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Original article

Prognosis of medically treated patients at least 80 years old with severe sclerotic aortic stenosis

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ABSTRACT

Background: The prevalence of severe sclerotic aortic stenosis (ScAS) in those at least ≧80 years old has been increasing in Japan; however, the prognosis of these Japanese patients without surgical treatment has not been reported.

Methods and results: Ninety consecutive patients with medically treated severe ScAS were prospectively studied. To assess further event-free survival rate (EFSR) from either cardiac (heart failure or cardiac death) events or noncardiac deaths, they were divided into three groups based on aortic valve area (AVA) at the initial diagnosis (group A: AVA ≦ 0.6 cm^2, group B: 0.6 cm^2 < AVA ≦ 0.8 cm^2, and group C: 0.8 cm^2 < AVA ≦ 1.0 cm^2). In comparison, 73 consecutive patients ≧80 years old with moderate ScAS (group M: 1.0 cm^2 < AVA ≦ 1.5 cm^2) were also enrolled. The EFSR in group A was significantly lower than that in the other groups ($p < 0.05$) while no difference was seen among the other groups although the EFSR from cardiac events in group B was lower than the moderate group ($p < 0.05$). Multivariate analysis showed that the cardiac risk factors were AVA ≦0.6 cm^2 and left ventricular ejection fraction (EF) ≦55%.

Conclusions: Since patients with AVA ≦0.6 cm^2 have a significantly worse prognosis, more symptoms, and higher prevalence of cardiac events, early aortic valve replacement should be considered in this group. Furthermore, patients having AVA ranging from 0.6 to 0.8 cm^2 have a worse prognosis in cardiac events compared to group M. In addition, EF ≦55% is another significant factor for cardiac events.

Introduction

An acute increase in the Japanese population at least ≧80 years old has resulted in a dramatic increase in patients with sclerotic aortic stenosis (ScAS). The mean age at the initial diagnosis of severe ScAS in the authors' previous study was 79 years in males and 82 years in females [1]. Varadarajan et al. [2] report, however, that only 20% of the elderly patients ≧80 years old with severe AS have undergone aortic valve replacement (AVR) because of their comorbidities or age. Although several reports have demonstrated the safety of AVR even in elderly patients [3,4], the rate of AVR in patients ≧80 years old remains low [2,5]. According to the 2008 American College of Cardiology/American Heart Association (ACC/AHA) practice guidelines for AS [6], the surgical indications for severe aortic stenosis (AS) [aortic valve area (AVA) <1.0 cm^2 or indexed AVA (AVAI) <0.6 cm^2] include symptomatic AS or left ventricular ejection fraction (EF) ≦50%. Debate still occurs in Japan, however, about whether AVA ≦1.0 cm^2 is an optimal indicator for AVR [7]. Since no report investigating the prognosis of Japanese patients with ScAS without AVR has yet been published, the appropriate severity of AS for AVR remains controversial [7]. To assess the prognosis of Japanese patients ≧80 years old with ScAS and without AVR; therefore, this prospective long-term follow-up study has been conducted.

Methods

Initially, 131 consecutive patients ≧80 years old with severe ScAS, AVA ≦1.0 cm^2, refusing AVR, or having contraindications for AVR at the initial diagnosis were enrolled in this study from November 17, 2003 to December 31, 2010. Exclusion criteria included those with bicuspid aortic valves, rheumatic AS, or regular hemodialysis treatments. In addition, 20 patients with critical

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conditions, such as shock, uncontrolled infection, neurological deficits, severe cirrhosis, and end-stage cancer with a predicted survival period less than 6 months, at the initial diagnosis were excluded.

One hundred and eleven patients, thus, were enrolled in this study. To compare the prognosis of severe ScAS, 74 consecutive patients ≧80 years old with moderate ScAS ($1.0\ cm^2 < AVA \leqq 1.5\ cm^2$) were also enrolled (group M); they were initially diagnosed in our hospital from January 1, 2004 to July 31, 2010. Enrollment criteria for group M were the same as described above for the severe ScAS group. Written informed consent was obtained in advance from all the patients for regular follow-up at the outpatient clinic. Patients who were unable to attend follow-up in the outpatient clinic were interviewed by telephone once or twice a year about their condition.

Blood pressure measurement, physical examination, echocardiogram, logistic EuroScore, and laboratory data were performed at the initial diagnosis. Since accurate evaluation of New York Heart Association classification of elderly patients is sometimes difficult due to restriction of activities, such as arthritis, lower back pain, or neurological deficits, the activities of daily living (ADL) were evaluated also during the initial diagnosis. The degree of ADL was classified as follows: no personal assistance needed = 0, partial personal assistance needed = 1, and total personal assistance needed = 2.

The AVA was measured by using a continuous equation, and the transaortic pressure gradient (AVPG) was calculated as 4 × (trans-(transaortic peak flow velocity)^2. Left ventricular volume was measured by the modified Simpson method by using two-dimensional echocardiography, and the left ventricular mass index was calculated by the reported equation [8]. Systemic vascular resistance was calculated as (80 × mean arterial pressure)/cardiac output. E' was used in the lateral mitral annulus velocity measured by the pulsed Doppler method. Both the transmitral velocities in the left ventricular rapid filling phase (E) and atrial kick (A) were also measured by pulsed Doppler method. The E/E' and E/A were calculated as indices of the left ventricular diastolic function.

For further assessment of the prognosis of ScAS based on the AVA, patients with severe ScAS were divided into three groups by the initial AVA (group A: $AVA \leqq 0.6\ cm^2$, group B: $0.6\ cm^2 < AVA \leqq 0.8\ cm^2$, and group C: $0.8\ cm^2 < AVA \leqq 1.0\ cm^2$). Primary endpoints were cardiac [heart failure (HF) or cardiac death] or noncardiac (noncardiac death) events. If patients had HF before they died by a cardiac or noncardiac cause, the cardiac event was considered as HF. When patients died, the dates and causes of death were found through the medical charts or family interviews.

In this study, HF was diagnosed according to the criteria of the Framingham study [9]. Liver dysfunction and chronic kidney disease were defined by those values exceeding the normal range in the study's laboratory.

The indications for AVR were in accordance with the 2008 ACC/AHA practice guidelines for AS [6]. Absolute indications of AVR included severe AS ($AVA < 1.0\ cm^2$) with symptoms and/or EF ≦50%. Undergoing coronary artery bypass graft surgery and/or surgery on the aorta or other heart valves were other indications for concomitant AVR. In patients ≧80 years old, however, many patients had no symptoms even if AS was severe. In such asymptomatic, severe ScAS, elderly patients, they were recommended to undergo AVR unless otherwise contraindicated.

Statistical analysis

Differences in age, body surface area (BSA), follow-up periods, echocardiographic parameters, logistic EuroScores, degrees of ADL, and laboratory data among the groups were analyzed by one-way ANOVA and Newman–Keuls test. Differences in symptoms, male/female ratios, rates of cardiac death, survival rates, comorbidities, and medications were analyzed by Fisher's exact test. Factors for cardiac death in severe ScAS were analyzed by univariate and multivariate analyses. The critical cut-off point of each parametric variable for univariate and multivariate analyses was determined by receiver operating characteristic curve. Both the event-free survival rates from cardiac and noncardiac events and from only cardiac events among all the severe groups and group M were analyzed by Kaplan–Meier analysis, and a significant difference of event-free survival rates from those endpoints was analyzed by log-rank test. Significant difference was accepted if $p < 0.05$.

Results

In the severe ScAS group, because 16 patients dropped out and 5 underwent AVR, only 90 patients could be followed up (group A: 24 patients, group B: 32 patients, and group C: 34 patients) to assess their prognosis without AVR. In group M, 73 patients were followed up because 1 patient underwent AVR. Table 1 lists the patients who underwent AVR after the study was begun. Four patients initially refused AVR despite the possibility of AVR but were all eventually successfully convinced otherwise. Only one patient had a contraindication at the enrollment of this study because of uncontrolled hyperthyroidism, but when controlled,

Table 1
Clinical characteristics of patients' having AVR after the study began.

	Patient				
	1	2	3	4	5
Age (years)	84	87	80	80	81
Sex	F	F	F	F	F
Symptoms	Chest pain dyspnea on exertion	Dyspnea	Chest pain dyspnea	None	Dyspnea on exertion
AVA (cm^2)	0.4	0.4	0.7	0.9	0.9
Ejection fraction (%)	72	66	76	64	59
Logistic EuroScore (%)	6.1	7.4	4.8	4.8	5.1
Degree of personal assistance of activities of daily living	0	0	0	0	0
Initial reason for avoiding AVR	Refused	Refused	Uncontrolled hyperthyroidism	Refused	Refused
Reason of AVR after enrollment in this study	Changed mind	Changed mind	Controlled hyperthyroidism	Changed mind	Changed mind

AVR, aortic valve replacement; AVA, aortic valve area.