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Late recurrence of left ventricular dysfunction after aortic valve replacement for severe chronic aortic regurgitation☆

Masashi Amano [a], Chisato Izumi [a,*], Sari Imamura [a], Naoaki Onishi [a], Yodo Tamaki [a], Soichiro Enomoto [a], Makoto Miyake [a], Toshihiro Tamura [a], Hirokazu Kondo [a], Kazuaki Kaitani [a], Kazuo Yamanaka [b], Yoshihisa Nakagawa [a]

[a] Department of Cardiology, Tenri Hospital, Tenri, Japan
[b] Department of Cardiovascular Surgery, Tenri Hospital, Tenri, Japan

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ABSTRACT

Background: Aortic valve replacement (AVR) for chronic aortic regurgitation (AR) with a decreased ejection fraction (EF) leads to improvement in left ventricular (LV) function, but there are no reports on late recurrence of LV dysfunction over long-term after AVR. This study aimed to identify frequency and predictors of late recurrent LV dysfunction after AVR.

Methods: We retrospectively investigated 58 consecutive patients undergoing AVR for severe chronic AR and with follow-up echocardiography for >5 years after AVR. Late recurrence of LV dysfunction was defined as an EF of <50% late after AVR and a 10% reduction in the EF compared with that observed at 1 year after AVR.

Results: The mean follow-up period was 10.3 ± 5.2 years. The preoperative EF was <50% in 21 (36%) patients, but it was normalized at 1 year after AVR in all patients except for one. However, late recurrence of LV dysfunction developed in 7 (12%) of the 58 patients. These patients showed significantly higher LV end-diastolic and end-systolic diameters before and at 1 year after AVR, a lower EF and relative wall thickness before AVR, a higher LV mass index at 1 year after AVR, and a higher incidence of preoperative and postoperative atrial fibrillation than those without late recurrence.

Conclusions: Late recurrent LV dysfunction may occur after AVR for severe chronic AR despite EF being once normalized. Early surgery proceeding remarkable LV enlargement and maintaining sinus rhythm are important for LV function over the long-term after AVR.

1. Introduction

In the current American Heart Association/American Colleague of Cardiology guidelines and the European Society of Cardiology/European Association for Cardio-Thoracic Surgery guidelines, aortic valve replacement (AVR) is recommended for patients with severe chronic aortic regurgitation (AR) who have symptoms and/or left ventricular (LV) dysfunction (ejection fraction (EF) <50%, LV end-diastolic diameter (LVDd) >65 or 70 mm, and/or LV end-systolic diameter (LVDs) >50 mm) [1,2]. This is because that previous studies have shown that outcomes of surgical intervention for patients with severe chronic AR and a low EF are poor [3–5], thus AVR is recommended before LV dysfunction develops [6]. On the other hand, the natural history of AR has also been well described and is characterized by a long asymptomatic period followed by a relatively rapid period of worsening after the onset of cardiac symptoms [7–9]. Therefore, patients with severe chronic AR sometimes exhibit LV dysfunction at the initial diagnosis. A recent report [10] described that survival after AVR in patients with preoperative severe LV dysfunction improved dramatically since 1985 and became equivalent to that of patients with non-severe LV dysfunction. In addition, it has been reported that LV function improves on a comparatively short-term after AVR [11,12]. However, in clinical settings, we have experienced some cases in which late recurrence of LV dysfunction developed despite EF being normalized early after AVR. There are few reports on the long-term chronological changes in LV function and no reports on recurrence of LV dysfunction after AVR. The present study aimed to evaluate chronological changes in LV function after AVR in patients with severe chronic AR, and to identify frequency and predictors of late recurrent LV dysfunction during long-term follow-up periods.

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

* Corresponding author at: Department of Cardiology, Tenri Hospital, 200 Mishima-cho, Tenri, Nara 632-8552, Japan.
E-mail address: izumi-ch@tenriyorozu.jp (C. Izumi).

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2. Methods

2.1. Study populations

We retrospectively investigated 58 consecutive patients (44 males, age at AVR: 56 ± 15 years) with severe chronic AR who underwent AVR at our institution between 1995 and 2010 and were followed up with echocardiography for >5 years after AVR in order to evaluate chronological changes in LV function during long-term follow-up periods. Patients who had other severe valvular disease or severe coronary artery disease, defined as >90% stenosis of more than one-vessel or old myocardial infarction, were excluded.

Late recurrence of LV dysfunction was defined as an EF of <50% late after AVR and a 10% reduction in the EF compared with that observed at 1 year after AVR. Furthermore, in order to determine the predictors of late recurrent LV dysfunction after AVR, preoperative laboratory data, medications, and clinical background data were evaluated. All patients gave their written informed consent on the local institutional form to participate in this study. The study protocol was approved by the institutional ethics committee at Tenri Hospital, judging it complaint to the principles outlined in the Helsinki Declaration.

2.2. Clinical characteristics

We investigated the pre- and postoperative clinical characteristics, including underlying disease, smoking habits, medications, and cardiac rhythm. The examined underlying disease included hypertension, hyperlipidemia, diabetes mellitus, cerebral infarction, chronic obstructive pulmonary disease, and connective tissue disease including aortitis. To evaluate the effects of medications, we investigated the use of antiplatelet drugs, anticoagulants, statins, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, β-blockers, diuretics, and digoxin. Preoperative laboratory data were investigated, including hemoglobin concentrations, white blood cell count, eosinophil count, estimated glomerular filtration rate (eGFR), and blood levels of urea nitrogen, creatinine, total cholesterol, and B-type natriuretic peptide. Moreover, the medications at 3 years after AVR were investigated. Patients were classified into the treatment group for a particular medication if they were taking it for >half of the follow-up period. Pre- and postoperative atrial fibrillation was investigated. Here, atrial fibrillation indicated permanent atrial fibrillation, which was defined as detection on an electrocardiogram at least three times during >6 months. Pre- and postoperative hospitalization due to heart failure and occurrence of ventricular tachycardia was also evaluated.

2.3. Echocardiographic examination and parameters

Comprehensive transthoracic echocardiography was performed before AVR, and 1 year and beyond 5 years after AVR, using high-quality, commercially available ultrasound systems [a Toshiba SSH 140-A Ultrasound System (Toshiba Medical Systems, Tochigi, Japan), an Acuson Sequoia C256 Echocardiography System (Acuson Corp, Mountain view, USA), a Vivid E9 Ultrasonic Unit (GE Health Care, Tokyo, Japan)]. By reviewing the recorded images of all study patients, LVDd, LVDs, septal wall thickness, and posterior wall thickness were measured from parasternal views and EF was measured using the modified Simpson's method by two experienced sonographers. LV mass was calculated using the formula for estimating LV mass from LV linear dimensions as described in the guidelines of the American Society of Echocardiography [13]. Moreover, we examined loading condition at each echocardiographic examination, which may influence EF.

2.4. Statistical analysis

Statistical analyses were performed using SPSS for Windows 22.0 (SPSS, Chicago, IL, USA). All data are expressed as mean ± SD values. Differences in parameters between 2 groups were determined using the Mann–Whitney *U*-test for continuous variables or Fisher's exact test for discrete variables. One-way repeated-measures analysis of variance (ANOVA) and a post hoc test (Turkey-Kramer test) were used to test for significance adjustment for multiple comparisons. Statistical significance was set at a p value of <0.05.

3. Results

3.1. Baseline characteristics

The baseline characteristics of all patients are described in Table 1. The mean follow-up period was 10.3 ± 5.2 years. The etiology of AR was as follows: degenerative valve in 24 patients, annuloaortic ectasia in 10, valve prolapse in 8, bicuspid valve in 8, rheumatic valve in 5, and others in 3. AVR was performed with a bioprosthesis (18 patients) or a mechanical prosthesis (40 patients). AVR alone was performed in 51 patients and concomitant replacement of the ascending aorta was performed in 7 patients.

3.2. Chronological changes in LV function

The chronological changes in echocardiographic data of LV function are shown in Fig. 1. The preoperative EF was <50% in 21 (36%) patients, but it was normalized at 1 year after AVR in all patients except for one. At 5–10 years after AVR, EF improved in one patient with EF of <50% at 1 year after AVR, however, 7 of the 57 patients with EF >50% at 1 year after AVR showed recurrent LV dysfunction. Therefore, late recurrence of LV dysfunction developed in 7 (12%) of the 58 patients.

Table 1
Clinical characteristics of the study population.

	58 patients
Pre- and postoperative characteristics	
Age (years)	56.3 ± 15.0
Sex (male), n (%)	44 (75.9)
Height (cm)	164.2 ± 9.1
Body weight (kg)	60.8 ± 13.0
Body mass index (kg/m^2)	22.4 ± 3.2
Body surface area (m^2)	1.7 ± 0.2
Extracorporeal circuit (min)	122.3 ± 37.1
Mean blood pressure (mmHg)	89.7 ± 11.3
Heart rate (bpm)	73.0 ± 14.5
LVDd (mm)	67.9 ± 7.5
LVDs (mm)	47.2 ± 9.2
EF (%)	53.5 ± 13.6
Hypertension, n (%)	31 (53.4)
Diabetes, n (%)	4 (6.9)
Cerebral infarction, n (%)	4 (6.9)
COPD, n (%)	2 (3.4)
Connective tissue disease, n (%)	4 (6.9)
Smoking habit, n (%)	23 (39.6)
Preoperative AF, n (%)	8 (13.8)
Preoperative occurrence of VT, n (%)	2 (3.4)
Preoperative hospitalization due to heart failure, n (%)	22 (37.9)
Postoperative AF, n (%)	14 (24.1)
Postoperative occurrence of VT, n (%)	3 (5.2)
Postoperative hospitalization due to heart failure, n (%)	5 (8.6)
Preoperative laboratory data	
Hb (g/L)	12.8 ± 1.7
WBC count (10^9/L)	6041 ± 2120
Eosinophils (%)	2.9 ± 2.2
BUN (mmol/L)	6.9 ± 2.8
Cr (μmol/L)	88.4 ± 26.5
eGFR (mL/min/1.73m^2)	61.5 ± 21.6
BNP (pmol/L)	136.0 ± 313.0
Total cholestelol (mmol/L)	4.6 ± 0.8
LDL (mmol/L)	2.9 ± 0.6
Preoperative medications	
ACE I/ARB, n (%)	37 (63.8)
β-blockers, n (%)	11 (19.0)
Digoxin, n (%)	14 (24.1)
Diuretics, n (%)	32 (55.2)
Statins, n (%)	5 (8.6)
Anti-platelets, n (%)	4 (6.9)
Anti-coagulates, n (%)	3 (5.2)
Postoperative medications (three years)	
ACE I/ARB, n (%)	27 (46.7)
β-blockers, n (%)	27 (46.7)
Digoxin, n (%)	9 (15.5)
Diuretics, n (%)	21 (36.2)
Statins, n (%)	11 (19.0)
Anti-platelets, n (%)	21 (36.2)
Anti-coagulates, n (%)	45 (77.6)

Values are presented as mean ± SD or n (%). LVDd = left ventricular end-diastolic diameter; LVDs = left ventricular end-systolic diameter; EF = ejection fraction; COPD = chronic obstructive pulmonary disease; AF = atrial fibrillation; VT = ventricular tachycardia; Hb = hemoglobin; WBC = white blood cell; BUN = blood urea nitrogen; Cr = creatinine; eGFR = estimated glomerular filtration rate; BNP = B-type natriuretic peptide; LDL = low-density lipoprotein; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker.

3.3. Predictors of late recurrent LV dysfunction

In order to clarify the predictors of late recurrent LV dysfunction, we compared the parameters between 7 patients with late recurrence of LV dysfunction and 51 patients without it. The etiology of AR in 7 patients