

Age-related changes in aortic valve with emphasis on the relation between pressure loading and thickened leaflets of the aortic valves[☆]

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Abstract

Background: The information of the prevalence of TAV and its relation to aortic stenosis in a large-scale human population is limited.

Methods: An echocardiographic study was performed prospectively in 2850 subjects to determine the relationship between age and the thickened aortic valves (TAV). Another simulated study was designed to test the hypothesis that the noncoronary leaflet may have a greater diastolic loading than the right or left coronary leaflet.

Results: The prevalence of TAV in this population was 14.4% (410/2850). It was 0% in the <39 years old; however, the prevalence of TAV increased progressively with age: it was 10.0% in the middle age group, 17.0% in the elderly group, and 53.7% in the octogenarian group (Chi-square test for linear trend, $\chi^2=67.10$, $p<0.001$). A greater frequency of TAV was noted at noncoronary leaflet (57.0%) than at either right (22.3%) or left (20.6%) coronary leaflet ($\chi^2=5.99$, $df=2$, $p<0.001$). The prevalence of aortic stenosis (AS) tended to increase with age (Chi-square test for linear trend, $\chi^2=37.85$, $p<0.001$). The simulated study demonstrated that the sinus of Valsalva without a coronary leaflet had a higher pressure loading than that with a coronary leaflet.

Conclusion: This study demonstrates that the prevalences of TAV and AS increase progressively with age. A greater frequency of TAV is found at the noncoronary leaflet than at either the right or left coronary leaflet. The simulated study supports our hypothesis that the noncoronary leaflet may bear a greater pressure loading than either the left or right coronary leaflet.

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1. Introduction

Aging changes in human aortic valves have been reported in both autopsy specimens and living patients [1–4]. Previous investigators have reported that the cardiac valves may show marked thickening and loss of elasticity

with aging [5]. Sahasakul et al. found that elderly subjects tended to have more thickened aortic valves (TAV) than young subjects on 200 autopsy cases [6]. Lindroos et al. reported the prevalence of aortic valve abnormalities in 501 cases but only in elders (older than 75 years of age) [7]. The information of the prevalence of TAV and its relation to aortic stenosis in a large-scale human population, especially young age subjects, is limited. A previous observation showed that the TAV occurred more frequently at the noncoronary leaflet than either the left or right coronary leaflet [8]. We hypothesize that the noncoronary leaflet might bear a greater pressure loading than the left or right coronary leaflet. The aims of this study were two-folds: (1) an echocardiographic investigation was performed prospectively to determine the prevalence of TAV,

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to evaluate its relation to aortic stenosis in different age groups, and to observe the frequency of TAV at different aortic leaflets; (2) another simulated study was designed to test the hypothesis that the noncoronary leaflet may have a greater diastolic loading than the left or right coronary leaflet.

2. Methods

2.1. Echocardiographic study

2.1.1. Study subjects

We prospectively evaluated the echocardiograms on two populations. The first population was a group of 180 consecutive healthy subjects (35–72 years old), selected from our physical check-up department. These subjects were residents in the nearby communities or the employees from several local industrial companies. The echocardiographic study was performed in these healthy subjects to determine the average value of aortic valve thickness. Another study population was a large group of 2850 consecutive subjects including 1668 men and 1182 women, aged 20 to 97 (mean 60.5) years old. These subjects were apparently healthy people who were referred to the echocardiographic laboratory evaluation due to routine physical check-ups, preoperative assessments of cardiac function before ophthalmic operations, or operations other than cardiovascular system. Patients with any condition, such as hypertension, congenital heart disease, connective tissue disease, rheumatic heart disease, bicuspid or quadricuspid aortic valve, prosthetic valve disease, infective endocarditis, and aortic dissection or aneurysm were excluded from this study due to the fact that these conditions may interfere with the interpretations of the results. According to age distribution, the study population was divided into 4 groups; each group was composed of patients within two decades: adult (<39 years old, $N=300$; 10.5%)*, middle age (40–59 years old, $N=778$; 27.3%)*, elderly (60–79 years old, $N=1690$; 59.3%)*, and octogenarian (≥ 80 years old, $N=82$; 2.8%)*. * N =case number.

2.1.2. Echocardiographic assessment

All patients received M-mode, two-dimensional, and color Doppler echocardiographic studies using a 2.5 MHz phased-array transducer which is incorporated with the Sonos 2500 or Sonos 5500 imaging systems (Agilent Technologies, Andover, Massachusetts). Routine parasternal long-axis, short-axis, apical four- and two-chamber, and apical long-axis views were studied in all subjects. In order to decrease the variation due to different ultrasonic settings, all echocardiographic studies were performed using fundamental imaging, rather than harmonic imaging. Slight tilting of the transducers to record the most obvious image with thickened aortic valve (TAV) in all views was

performed. The aortic valve was considered as a thickened aortic valve only if aortic leaflet over the echocardiogram was thickened at both parasternal long- and short-axis views. To determine the average value of aortic valve thickness, a group of 180 consecutive healthy subjects (the first group) was studied. They were apparently healthy without hypertension or any discomfort. The thickness of aortic valve was measured using a track ball and built-in software from the echo-machine at both the parasternal long-axis and short-axis views. With assistance of the cine-loop and frame-by-frame search, the thickest point at the edge of any aortic leaflet at late-systole was measured and regarded as the aortic valve thickness. Since all subjects were in normal sinus rhythm, the average thickness of the aortic valve in three consecutive cardiac cycles was used in the analysis. In order to evaluate the inter-observer variability, two experienced cardiologists measured the aortic valve thickness in the first 50 cases of the first group in separate time (more than 2 h) within the same day. The intra-observer variability was also studied by the same observer in these 50 cases with 5–10 days apart. From this study, we found that 17 out of 180 cases (9.4%) had thickened aortic valves. The mean values of aortic valve thickness in those with a thickened leaflet was 2.71 ± 0.65 mm and 2.78 ± 0.52 mm for the parasternal long- and short-axis views, respectively. The aortic valve thickness in those without a thickened leaflet was 1.37 ± 0.29 mm and 1.41 ± 0.31 mm from the parasternal long- and short-axis view, respectively. The mean value plus 2 S.D. was considered to be the upper limit of normal. It was 1.95 mm and 2.03 mm for the long- and short- axis views, respectively. Therefore, the thickened aortic valve was considered only if the thickness of aortic valve was more than 2.1 mm. Besides the thickness, the calcification of the aortic valve was also assessed. Calcification was considered if the echodensity of aortic valve was denser than that in the anterior aortic wall.

The maximal and mean pressure gradients across the aortic valves were measured using continuous wave Doppler echocardiographic examination [9]. Aortic stenosis (AS) was diagnosed by documenting aortic valve leaflet thickening with reduced systolic opening on two-dimensional echocardiography and a peak pressure gradient of at least 20 mm Hg or more by Doppler echocardiography across a stenotic aortic valve. If the mean pressure gradient was ≥ 50 mm Hg, the patients were considered as having severe aortic stenosis [10,11]. AS patients were divided into only severe- and non-severe-AS groups. As significant aortic regurgitation may increase the flow velocity and affect the calculation of pressure gradient, patients with moderate or severe aortic regurgitation were not included in this study. The same cardiologists, blinded to the clinical data and history of the patients, measured the aortic valve thickness and interpreted the echocardiographic findings of all patients throughout the study.

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