-free rates were low, 61.6% at 3 years and 55.3% at 5 years. This may imply that poor left ventricular function remains even after open mitral valve surgery with good control of mitral regurgitation. Multidisciplinary therapy should be provided to these subsets, including pharmacotherapy, diet, rehabilitation, and cardiac resynchronization therapy, even after the surgery.

Concerning risk factors for long-term survival, the clinical frailty scale score was the only predictor of long-term mortality in the present study. Th clinical frailty scale is a simple method to semi-quantitatively assess patient frailty.[18] It has been reported that it can predict late mortality in certain cases.[19,20] Since the present study showed worse long-term survival in patients with high clinical frailty scale scores, the operative indications need to be considered carefully in such ill patients, because surgical stress or trauma could make the patients' frailty worse. For patients with a high clinical frailty scale score, percutaneous transcatheter mitral valve edge-to-edge repair might be a better option, because it is far less invasive than open heart surgery.

The present study had several limitations. First was the retrospective design of the study. Once we selected open heart surgery for the patients, huge selection bias existed.

Second, the number of patients was small, and data in the present study represent our clinical experience with a consecutive series of surgical correction for mitral regurgitation with poor left ventricular function.

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However, the present results reflect real-world clinical practice and imply that open heart surgery could be appropriate for selected patients even with poor left ventricular function.

The last limitation was that, because of the retrospective nature of the investigation, this study did not have a control group. Whether surgical correction of secondary mitral regurgitation provides greater benefit than other therapeutic options over the long-term is unknown. However, considering that several articles have reported a poor prognosis for patients with secondary mitral regurgitation and our good operative results, we feel encouraged to provide open mitral valve surgery if the patient can tolerate the surgery.

Conclusions

In conclusion, the perioperative results of mitral valve surgery for secondary mitral valve regurgitation with poor left ventricular function were good. The present results suggest that open mitral valve surgery could be appropriate for secondary mitral valve regurgitation with poor cardiac function. However, since the clinical frailty scale score affects long-term survival significantly, operative indications should be considered carefully in patients with a high clinical frailty scale score.

Further accumulation of data is mandatory to determine which modality should be used for patients with secondary mitral regurgitation and poor left ventricular function.

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Author contributions

HK contributed the article design, concept, data interpretation, drafting and revision of the article. AK contributed data analysis and data interpretation. YK contributed the concept, and data interpretation. MT and AC contributed data collection and data analysis.

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Figure legends

Figure 1. Kaplan-Meier analysis of survival from all-cause death

Figure 2. Kaplan-Meier analysis of freedom from heart failure re-admission

Figure 3. Kaplan-Meier with log-rank analysis of survival for high and low clinical frailty scale scores

Table 1. Pre-operative characteristics of the 69 patients

Variable n (%), mean ±SD

Age (y) 65.5 ±11.0

Males 58 (84.1%)

Body surface area (m^2) 1.64 ± 0.20

Body mass index (kg/m^2) 22.4 ± 4.6

NYHA III/IV 50 (72.5%)

Preoperative IABP required 9 (13.0%)

Emergency 2 (2.9%)

Euro II score 15.2 ± 0.14

Clinical Frailty Score 3.32 ± 0.73

Comorbidities

Hypertension 31 (44.9%)

Dyslipidemia 40 (58.0%)

Diabetes mellitus 38 (55.1%)

Atrial fibrillation 20 (29.0%)

Hemodialysis 6 (8.7%)

COPD 31 (44.9%)

Smoking history 42 (60.9%)

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Liver dysfunction 18 (26.1%)

Carotid artery stenosis 1 (1.4%)

Peripheral artery disease 6 (8.7%)

Prior cardiac surgery 7 (10.1%)

Prior myocardial infarction 14 (20.3%)

Prior percutaneous coronary intervention 17 (24.6%)

eGFR (ml/min/1.73 m^2) 48.5 ± 20.6

Hematocrit (%) 40.2 ± 5.5

Total bilirubin (mg/dl) 1.28 ± 0.66

Etiology

Ischemic 35 (50.7%)

Non-ischemic 34 (49.3%)

Preoperative echocardiogram

LV ejection fraction (%) 21.2 ± 9.1

Left atrial diameter (mm) 49.3 ± 7.4

LV diameter in diastole (mm) 65.1 ± 8.3

LV diameter in systole (mm) 58.6 ± 8.4

Mitral regurgitation 3.4 ± 0.6

Tricuspid regurgitation 2.3 ± 1.0

COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; IABP = intra-aortic balloon pump; LV = left ventricular; NYHA = New York Heart Association functional classification; SD = standard deviation.

Table 2. Peri-operative results of the 69 patients

Variable *n* (%), mean ±SD

Mitral valve replacement 33 (47.8%)

Mitral valve plasty 36 (52.2%)

Subvalvular apparatus procedure 23 (63.9%)

Concomitant Procedure

Coronary artery bypass grafting 29 (42.0%)

Distal anastomoses/patient 3.0 ± 1.4

Tricuspid valve plasty 28 (40.6%)

Maze 18 (26.1%)

Left ventricular restoration 7 (10.1%)

Operation time (min) 289.5 ± 89.0

Cardiopulmonary bypass time (min) 158.3 ± 55.3

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Aortic cross-clamp time (min) 88.5 ± 41.7

Transfusion 50 (72.5%)

Mean ventilation time except prolonged ventilation (h) 8.4 ± 9.0

Mean intensive care unit stay (days) 2.3 ± 3.9

Mean postoperative hospitalization (days) 23.6 ±22.6

Morbidities

Prolonged ventilation (>72 h) 2 (2.3%)

Re-intubation 4 (5.8%)

Re-exploration 1 (1.4%)

Required hemodialysis 5 (7.2%)

Cerebral infarction 1 (1.4%)

Transient ischemic attack 2 (2.9%)

Postoperative atrial fibrillation 29 (42.0%)

Deep wound infection 0 (0%)

Operative/in-hospital death 0 (0%)

Postoperative Echocardiogram

LV ejection fraction (%) 24.3 ± 8.5

Left atrial diameter (mm) 46.0 ± 6.6

LV diameter in diastole (mm) 62.5 ± 8.9

LV diameter in systole (mm) 56.1 ± 9.5

Mitral regurgitation 0.75 ± 0.9

Tricuspid regurgitation 1.7 ± 0.7

LV = left ventricular; SD = standard deviation

Table 3. Results of the log-rank test stratified by variables

Variable Yes (n) No (n) Log-rank p value

Sex 55 (male) 11 (female) 0.133

Ischemic etiology 35 31 0.585

Ejection fraction <20% 26 40 0.811

Clinical Frailty Scale score [?]4 14 52 0.046

Comorbidities

Hypertension 29 37 0.78

Diabetes mellitus 38 28 0.51

Dyslipidemia 39 27 0.535

Preoperative atrial fibrillation 19 47 0.694

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Peripheral artery disease 6 60 0.083

Hemodialysis 6 60 0.867

History of smoking 42 24 0.259

Prior PCI 17 49 0.536

Prior myocardial infarction 14 52 0.592

Main procedure

Mitral valve replacement 31 35 0.236

Concomitant procedures

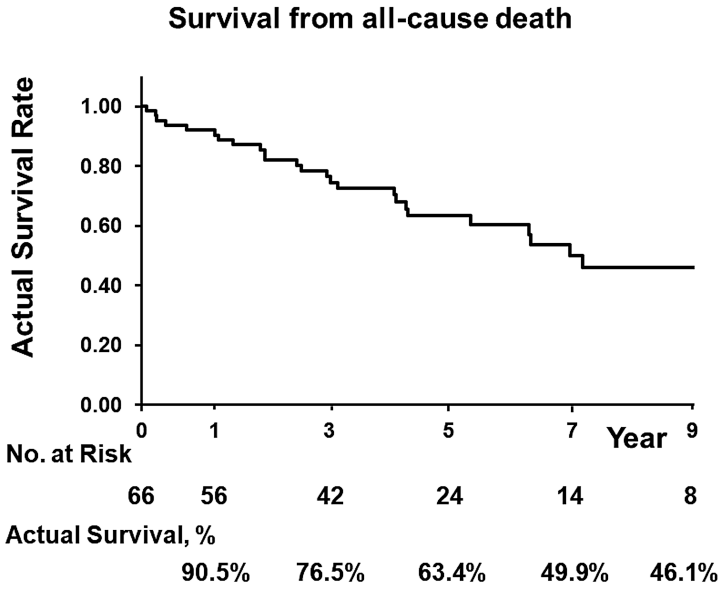
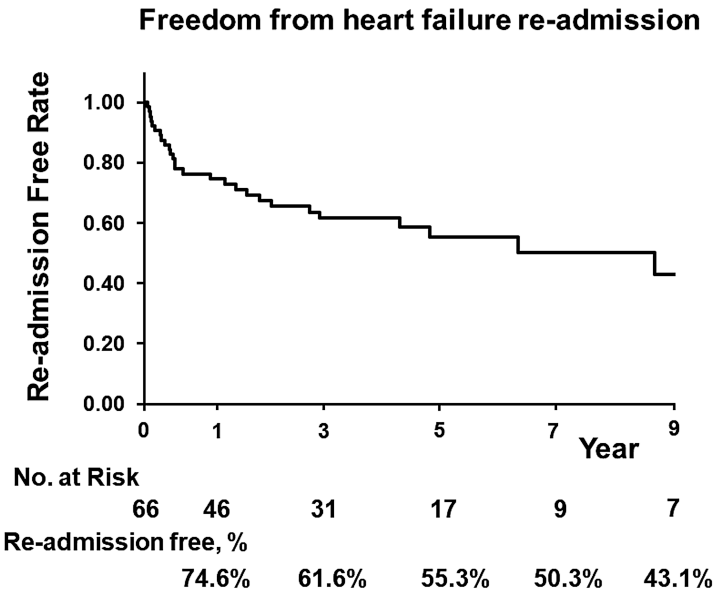
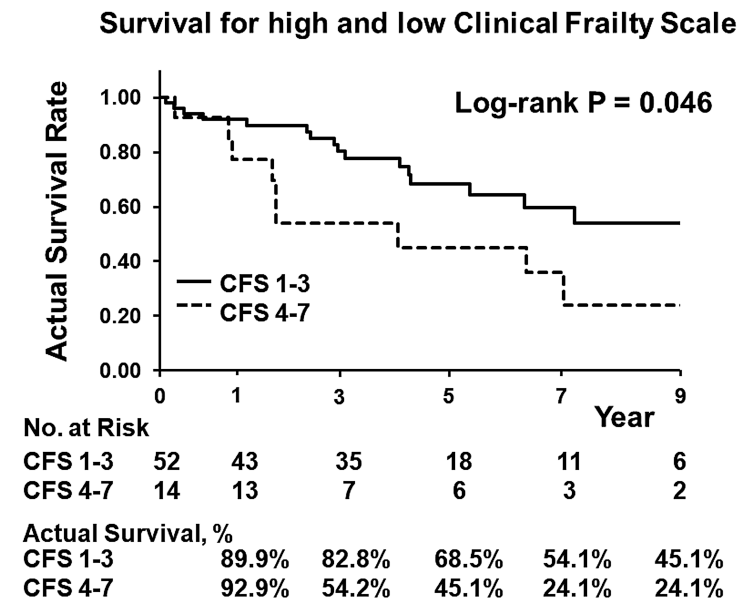
Coronary artery bypass grafting 29 37 0.919

Tricuspid valve plasty 27 39 0.893

Maze 18 48 0.363

Left ventricular restoration 7 59 0.167

PCI = percutaneous coronary intervention.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