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ORIGINAL ARTICLE

Abnormal Tei index predicts poor left ventricular mass regression and survival after AVR in aortic stenosis patients

Koji Tao (MD)[a,*], Ryuzo Sakata (MD, FJCC)[a], Yoshifumi Iguro (MD)[a], Tetsuya Ueno (MD)[a], Masahiro Ueno (MD)[a], Yasuhiro Tanaka (MD, FJCC)[b], Yutaka Otsuji (MD, FJCC)[c], Chuwa Tei (MD, FJCC)[b]

[a] *Department of Cardiovascular Surgery, Graduate School of Medicine, Kagoshima University, Kagoshima, Japan*

[b] *Cardiovascular Medicine, Graduate School of Medicine, Kagoshima University, Kagoshima, Japan*

[c] *The Second Department of Internal Medicine, University of Occupational and Environmental Health Japan School of Medicine, Fukuoka, Japan*

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Summary
Background: A Tei index is known to reflect overall cardiac performance including systolic and diastolic function in a variety of heart disease. We investigated the relationship between preoperative Tei index and postoperative left ventricular (LV) mass regression and survival after aortic valve replacement (AVR) for aortic valve stenosis (AS).
Methods: One hundred fifty-four patients with AS were classified into a group with abnormal (Abn) LV function ($n = 47$, $0.45 \leq$ Tei index) and a group with normal (Nor) LV function ($n = 107$, Tei index < 0.45). The pre- and postoperative echocardiographic variables including LV dimension, LV wall thickness, and LV mass regression as well as 6-year survival were compared between the two groups.
Results: There was a significant difference in both absolute and relative LV mass index (LVMI) regression ($P = 0.004$ and 0.0007). Multiple linear regression analysis revealed that the preoperative LVMI, Tei index, and follow-up period were independent predictors of LVMI regression after AVR. Thirteen patients died (valve-related

Abbreviations: AS, aortic stenosis; AVA, aortic valve area; AVR, aortic valve replacement; BSA, body surface area; CABG, coronary artery bypass grafting; EOA, effective orifice area; EOAI, indexed effective orifice area; IVS, interventricular septal thickness; LV, left ventricular; LVEF, left ventricular ejection fraction; LVDD, left ventricular end-diastolic diameter; LVM, left ventricular mass; LVMI, left ventricular mass index; NYHA, New York Heart Association; PG, pressure gradient; PPM, prosthesis-patient mismatch; PW, posterior wall thickness.

* Corresponding author.
E-mail address: koji-tao@sea.plala.or.jp (K. Tao).

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death in 5). Although the overall survival rate in the Nor-LV group (92.8%) was significantly better than that in the Abn-LV group (71.6%), there was no significant difference in survival free from valve-related death.
Conclusions: Preoperative Tei index can be one of the significant predictors of LVMI regression and overall survival after AVR.

Introduction

Reduction of the left ventricular mass (LVM) with consequent improvement in cardiac function is an essential objective of aortic valve replacement (AVR) in patients with aortic stenosis (AS). However, because of small valve annulus often seen in AS, an inappropriately smaller size of prosthetic valves have to be implanted in some cases. Since the concept of prosthesis-patient mismatch (PPM) was first described by Rahimtoola in 1978, the impact of the PPM on postoperative LV mass regression or survival has been intensively investigated, however, it remains controversial [1].

Recently, Ruel and coworkers showed coexistence of the LV systolic dysfunction with low ejection fraction amplified the risk of the PPM on LVM regression and survival [2]. Apart from the LV ejection fraction, the Tei index is a combined measure of both systolic and diastolic LV function [3]. In the present study, we focused on the influence of the preoperative LV performance estimated by the Tei index on LVM regression and survival at the late stage after AVR.

Patients and methods

From January 2000 to December 2006, 343 patients underwent AVR, and we selected 154 consecutive patients with aortic stenosis that received a mechanical or bioprosthetic valve. Patients undergoing other concomitant surgical procedures were permitted to enter the study. Exclusion criteria included severe aortic regurgitation, severe mitral regurgitation, mitral stenosis, coronary artery bypass grafting (CABG) for unstable angina, and acute or healed myocardial infarction. Perioperative data were obtained by retrospective review of hospital records and echocardiographic reports. Follow-up information was obtained directly in our hospital and through comprehensive questionnaires and by telephone interview with surviving patients, family members, or the patient's personal physician. The study was approved by our institution's review board (IRB) and informed consent was obtained from all patients. The Tei index was calculated as (ICT + IRT)/ET (ICT: isovolemic contraction time, IRT: isovolemic relaxation time, and ET: ejection time). The normal Tei index is 0.39 ± 0.05; it is assumed that a value of >0.45 is indicative of LV dysfunction. Ono and coworkers reported that the patients with various heart disease whose Tei index more than 0.45 showed significantly increased BNP levels than the patients with Tei index less than 0.45. Based on their conclusion, we set the cut-off value of Tei index as 0.45 [4]. The patients ($n = 154$) were divided into two groups based on a preoperative Tei index ≥ 0.45 ($n = 47$; Abn-LV group) or <0.45 ($n = 107$; Nor-LV group) for comparative analysis. Postoperative echocardiography was performed from 7 days to 6 years (mean, 1.98 ± 1.8 years) following the operation in all patients, and the preoperative and postoperative values of transvalvular pressure gradient (PG), LV systolic and diastolic function, and the absolute and relative regression in LVM index (LVMI) were compared between the Abn-LV and the Nor-LV groups.

Surgical techniques

The operation was performed by two senior surgeons (RS) and (YI). The patients were placed on cardiopulmonary bypass by aortic and bicaval cannulation. After antegrade cold cardioplegia solution was infused, an oblique aortotomy was made to expose the aortic valve. The vent tube was inserted from the right superior pulmonary vein. Selective infusion of cardioplegia solution was repeated every 30 min during cardiac arrest. Prosthesis size was selected according to the size of the aortic annulus; the prosthesis was usually implanted by means of multiple, interrupted, everting, mattress sutures reinforced with Teflon pledgets placed in an intra-annular position or was implanted in a supra-annular position using the technique of multiple, interrupted, noneverting pledgets vertical mattress sutures.

Doppler echocardiographic measurements

Preoperative and postoperative echocardiographic studies were performed by experienced echocardiographers using a 2- or 3-MHz transducer and phased array sector scanner (HDI 5000, ATL Ultrasound, Inc., Bothell, WA, USA; Sonos 5500, Phillips Medical Systems, Andover, MA, USA). The preoperative echocardiograms were recorded 0—7 days before surgery and postoperative echocardiograms were obtained at least 7 days after the operation. Standard parasternal, apical, subcostal, and suprasternal views were obtained. Hemodynamic variables were calculated using standard formulae. The measurement and significance of the Tei index are described in detail elsewhere [3]. The transvalvular PG was determined using the modified Bernoulli equation [5]; aortic valve area (AVA) was calculated by the continuity equation [5]; and LVM was calculated by the Devereux formula [6]. LV systolic performance was evaluated by means of the left ventricular ejection fraction (LVEF) calculated from biplane images using a modification of Simpson's method. LV diastolic performance was evaluated by means of the E/A and deceleration time (DcT). The indexed effective orifice area (EOAI) for each prosthesis was easily calculated from the normal reference value of effective orifice area (EOA) divided by the patient's body surface area [6].

Pibarot et al. defined PPM as clinically insignificant if the EOAI > $0.85\,\mathrm{cm^2/m^2}$, as moderate if it was >$0.65\,\mathrm{cm^2/m^2}$ but $\leq 0.85\,\mathrm{cm^2/m^2}$, and as severe if it was $\leq 0.65\,\mathrm{cm^2/m^2}$ [7]. In the present study, PPM was also defined as an EOAI $\leq 0.85\,\mathrm{cm^2/m^2}$, based on the recommendation of Pibalot et al.

Statistical analysis

The data were statistically analyzed using JMP 6.0.3 software (SAS, Inc., Chicago, IL, USA). The continuous variables were expressed as mean values ± standard deviation (S.D.). The normality of the distributions in the two groups was tested by means of the Shapiro—Wilk test. A Student's *t*-test or Wilcoxon test for continuous variables, and a chi-square test or Fisher's exact test for discrete variables were used, as appropriate. The relationship between the preoperative peak PG, mean PG, EOAI, the preoperative LVMI, follow-up period and the absolute LVMI regression were evaluated by means of simple linear regression analysis in order to calculate *r* (Pearson's correlation coefficient). The variables with a *P* value <0.10 in the univariate regression analysis were entered into a multiple linear regression analysis to identify the independent predictors of absolute LVMI regression. A *P* value <0.05 was considered significant.

Results

Preoperative data

Table 1 shows patients' preoperative and operative characteristics classified into an Abn-LV group ($n = 47$, Tei index < 0.45) and a Nor-LV group ($n = 107$, Tei index < 0.45). The mean age, BSA, AVA, peak aortic PG, and mean aortic PG were not significantly different between the two groups. There were no significant differences in prevalence of female gender, hemodialysis, New York Heart Association (NYHA) class III or IV, and concomitant procedures between the two groups. However, the Abn-LV group had more patients with an LVEF ≤40% compared with the Nor-LV group.

Implanted valves

There were 126 mechanical prostheses (81.8%) and 28 bioprostheses (18.2%) implanted. Among the patients, 80 received a St. Jude Medical Hemodynamic Plus prosthesis (St. Jude Medical, Inc., St. Paul, MN, USA), 13 received a Sorin Bicarbon Slimline prosthesis (Sorin Biomedica, Saluggia, Italy), 11 received a St. Jude Medical standard prosthesis (St. Jude Medical, Inc., St. Paul, MN, USA), 7 received a Carbomedics Top Hat prosthesis (Carbomedics, Inc., Austin, TX, USA), 6 received a St. Jude Medical Regent prosthesis (St. Jude Medical, Inc., St. Paul, MN, USA), 6 received an ON-X prosthesis (Medical Carbon Research Institute, Austin, TX, USA) and 3 received an ATS Advanced Performance prosthesis (ATS Medical, Inc., Minneapolis, MN, USA). All patients in the bioprosthetic group received Carpentier—Edwards perimount bioprosthesis (Edwards Lifesciences Corp., Inc., Irvine, CA, USA). The distribution of patients in regard to prosthesis size was 17 mm in 16 patients, 19 mm in 57 patients, 21 mm in 56 patients, 23 mm in 19 patients, and 25 mm in 3 patients. Concomitant surgical procedures included CABG in 33, combined valvular disease in 2 and ascending aorta replacement in 18. We tried to implant prosthetic valves as large as possible without an aortic-root enlargement procedure, and subsequently, only one patient underwent Nick's procedure and was implanted with an SJM 17 mm HP valve.

Operative data

The mean EOAI was not different between the two groups. There were 22 PPM patients (Abn-LV, 5; Nor-LV, 17) in both groups, and the mean EOAI of the PPM patients was not statistically different between the

Table 1 Preoperative and operative patient characteristics.

Characteristic	Abn-LV	Nor-LV	*P*-Value
Number of patients	47	107	–
Age (years), mean ± S.D.	72.9 ± 9.0	70.0 ± 10.2	0.0954
Sex (female)	55.3%	56.1%	0.9307
BSA (m^2), mean ± S.D.	1.49 ± 0.18	1.50 ± 0.15	0.8360
Aortic valve area (cm^2), mean ± S.D.	0.58 ± 0.18	0.59 ± 0.19	0.7102
Peak aortic gradient (mmHg) mean ± S.D.	92.9 ± 27.0	101.4 ± 32.3	0.1209
Mean aortic gradient (mmHg), mean ± S.D.	54.4 ± 18.3	58.5 ± 18.8	0.2114
Valve pathology			
AS/ASR	34/13	73/34	0.6095
Bicuspid	34.0%	33.7%	0.9627
Hemodialysis	8.5%	4.7%	0.3498
Atrial fibrillation	6.4%	3.7%	0.4681
LVEF ≤ 40%	12.8%	2.8%	0.0152
NYHA class III or IV	28.3%	20.2%	0.2764
AVR only/AVR and concomitant procedure	28/19	70/37	0.4874
Bioprosthesis/mechanical prosthesis	9/38(19.2%)	19/88(17.8%)	0.8366
EOAI (cm^2/m^2)	0.99 ± 0.13	0.96 ± 0.13	0.2050
PPM (EOAI ≤ 0.85 cm^2/m^2)	5(10.6%)	17(15.9%)	0.3913
Aortic cross-clamp time (min)	98.1 ± 23.3	95.9 ± 25.8	0.6244
Cardiopulmonary bypass time (min)	139.0 ± 31.6	133.7 ± 34.8	0.3736

AS, aortic stenosis; AVR, aortic valve replacement; BSA, body surface area (m^2); LVEF, left ventricular ejection fraction (%); NYHA, New York Heart Association.

two groups. There was no severe PPM patient in either group.

Early mortality

Although there were no deaths within 30 days after the operation, 2 patients (1 in Abn-LV group) died during the same hospitalization period. The cause of death was sepsis in one and brain death in one resulting from ventricular fibrillation induced by a Swan—Ganz catheter during the induction of anesthesia. None of these deaths was related to the prosthetic valve size or LV dysfunction.

Late mortality

The follow-up period ranged from 0.27 to 6.8 years (median, 3.48 years). Eleven patients (Abn-LV, 6; Nor-LV, 5) died during the follow-up period. Among the patients who died, five deaths (3 in Abn-LV group) were valve-related including four sudden deaths and one cerebral hemorrhage. Among the six non-valve-related deaths, three patients died from respiratory failure, one patient died from sepsis, one from non-occlusive mesenteric ischemia, and one from low output syndrome (LOS). The overall survival rate at 1, 3, and 6 years was 93.5%, 86.7%, and 71.6% in the Abn-LV group, respectively; and 97.2%, 94.8%, and 92.8% in the Nor-LV group ($P = 0.0307$) (Fig. 1). Survival free from valve-related death at 1, 3, and 6 years was 97.8%, 90.7%, and 90.7% in the Abn-LV group, respectively; and 99.0%, 99.0%, and 96.9% in the Nor-LV group ($P = 0.0696$) (Fig. 1). There was a significant difference in overall survival, but no significant difference in survival free from valve-related death between the two groups. However, the Nor-LV group showed a trend toward higher survival free from valve-related death rate.

Prosthetic valve hemodynamics

Follow-up echocardiography was performed at 1.52 ± 1.76 years following the operation in the Abn-LV group and at 2.18 ± 1.77 years in the Nor-LV group ($P = 0.0343$). There was no significant difference in the postoperative peak and mean PGs between the two groups. No structural or functional abnormalities of the prostheses were found during the postoperative examination.

Left ventricular morphologic changes

The preoperative and postoperative echocardiographic data are shown in Table 2. In both groups, LVDd, LVDs, IVS + PW, LVM, and LVMI all decreased significantly after AVR, where interventricular septal (IVS) and PW are standard measures

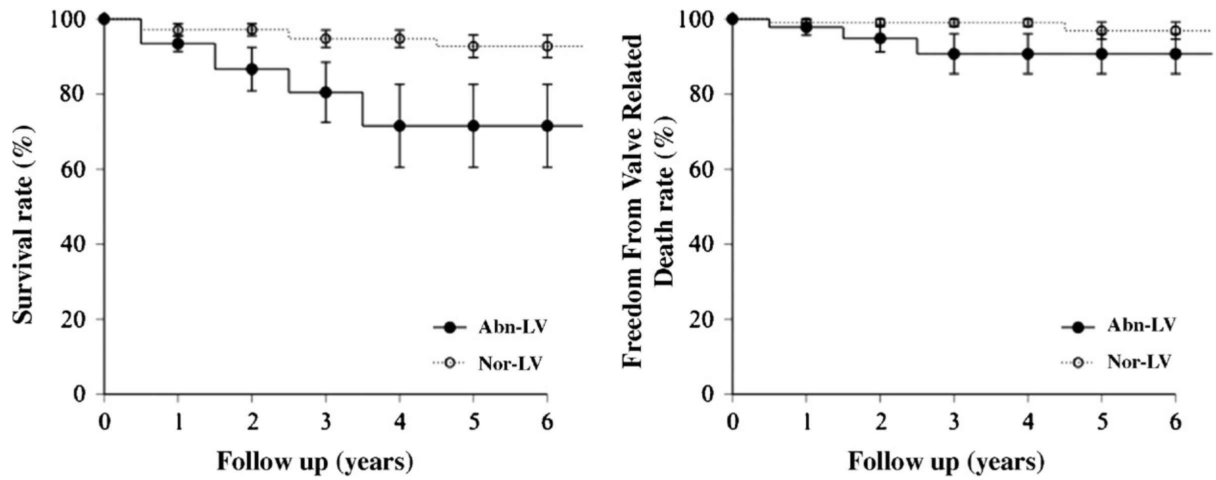

Figure 1 Actuarial survival curve and actuarial freedom from valve-related death. The overall survival rate in the Abn-LV group was significantly worse than that in the Nor-LV group (left). There was no significant difference in actuarial freedom from valve-related death between two groups (right).

(in millimeters) of IVS thickness and posterior wall thickness (PW). There were no significant differences in these parameters between the two groups. However, there was a significant difference in absolute and relative IVS + PW regression and LVM regression or LVMI regression between the two groups.

Left ventricular functional changes

There was a significant difference in preoperative LVEF between the two groups, but there was no difference in postoperative LVEF. There was no improvement in LVEF after the operation in either group. Preoperative E/A in the Abn-LV group was significantly lower than that in the Nor-LV group whereas there was no significant difference between two groups after AVR. The postoperative Tei index was 0.55 ± 0.17 in the Abn-LV group and 0.43 ± 0.15 in the Nor-LV group ($P = 0.0007$). In the Nor-LV group, the Tei index significantly increased after AVR (Table 2).

Predictors of left ventricular mass regression

In univariate regression, the EOAI and preoperative LVEF were not significantly correlated with LVMI regression. However, the absolute LVMI regression was significantly correlated with the preoperative IVS + PW, peak and mean aortic PG, preoperative Tei index, preoperative LVMI and follow-up period; and these variables were entered into a multiple linear regression analysis. In this analysis, female sex, preoperative Tei index, preoperative LVMI and follow-up period were all independent predictors of LVMI regression after AVR (Table 3).

Discussion

PPM, LVM regression, and survival

In the past two decades, numerous studies have focused on the relationship among three important issues related to AVR for AS, including the PPM, LVM regression, and survival. However, a retrograde fashion in most of these investigations including patients with different preoperative conditions might have contributed, to some extent, to the varying results and conclusions.

PPM and patients' survival

The impact of PPM on early and long-term patients' survival has been intensively investigated and a majority of the literature showed their positive relationship. Blais et al. showed that PPM (severe, EOAI ≤ 0.65; moderate, $0.65 < \text{EOAI} \leq 0.85$) was a strong and independent predictor of short-term mortality among patients undergoing AVR [8]. However, Pibarot et al. studied the impact of PPM (EOAI ≤ 0.85) on 7-year survival after AVR and found no difference between those with and without mismatch [7]. In our previous study, the presence of PPM did not significantly affect the long-term survival of patients [9].

PPM and LVM regression

The relationship between the PPM and LVM regression also remains controversial. Del Rizzo et al.

Table 2 Preoperative and postoperative left ventricular morphologic and functional changes.

Parameters	Abn-LV 47	Nor-LV 107	*P*-Value
Echocardiography follow-up (years)	1.52 ± 1.76	2.18 ± 1.77	0.0343
LVDd (mm) mean ± S.D.			
Preoperative	46.4 ± 7.12	46.2 ± 6.08	0.8851
Postoperative	44.3 ± 6.83**	42.8 ± 5.46**	0.1493
LVDs (mm) mean ± S.D.			
Preoperative	30.8 ± 9.28	27.9 ± 7.26	0.0409
Postoperative	28.6 ± 8.30**	26.6 ± 5.67*	0.0879
IVS + PW (mm) mean ± S.D.			
Preoperative	29.6 ± 5.36	30.6 ± 5.57	0.3009
Postoperative	26.6 ± 4.89**	25.7 ± 4.51**	0.2332
Absolute IVS + PW regression (mm) mean ± S.D.	3.00 ± 5.23	5.03 ± 4.52	0.0160
Relative IVS + PW regression (%) mean ± S.D.	8.40 ± 18.0	15.3 ± 13.3	0.0090
LVM (g) mean ± S.D.			
Preoperative	285.1 ± 86.2	301.5 ± 93.0	0.3040
Postoperative	229.0 ± 75.5**	206.3 ± 64.9**	0.0593
Absolute LVM regression (g), mean ± S.D.	56.1 ± 78.3	95.8 ± 73.4	0.0029
Relative LVM regression (%), mean ± S.D.	16.9 ± 25.3	29.7 ± 18.0	0.0005
LVMI (g/m^2), mean ± S.D.			
Preoperative	191.9 ± 53.6	201.2 ± 57.4	0.3486
Postoperative	152.9 ± 44.5**	136.5 ± 38.1**	0.0210
Absolute LVMI regression (g/m^2), mean ± S.D.	39.0 ± 53.0	64.7 ± 48.9	0.0040
Relative LVMI regression (%), mean ± S.D.	17.3 ± 25.2	29.8 ± 18.2	0.0007
Relative wall thickness, mean ± S.D.			
Preoperative	0.66 ± 0.18	0.68 ± 0.17	0.5589
Postoperative	0.62 ± 0.16*	0.61 ± 0.14**	0.7897
LVEF (%), mean ± S.D.			
Preoperative	61.3 ± 16.0	68.2 ± 12.3	0.0040
Postoperative	64.2 ± 12.7	67.1 ± 10.1	0.1250
E/*A*, mean ± S.D.			
Preoperative	0.64 ± 0.22	0.82 ± 0.54	0.0331
Postoperative	0.95 ± 0.73	0.92 ± 0.36	0.7428
DcT (ms), mean ± S.D.			
Preoperative	259.5 ± 92.6	269.6 ± 88.3	0.5423
Postoperative	245.7 ± 78.4	236.1 ± 59.3	0.4920
Tei index, mean ± S.D.			
Preoperative	0.58 ± 0.13	0.30 ± 0.09	<0.0001
Postoperative	0.55 ± 0.17	0.43 ± 0.15**	0.0007

IVS, interventricular septal thickness (mm); PW, posterior wall thickness (mm); LVM, left ventricular mass (g); LVMI, left ventricular mass index (%); LVEF, left ventricular ejection fraction (%); DcT, deceleration time.

* Postoperative vs. preoperative $P < 0.05$.

** Postoperative vs. preoperative $P < 0.001$.

found a strong, independent relationship between the EOAI and the extent of LVM regression in 1103 patients who underwent AVR with a stentless porcine valve [10]. Tasca et al. showed that in patients with pure AS, PPM was associated with less regression of LVM. In their series of studies, a larger projected EOAI, female gender, and a higher preoperative LVM were independent predictors of greater LVM regression [11,12]. Contrary to these reports, Hanayama et al. found no significant relationship between PPM and regression of LV hypertrophy, and concluded that the most important independent predictor of incomplete LVM regression was the extent of preoperative LVMI rather than the size of aortic prostheses, the presence of PPM, or the mean and peak PG [13]. Recently, Imanaka et al.

Table 3 Independent predictors of absolute LV mass regression in multiple regression analysis.

Predictive variable	Univariate analysis	Multivariate analysis		
	P-Value	Standardized coefficients (β)	S.E.	*P*-Value
Age	0.3460	—	—	—
Sex (female)	0.0939	0.06387	3.238775	0.2728
IVS + PW	<0.0001	—	—	0.9274
LVEF	0.5897	—	—	—
Tei index	0.0026	−0.18645	16.98942	0.0009
Tei index < 0.45	0.0023	—	—	0.4212
EOAI	0.9883	—	—	—
PPM	0.5505	—	—	—
Preoperative LVMI	<0.0001	0.683681	0.052529	<0.0001
RWT	0.0016	—	—	0.9679
Preoperative peak PG	0.0147	—	—	0.8903
Preoperative mean PG	0.0122	—	—	0.6417
Follow-up period	0.0004	0.149999	1.594038	0.0084

Model: $r = 0.75$, $r^2 = 56\%$, $P < 0.0001$. IVS, interventricular septal thickness (mm); PW, posterior wall thickness (mm); EOA, effective orifice area (cm^2/m^2); LVM, left ventricular mass (g); LVMI, left ventricular mass index (g/m^2).

showed that systolic blood pressure following AVR was the single variable that significantly influenced regression of LV mass [14]. In our previous study, moderate PPM does not appear to alter LVMI regression, NYHA class, or intermediate-term outcome in AS patients undergoing AVR with mechanical prostheses [9].

LVM regression and patients' survival

Mehta et al. showed that increased LVMI was associated with increased adverse in-hospital clinical outcome in patients undergoing AVR [15]. Kratz et al. reported that late deaths after AVR are often caused by sudden cardiac arrest, arrhythmias, or congestive heart failure and these late events may be caused or influenced by LV hypertrophy [16]. In our present study, although two in-hospital deaths were not related to the PPM, it is noteworthy that three out of 4 sudden deaths occurred in the patients with increased LVM in the intermediate term. These reports suggest a positive relationship between LVM regression and patients' survival.

These mixed results, especially related to the PPM, may suggest that the postoperative LVM regression and survival of such critically ill patients are multi-factorial and the PPM alone is not sufficient as their definitive predictor.

Tei index, LVM regression, and survival

It is noteworthy that significant differences were detected in absolute and relative LVMI regressions and in the frequency of postoperative increase of LVM between the two groups without significant difference in the frequency of the PPM. In addition, the EOAI had no direct correlation with absolute and relative regression of LV wall thickness and LVMI. Intimate correlation between the Tei index and LVM regression was further confirmed by multiple linear regression analysis, showing the Tei index was one of the important independent predictors of greater LVM regression. Because of the intimate relationship between the LVM regression and patients' survival mentioned before, it is not surprising that the overall survival of abnormal Tei index group was significantly worse than that of normal Tei index group.

Study limitations

There are several limitations to the present study. First, the study was not performed in a prospective manner. Second, there was a significant difference ($P = 0.03$) in the interval of echocardiographic follow-up. Third, isovolemic contraction and relaxation times were not measured independently, which made us unable to do further investigations about the postoperative changes of the Tei index in both groups. Fourth, many different types of mechanical valves were implanted. Despite these limitations, we believe the present study will shed some scientific light on still unexplained issues, related to AVR for AS patients.

Conclusion

The Tei index can be an independent predictor alternative to the PPM in postoperative LVM regression and long-term patients' survival after AVR for AS.

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