Long Term Results and Predictors of Left Ventricular Function Recovery after Aortic Valve Replacement for Chronic Aortic Regurgitation

Hiroyuki Saisho[a], Koichi Arinaga[a], Satoshi Kikusaki[a], Yuichiro Hirata[a],

Kumiko Wada[a], Tatsuyuki Kakuma[b], Hiroyuki Tanaka[a]

a Department of Surgery, Kurume University School of Medicine, Kurume, Japan.

b Biostatistics Center, Kurume University, Kurume, Japan.

Abstract

Backgrounds:

In most patients with aortic regurgitation (AR), aortic valve replacement (AVR) improves left

ventricular (LV) function, but some patients will not have favorable remodeling. Our objectives

were to review long term clinical results of AVR for AR and to examine what factors affect the

normalization of LV function after AVR for chronic AR.

Methods and Results:

Between 1989 and 2010, 177 patients underwent isolated AVR for chronic pure AR. The

patients were divided into 2 groups based on indexed end-systolic LV diameter (iESD): Group

L (iESD)$\geqq$25 mm/m^2)(130 patients) and Group S (iESD<25 mm/m^2)(47 patients). There was

no significant difference between groups in late mortality, freedom from cardiac-related death

and rehospitalization for heart failure at late follow up after operation. At postoperative

follow-up, 16 % of patients had not recovered normal LV systolic function. By means of

multivariate analysis, iESD and cardiac index (CI) were independent predictors of recovery of

LV function and iESD>26.7 mm/m^2 and CI<2.71 l/min/m^2 were the best cut-off values.

Conclusion:

Early and late surgical results of AVR for chronic AR were good, but for the preservation of

postoperative normal LV function, AVR for AR patients should be performed before iESD

reaches 26.7 mm/m^2.

Introduction

Chronic aortic regurgitation (AR) involves both volume and pressure overload at the left ventricle (LV) and the goals of treatment are to prevent death, diminish symptoms, and prevent the development of heart failure [1].

Aortic valve replacement (AVR) is an established treatment for AR and the long term results of AVR for chronic AR are satisfactory. However, in some cases postoperative LV dilatation and function are inadequate. Indeed, Henry et al. showed that cases with end-systolic LV diameter (ESD) $\geqq$ 55mm and % fractional shortening $< 25\%$ had poor prognosis and more frequent post-operative complications [2]

LV systolic function and LV dimensions have been regarded as important parameters when considering appropriate timing of AVR for patients with AR [3]. However, it is unclear when the operation should be undertaken in such patients.

Recent studies have suggested the use of indexed LV dimensions in chronic AR to optimize surgical indications because decisions based on raw data might be inappropriate for patients with extreme body surface area (BSA) such as Japanese [4-7]. In the 2012 ESC/EACTS guidelines, indexed ESD (iESD) was newly added as a parameter for class IIa indication of AVR for AR: surgery for severe AR should be considered in asymptomatic patients with ejection fraction (EF) $> 50\%$) with severe LV dilatation (end diastolic diameter (EDD) > 70

4

mm or end systolic diameter (ESD) > 50 mm or indexed ESD (iESD) > 25 mm/m^2 with small

body size). In a recent revision of the AHA/ACC guidelines, iESD was newly included as a

decision-making criterion for operation regardless of body size [8]. However, there are few

studies examining predictive factors for prognosis after AVR for AR in Japanese patients.

In this study, we retrospectively reviewed 177 patients who underwent AVR for AR at our

hospital for 22 years and evaluated the early and long term clinical results of AVR for AR and

examined several predictors of recovery of LV function after the operation.

Patients and Methods

The Ethics Committee of Kurume University School of Medicine and the Institutional

Review Board approved this study. Individual patient consent was waived because the study

was retrospective.

Patients

From 1989 to 2010, 177 patients underwent primary isolated AVR for chronic pure AR at

Kurume University Hospital. Indications of AVR were symptomatic severe AR and

asymptomatic severe AR with LV systolic dysfunction (EF $\leqq$ 50%) or dilatation (EF > 50%

with EDD > 70mm and ESD > 50mm). To select only patients with chronic pure severe AR,

patients were excluded who had mild or greater aortic stenosis or local asynergy of wall motion

on preoperative transthoracic echocardiography (TTE). Patients were also excluded who had

previous cardiac surgery, concomitant coronary artery bypass graft, other heart valve surgery or

aortic surgery. Moreover, patients with acute AR, including aortic dissections or infective

endocarditis, were also excluded.

Subjects were 122 men and 55 women with a mean age of 58.4 ± 15.4 years (range, 21 to 84

years). The mean BSA was 1.57 ± 0.17 m^2 (range, 1.18 to 2.00 m^2). The etiologies of AR were

degeneration in 97 patients (55 %), congenital anomaly in 39 patients (22 %; bicuspid valve 32,

quadricuspid valve 7), rheumatic fever in 20 patients (11 %), annular dilatation in 14 patients

(8 %) and aortitis in 7 patients (4 %).

Preoperative variables are shown in Table 1. We divided these patients into 2 groups based on

iESD (Group L: iESD > 25 mm/m^2, Group S: iESD $\leqq$ 25 mm/m^2) and 130 patients (73.4 %)

had LV dilatation of iESD > 25 mm/m^2.

Data Collection and Follow-Up

Preoperative and perioperative data were collected from medical records and follow-up data

were obtained from our outpatient clinic records or by correspondence with referring physicians.

Hospital survivors were followed up annually at our outpatient clinic. Patients were contacted

directly by telephone or through the referring physician, and additional data were collected from

clinical records. Deaths and complications were properly defined according to published

guidelines of The Society of Thoracic Surgeons [9]. EF and LV dimensions were measured and

the normalization of LV systolic function was defined as EF $\geqq$ 55 % according to

recommendations by the American Society of Echocardiography [10].

Statistical Methods

Continuous variables were expressed as mean ± standard deviation. Simple comparisons were

performed using a standard χ^2 test or a non-paired *t* test. The paired t-test was used to compare 2

groups, while ANOVA was used to compare more than 2 groups. Survivals and freedom from

late complications were estimated using the Kaplan-Meier method. Survival curves were

compared using a log-rank test. The risk factors for recovery of LV systolic function were

analyzed by both univariate and multivariate analysis with the Cox proportional hazards model.

For continuous variables, diagnostic cut-off values with the most favorable sensitivities and

specificities were identified by receiver operating characteristics (ROC) curve analysis.

Results

Clinical Outcome

There were 2 hospital deaths (1.1 %), caused by low cardiac output syndrome and pneumonia

respectively and both were Group L.

Among the 175 operative survivors, 168 patients (96.0 %) were followed up. The mean

follow-up period was 11.8 ± 6.5 years (range, 2 months to 24.8 years) for a total of 2081.3

patient-years. During the follow-up period, 38 patients (21.5 %) died of various causes,

including 4 cardiac-related deaths (2.3 %) (heart failure in three patients, arrhythmia in one

patient). Of all cardiac-related deaths, three were in Group L and one was in Group S.

The actuarial survival, including early death at 10 and 20 years was 89.9 % and 55.2 % in

Group L, and 82.7 % and 71.6 % in Group S (P = 0.72), respectively. Differences in the

actuarial survival were not significant (Fig 1 A).

The actuarial freedom from cardiac-related death at 10 and 20 years was 99.2 % and 97.5 %

in Group L, and 95.0 % and 79.1 % in Group S (P = 0.25), respectively. Differences in the

actuarial freedom from cardiac-related death were not significant (Fig 1 B).

Eight patients were admitted to our hospital due to heart failure for an incidence of 0.4 % per

patient-year. Of them, 5 patients were in Group L, and 3 patients were Group S. The details of

rehospitalization due to heart failure are presented in Table 2. The actuarial freedom from

rehospitalization due to heart failure at 10 and 20 years was 98.0 % and 92.4 % in Group L, and

97.2 % and 71.8 % in Group S (P = 0.31), respectively. Differences in the freedom from

rehospitalization due to heart failure were not significant (Fig 1 C).

Time course of Echocardiographic Data

Echocardiography was performed within 1 week before the operation, at the immediate

postoperative period (7 days after the operation), at early follow up (1 year after the operation)

and at late follow-up period (mean 6.7 years (range, 3 years to 10 years)). Fig 2 shows the

variables before and after the operation in the 2 groups. The mean iEDD and iESD in both

groups just after the operation were significantly improved from preoperative values (iEDD :

42.9 ± 5.4 to 34.2 ± 4.7 mm/m^2, iESD : 30.4 ± 5.5 to 24.9 ± 4.9 mm/m^2 in Group L, and iEDD :

35.4 ± 3.1 to 31.1 ± 3.5 mm/m^2, iESD : 22.1 ± 1.8 to 20.8 ± 3.6 mm/m^2 in Group S). The

improvement in these variables was maintained in both groups at early postoperative follow-up

and at long term period. The mean iEDD and iESD in Group L were significantly larger at the

immediate postoperative period, but after that, there were no significant differences between the

2 groups.

The mean preoperative EF was 54.8 ± 9.7 % in Group L and 66.6 ± 6.0 % in Group S (P <

0.05). There was a temporal decrease in both groups immediately after the operation, but it

improved and maintained normal values during follow up, and no significant difference was

recognized between the 2 groups.

9

Predictors of the normalization of LV systolic function

Postoperative follow-up echocardiograms were obtained in 144 of the 177 patients and 23 of

these patients (16.0%) were unable to recover to the normal value of EF. Several factors

affecting recovery of postoperative LV systolic function were identified by univariate and

multivariate analyses (Table 3).

By means of univariate analysis, we determined that ESD, iESD, EF, cardiac index (CI),

history of atrial fibrillation (AF) and smoking were associated with postoperative normalization

of EF. EDD and iEDD were not predictive of normal EF in the postoperative period. By means

of multivariate analysis, iESD and CI were found to be significant factors and patients with

lower EF, history of AF and habit of smoking had poorer recovery of LV systolic function.

Receiver operating characteristic curve analyses showed that the best cut-off values for

predicting of EF recovery after surgery were iESD of 26.7 mm/m^2, EF of 50.2 %, and CI of 2.71

$l/min/m^2$.

To score the risk of poor recovery of LV systolic function with the above factor, we assigned

2 points to a larger iESD($\geqq$ 26.7 mm/m^2), lower EF($<$ 50.2 %), history of AF and habit of

smoking and 3 points to lower CI($<$ 2.71 $l/min/m^2$). As a result, we found that patients with a

score of 5 or more had poor recovery of LV systolic function after AVR, with a sensitivity and

10

specificity of 82.6% and 64.5%, respectively.

Discussion

In the new 2012 ESC/EACTS guidelines, iESD was used as a parameter for decision making

for AVR for chronic AR, that is, asymptomatic patients with severe AR and severe LV

dilatation (iESD > 25 mm/m^2) were newly added as a class IIa indication for AVR. This

revision was based on a report that the use of iESD improves the prediction of unfavorable

outcome after AVR in patients with low BSA and that iESD > 25 mm/m^2 should be used as a

cut-off point for surgery rather than ESD > 50 mm in patients with low BSA. [4]. Indeed,

Daimon et al. showed that BSA of Japanese is very low and LV dimensions are small compared

with the reference values in the guidelines from the American Society of Echocardiography [11].

In this study, the mean BSA was 1.57 ± 0.17 m^2, which demonstrates that our patients were

smaller than those in other reports, especially those from Western countries [6, 11, 12]. This

difference in physique between Japanese and Western populations will have a great effect on

how the grade of LV dilatation influences the results of AVR.

In this study, we found that iESD of 26.7 mm/m^2 was the best cut-off values for predicting EF

recovery after surgery, and this result supports the new guideline from the viewpoint of the LV

reverse remodeling effect. However, there was no significant factor in late survival,

cardiac-related death and freedom from rehospitalization due to heart failure despite the use of indexed LV dimensions.

The present results revealed that patients who had isolated AVR for chronic AR had good clinical results regardless of the severity of LV dilatation and hospital mortality at our hospital (1.1%) was lower than other previous studies (1.7 % to 14 %) [4, 5, 6, 13, 14] and late survival was good. These good results are thought to be due to improved operative techniques, intensive care and medical therapy, as well as low incidence of cardiac-related complications.

The timing of operation for asymptomatic severe chronic AR remains controversial. Preoperative ESD has been reported as a poor prognostic factor in patients with severe AR after AVR. Henry et al. showed that cases with ESD $\geqq$ 55mm and % fractional shortening $< 25\%$ had a poor prognosis and more frequent post-operative complications [3]. Some clinicians looked negatively at the operation because they believed myocardial changes in these patients to be at an irreversible stage [15]. The Euro Heart Survey revealed that only 22 % of chronic AR patients with LVEF of from 30 to 50 % received the operation and only 3 % of those with LVEF < 30 % did [16]. This situation may be because of the clear relationship between lower preoperative LVEF and worse postoperative survival. Therefore, 55 mm of ESD has been widely accepted as a cut off value indicating poor prognosis and there is still a major reluctance to offer AVR to these patients in the current era.

12

Even though many of them develop irreversible changes, some cases manifest a meaningful recovery of LV function after AVR, [14, 15, 17, 18]. Some studies showed there was no significance difference in survival rate between cases with severe LV dysfunction and those with normal LV function after AVR [19, 20]. Our study had 18 patients (10.2%) with ESD $\geqq$ 55mm and there was no operative mortality and no significant difference in postoperative course at late follow up compared with patients with ESD < 55mm.

The current ACC/AHA guidelines do not recommend AVR for patients with LVEF > 50 %, EDD < 70 mm, and ESD < 50 mm in the absence of concomitant cardiac or aortic surgery [21] and few studies have evaluated the impact of AVR on survival in the asymptomatic phase of the disease. Turk et al. investigated whether AVR would yield a survival benefit in asymptomatic severe AR patients with those parameter values and showed that AVR was associated with significant survival benefit [22]. Considering the declining operative mortality of AVR and the improvement of perioperative management, these results possibly support a strategy of earlier surgery for AR and despite serving as a class III indication, AVR could be indicated in severe asymptomatic AR patients with normal LVEF and lesser LV dilatation.

AR is the combined condition of volume overload and pressure overload and LVEF and ESD have been focused on as measures of LV pump performance and EDD as a measure of the severity of the volume overload in asymptomatic patients with AR. After the removal of this

13

condition with surgical repair, enlarged LV dimensions, mainly EDD, are usually reduced

within a few weeks after the operation, because the effect of preload decrease appears to be

dominant at this time. Therefore, LVEF decreases temporarily [22 - 24]. In our study, both

groups had great reduction in iEDD and iESD, but the decrease in iESD in Group S was smaller

than in Group L. That's why the grade of LVEF decline was greater in Group L but Group S

had significantly better LVEF than Group L. After discharge, Group L had additional

improvement in LV dimensions, and LV function reached a plateau at the early period after the

operation. This chronological change could result from the reduced afterload with gradual

improvement in LV function after surgery or it might show an actual improvement in contractile

function and would indicate that it takes about one year to make sure of the improvement of LV

function with AVR. That is why we choose this period as the appropriate timing for judging the

effect of the operation.

The other predictors we identified, CI, history of AF and habit of smoking should also be

considered in assessing the postoperative prognosis of these patients.

In the presence of severe AR, stroke volume (SV) depends on the regurgitant volume and on

the pumping capacity of LV. Some studies have clearly suggested a link between SV and the

presence and extent of viable myocardium in patients with heart failure from systolic

dysfunction [25,26]. CI is associated with SV in this condition, and the preservation of elevated

14

CI with decreased systolic function could suggest that there is enough viable myocardium and the operation can lead this heart to eventual favorable remodeling.

There are few studies about the relationship between AF, habit of smoking and recovery of LV function after surgery. Persistent AF is reported to be independently associated with increasing diffuse fibrosis of LV and AF itself may play an independent role in adverse cardiac remodeling [27]. Smoking that includes more than 4000 chemical substances, promotes cardiomyocyte apoptosis by inducing oxidative stress and is suggested to be related to LV dysfunction [28, 29]. Further studies are necessary to evaluate how these conditions affect the postoperative clinical course.

To our knowledge, this is the first study to evaluate the effect of AVR on LV reverse remodeling from the point of preoperative factors including hemodynamics indices such as iESD and CI and to score the risk in Japanese patients. These days, the improvement in operative results is shifting the timing of AVR for AR earlier, and this prediction score is thought to be a useful decision-making tool for the operation.

The limitations of this study are as follows. First, our study is a retrospective study and despite our efforts to control for confounding data and selection bias, it is not possible to control for all confounders. Second, as a single center study, our sample size is relatively small and susceptible to a type II error. Therefore we could not come to definite conclusions. However,

the follow-up periods were more than 20 years, which was adequate for examining the effect of

isolated AVR for chronic AR.

Conclusion

The results of AVR for chronic AR were satisfactory in terms of early and late survival and

no factor significantly affected the clinical results. However, for the preservation of

postoperative normal LV systolic function, AVR for AR patients should be indicated before

iESD reaches 26.7 mm/m^2. This result supports the new guidelines from the viewpoint of the

LV reverse remodeling effect.

Disclosure Statement

All authors have no conflict of interest.

References

[1] Tornos MP, Sambola A, Permanyer-Miralda G, Evangelista A, Gomez Z, et al. Long-term outcome of surgically treated aortic regurgitation: influence of guideline adherence toward early surgery. J Am Coll Cardiol 2006; 47:1012–7

[2] Henry WL, Bonow RO, Borer JS, Ware JH, Kent KM, et al. Observations on the optimum time for operative intervention for aortic regurgitation. I. Evaluation of the results of aortic valve replacement in symptomatic patients. Circulation 1980; 61:471-83.

[3] Taniguchi K, Sawa Y. Contemporary reviews by surgeon: timing of operation for chronic aortic regurgitation. Gen Thorac Cardiovasc Surg 2012; 60:735–43

[4] Sambola A, Tornos P, Ferreira-Gonzalez I, Evangelista A. Prognostic value of preoperative indexed end-systolic left ventricle diameter in the outcome after surgery in patients with chronic aortic regurgitation.Am Heart J 2008; 155**:** 1114 – 20.

[5] Brown ML, Schaff HV, Suri RM, Zhuo L, Sundt TM, et al. Indexed left ventricular dimensions best predict survival after aortic valve replacement in patients with aortic valve regurgitation.Ann Thorac Surg 2009; 87**:** 1170 – 6.

[6] Cho SH, Byun CS, Kim KW, Chang BC, Yoo KJ, et al. Preoperative indexed left ventricular dimensions to predict early recovery of left ventricular function after aortic valve replacement for chronic aortic regurgitation. Circ J 2010; 74:2340–5.

[7] Vahanian A, Alfieri O, Andreotti F, Antunes MJ, Baron-Esquivias G, et al. Guidelines on the

management of valvular heart disease (version 2012). The Joint Task Force on the Management

of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European

Association for Cardio-Thoracic Surgery (EACTS) Eur Heart J 2012; 33, 2451–96

[8] Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP III, et al. 2014 AHA/ACC

guideline for the management of patients with valvular heart disease: executive summary: a

report of the American College of Cardiology/American Heart Association Task Force on

Practice Guidelines. J Am Coll Cardiol 2014; 63:2438–88.

[9] Cary W. Akins, D. Craig Miller, Marko I. Turina, Nicholas T.Kouchoukos, Eugene H.

Blackstone, et al. Guidelines for Reporting Mortality and Morbidity After Cardiac Valve

Interventions　Ann Thorac Surg. 2008;85:1490–5

[10] Lan RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, et al. Recommendations for

chamber quantification: a report from the American Society of Echocardiography's guidelines

and standards committee and the chamber quantification writing group, developed in

conjunction with the European Association of Echocardiography, a branch of the European

Society of Echocardiography. J Am Soc Echocardiogr 2005; 18:1440–63.

[11] Daimon M, Watanabe H, Abe Y, Hirata K, Hozumi T, et al. Normal values of

echocardiographic parameters in relation to age in a healthy Japanese population. Circ J 2008;

72: 1859 – 66.

[12] Sénéchal M, Bernier M, Dagenais F, Dubois M, Dubois-Sénéchal I, et al. Usefulness of Preoperative Stroke Volume as Strong Predictor of Left Ventricular Remodeling and Outcomes After Aortic Valve Replacement in Patients With Severe Pure Aortic Regurgitation Am J Cardiol 2011;108:1008 –13

[13] Enriquez-Sarano, Tajik A. Aortic regurgitation. N Engl J Med 2004; 351:1539–46

[14] Chaliki HP, Mohty D, Avierinos JF, Scott CG, Schaff HV, et al. Outcomes after aortic valve replacement in patients with severe aortic regurgitation and markedly reduced left ventricular function. Circulation 2002; 106:2687–93.

[15] Klodas E, Enriquez-Sarano M, Tajik AJ, Mullany CJ, Bailey KR, et al. Aortic regurgitation complicated by extreme left ventricular dilation: Long-term outcome after surgical correction. J Am Coll Cardiol 1996; 27**:** 670 – 7.

[16] Iung B, Baron G, Butchart EG, Delahaye F, Gohlke-Ba¨rwolf C, et al. A prospective survey of patients with valvular heart disease in Europe: the Euro Heart Survey on Valvular Heart Disease. Eur Heart J 2003; 24:1231–43.

[17] Taniguchi K, Nakano S, Kawashima Y, Sakai K, Kawamoto T, et al. Left ventricular ejection performance, wall stress, and contractile state in aortic regurgitation before and after aortic valve replacement. Circulation 1990; 82:798–807.

[18] Bonow RO, Dodd JT, Maron BJ, O'Gara PT, White GG, et al. Long-term serial changes in

left ventricular function and reversal of ventricular dilatation after valve replacement for chronic

aortic regurgitation. Circulation 1988; 78:1108–20.

[19] Bhudia SK, McCarthy PM, Kumpati GS, Helou J, Rajeswaran J, et al. Improved outcomes

after aortic valve surgery for chronic aortic regurgitation with severe left ventricular

dysfunction. J Am Coll Cardiol 2007; 49:1456-71.

[20] Kamath AR, Varadarajan P, Turk R, Sampat U, Patel R, et al. Survival in patients with

severe aortic regurgitation and severe left ventricular dysfunction is improved by aortic valve

replacement: results from a cohort of 166 patients with an ejection fraction < or =35%.

Circulation 2009; 120:S134-8.

[21] Bonow RO, Carabello BA, Chatterjee K, Leon AC, de Faxon DP Jr, et al. Focused update

incorporated into the ACC/AHA 2006 guidelines for the management of patients with valvular

heart disease: a report of the American College of Cardiology/ American Heart Association

Task Force on Practice Guidelines (writing committee to revise the 1998 guidelines for the

management of patients with valvular heart disease): endorsed by the Society of Cardiovascular

Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of

Thoracic Surgeons. Circulation 2008; 118:e523–661.

[22] Turk R, Varadarajan P, Kamath A, Sampat U, Khandhar S, et al. Survival benefit of aortic

valve replacement in older patients with asymptomatic chronic severe aortic regurgitation. Ann

Thorac Surg 2010; 89:731–7.

[23] Kang HJ, Kim YJ, Sohn DW, Oh BH, Lee MM, et al. Prediction of postoperative left

ventricular systolic function with Doppler-derived dP/dt in patients with chronic aortic

regurgitation. J Am Soc Echocardiogr 2003; 16: 1111 – 5.

[24] Hirooka K, Yasumura Y, Tsujita Y, Hanatani A, Nakatani S, et al. Enhanced method for

predicting left ventricular reverse remodeling after surgical repair of aortic regurgitation:

Application of ultrasonic tissue characterization. J Am Soc Echocardiogr 2002; 15: 695 – 701.

[25] Sénéchal M, Lancellotti P, Garceau P, Champagne J, Dubois M, et al. Usefulness and

limitation of dobutamine stress echocardiography to predict acute response to cardiac

resynchronization therapy. Echocardiography 2010; 27:50 –7.

[26] Tribouilloy C, Lévy F, Rusinaru D, Guéret P, Petit-Eisenmann H, et al. Outcome after

aortic valve replacement for low-flow/low-gradient aortic stenosis without contractile reserve on

dobutamine stress echocardiography. J Am Coll Cardiol 2009; 53:1865–73

[27] Liang-han Ling, Peter M. Kistler, Andris H. Ellims, Leah M. Iles, Geraldine Lee, et al.

Diffuse Ventricular Fibrosis in Atrial Fibrillation. J Am Coll Cardiol 2012; 60:2402–8

[28] Zhou X, Sheng Y, Yang R, Kong X. Nicotine promotes cardiomyocyte apoptosis via

oxidative stress and altered apoptosis-related gene expression. Cardiology 2010; 115:243–50.

[29] Ibe W, Saraste A, Lindemann S, Bruder S, Buerke M, et al. Cardiomyocyte apoptosis is

related to left ventricular dysfunction and remodeling in dilated cardiomyopathy, but is not

affected by growth hormone treatment. Eur J Heart Fail 2007; 9:160–7.

Figure legends

(Table 1) Comparison of preoperative patients' characteristics

Characteristics	All patients	Group L	Group S	P value
Number of patients	177	130	47	
Age (years)	58.4 ± 15.4 (21〜84)	58.7 ± 15.4 (26〜84)	57.7 ± 15.6 (21〜84)	0.71
Male / Female	122 / 55	90 / 40	32 / 15	0.83
BSA (m^2)	1.57 ± 0.17	1.56 ± 0.16	1.60 ± 0.17	0.11
NYHA Ⅲ or Ⅳ	37 (20.9%)	26 (20.0%)	11 (23.4%)	0.09
EDD (mm)	63.6 ± 8.5 (45〜88)	66.0 ± 8.1 (47〜88)	57.1 ± 5.8 (45〜67)	<0.01
iEDD (mm/m^2)	40.9 ± 6.0 (29〜62)	42.9 ± 5.5 (35〜62)	35.4 ± 3.1 (29〜42)	<0.01
ESD (mm)	43.7 ± 8.6 (28〜68)	46.7 ± 7.9 (32〜68)	35.6 ± 4.4 (28〜45)	<0.01
iESD (mm/m^2)	28.2 ± 6.0 (17〜49)	30.4 ± 5.5 (25〜49)	22.1 ± 1.8 (17〜24)	-
EF (%)	58.0 ± 10.3 (31〜74)	54.8 ± 9.7 (31〜72)	66.6 ± 6.0 (57〜79)	<0.01

BSA: body surface area

NYHA: New York Heart Association

EDD: end diastolic diameter

iEDD: indexed end diastolic diameter

ESD: end systolic diameter

iESD: indexed end systolic diameter

EF: ejection fraction

Group L: iESD > 25 mm/m^2, Group S: iESD $\leqq$ 25 mm/m^2
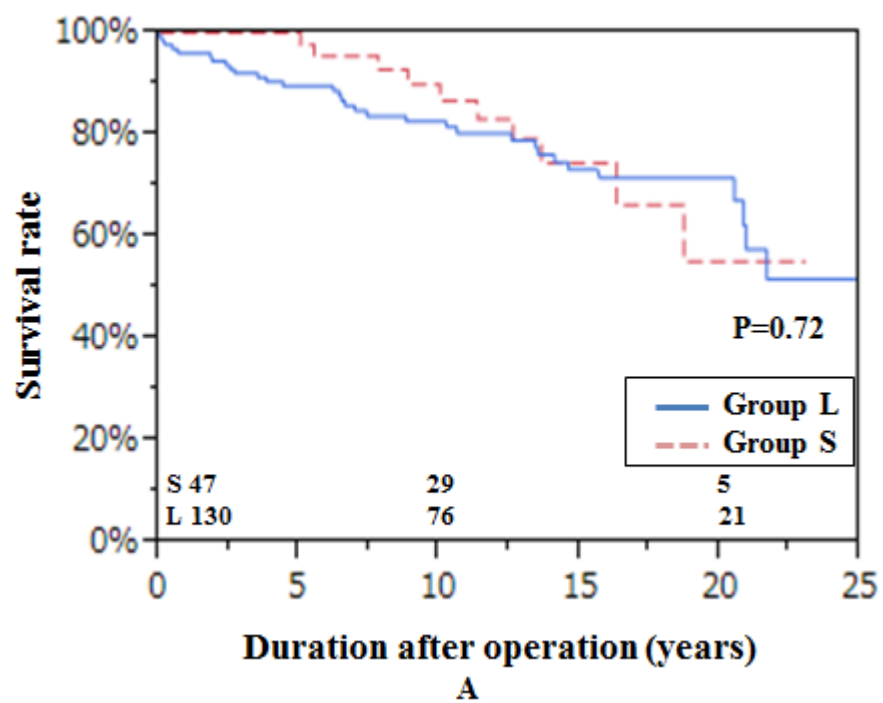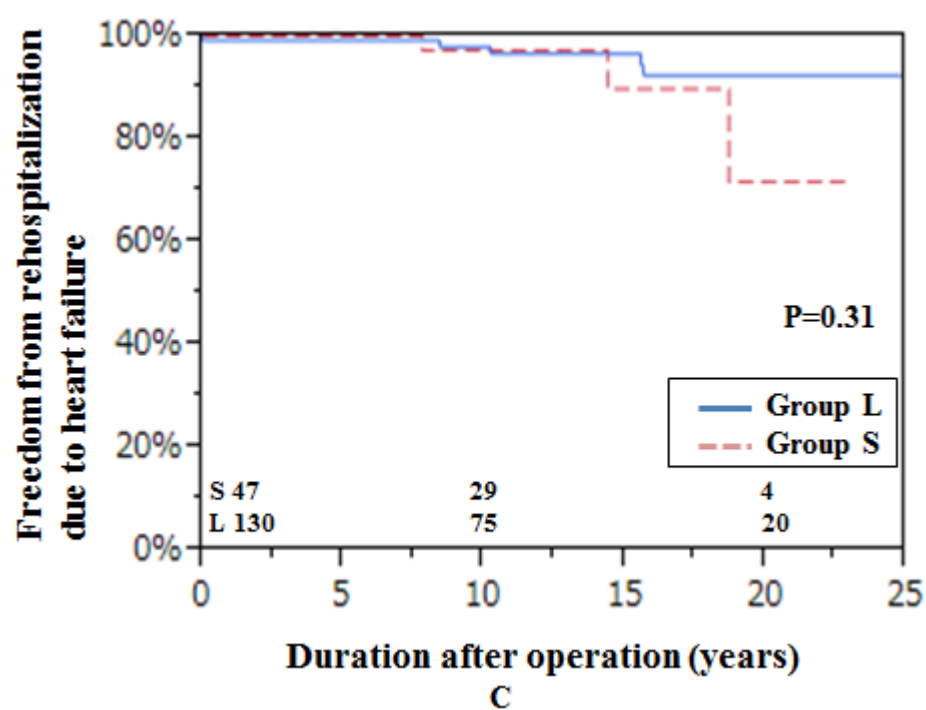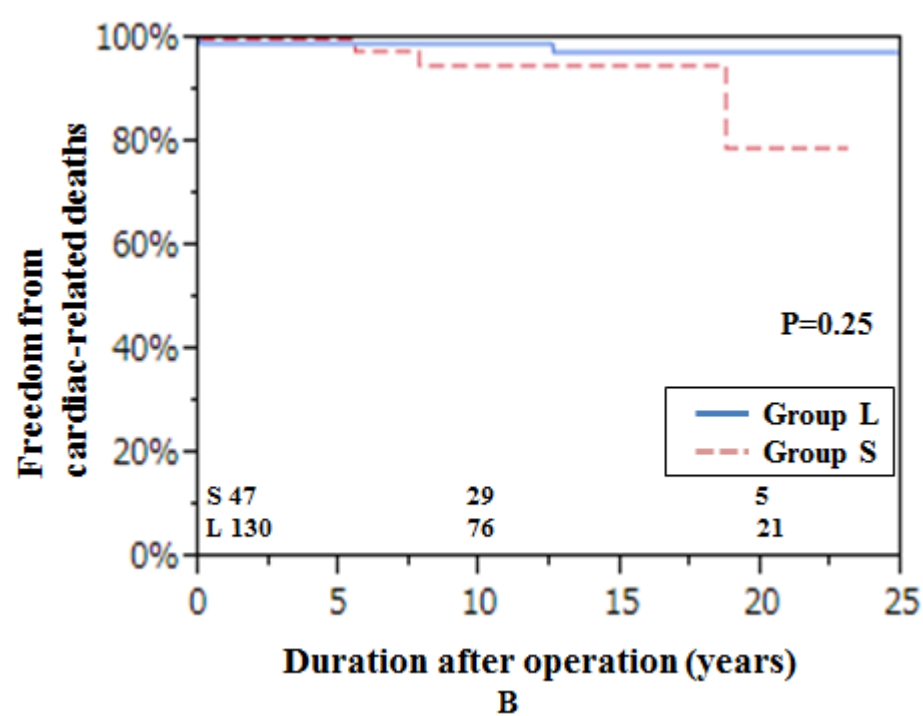
P value: Group L vs Group S

(Fig 1)

(A) Actuarial survival rate

(B) Freedom from cardiac-related deaths

(C) Freedom from rehospitalization due to heart failure

Group L: iESD > 25 mm/m^2, Group S: iESD $\leqq$ 25 mm/m^2

B

C

(Fig 2)

(A) Preoperative, immediate postoperative, early postoperative and late postoperative iEDD

(B) Preoperative, immediate postoperative, early postoperative and late postoperative iESD

(C) Preoperative, immediate postoperative, early postoperative and late postoperative EF.

iEDD: indexed end diastolic diameter

iESD: indexed end systolic diameter
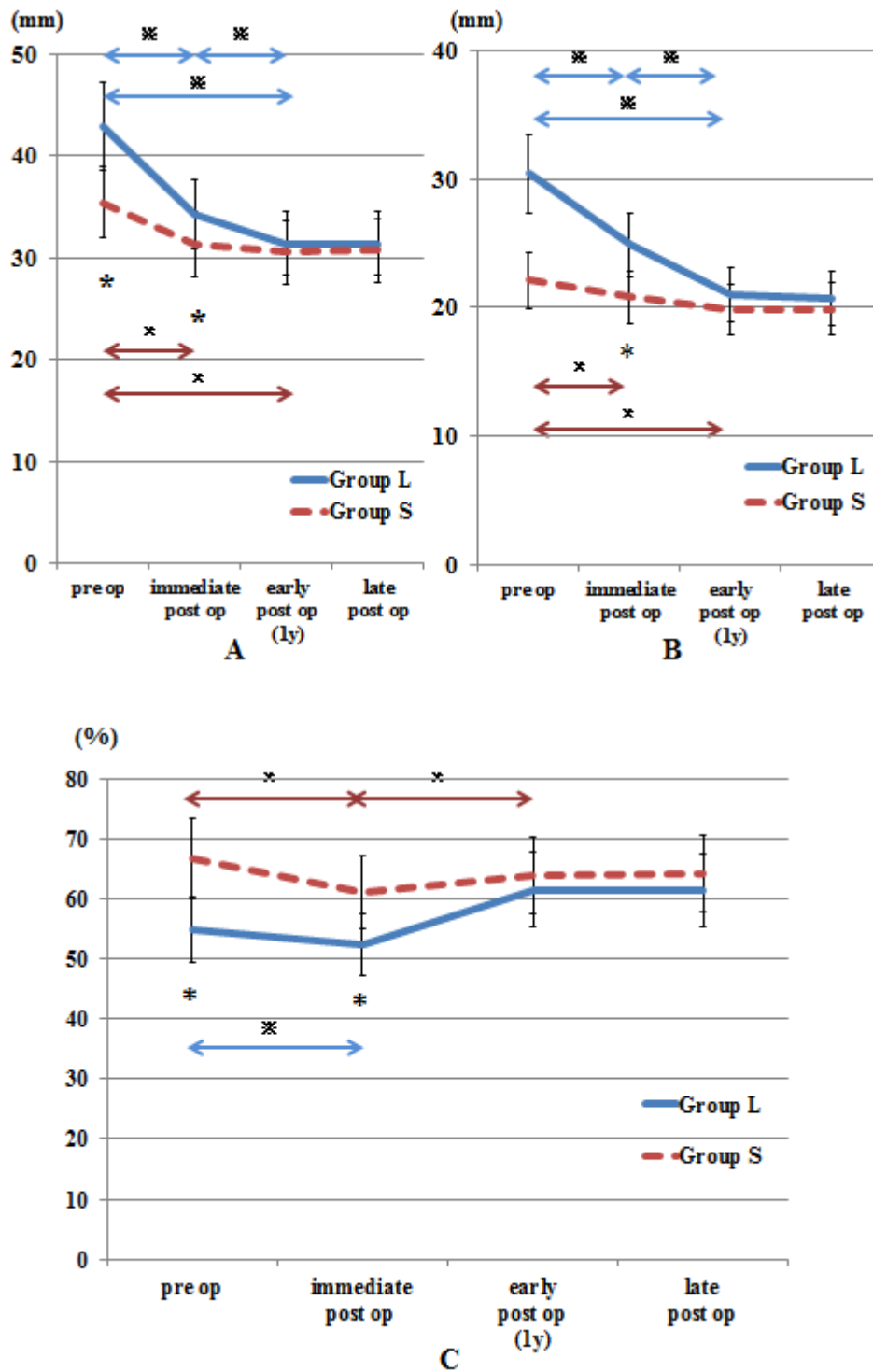
EF: ejection fraction

op: operation

1y: 1 year

Group L: iESD > 25 mm/m^2, Group S: iESD $\leqq$ 25 mm/m^2

* : Significant difference ($p < 0.05$) between 2 groups.

※ : $p < 0.05$ between 2 periods in Group L

× : $p < 0.05$ between 2 periods in Group S

(Table 2) Summary of eight rehospitalized patients

Patient	Pre-ope iEDD / iESD (mm/m^2)	Pre-opeEF (%)	Cause of rehospitalization	Outcome	Duration from surgery (mo)
64 M	35 / 19	75	CHF following thrombosed valve	death	66
67 M	57 / 40	51	CHF with exacerbation of MR	death	93
47 M	56 / 44	43	CHF due to difficulty with volume control for HD	death	101
66 F	37 / 24	64	CHF with new occurrence of AF and exacerbation of MR	death	234
69 M	37 / 29	42	CHF with exacerbation of MR	alive	128
72 M	35 / 24	60	unknown	alive	174
51 M	40 / 30	48	CHF with exacerbation of MR	alive	186
40 M	45 / 40	27	CHF with CRT for trifasoicular block	alive	186

iEDD: indexed end diastolic diameter

iESD: indexed end systolic diameter

EF: ejection fraction

CHF: congestive heart failure

MR: mitral regurgitation

HD: hemodialysis

AF: atrial fibrillation

CRT: cardiac resynchronization therapy

mo: month

(Table 3) Multivariable Cox proportional hazards regression model of recovery of LV systolic

function

Variable	Odds ratio [95% Confidence Interval]	P value
iESD	3.72 [1.05-13.2]	0.04
EF	3.14 [0.92-10.71]	0.06
CI	4.76 [1.38-16.39]	0.01
AF	5.22 [0.99-27.46]	0.05
smoking	2.82 [0.93-8.53]	0.06

LV: left ventricle

iESD: :indexed end systolic diameter

EF: ejection fraction

CI: cardiac index

AF: atrial fibrillation