Original article

When and how aortic stenosis is first diagnosed: A single-center observational study

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ABSTRACT

Background: The development of clinical symptoms is associated with cardiovascular events in patients with aortic stenosis (AS). Thus, early diagnosis of AS is clinically important. However, there are few data on symptom status or the severity of AS when patients are first diagnosed, or on how AS is detected in routine practice. We aimed to investigate when and how AS patients are first diagnosed in our hospital.
Methods: We retrospectively enrolled 198 AS patients diagnosed from 1989 to 2009, and identified their symptoms and AS severity at the time of the first diagnosis. We also assessed the reasons why they came to the hospital based on their medical records.
Results: Of the 198 patients, 82 (41.6%) had voluntarily visited or been referred to our hospital after developing clinical symptoms (Symptomatic group). The remaining 116 patients (58.4%) had been asymptomatic, and cardiovascular disease was suspected during an annual or occasional health checkup (Asymptomatic group). The initial findings in the Asymptomatic group that led to the diagnosis of AS were: a systolic murmur on auscultation (62%), abnormal electrocardiography (27%), or abnormal echocardiography (11%). The Symptomatic group had significantly greater AS severity and an increased left ventricular mass index, and experienced more cardiac events (valve replacement or cardiac death) during the follow-up period.
Conclusions: About 40% of the AS patients in this study were not diagnosed until they developed clinical symptoms, suggesting that many other patients in the community might have a latent risk of cardiovascular events. Auscultation plays an important role in the early diagnosis of AS.

Introduction

In the modern era, the prevalence of degenerative calcified aortic valve (AV) disease has increased. With the growth of aging societies and consequent increase in the prevalence of atherosclerosis [1], degenerative calcified valve disease has become the most common cause of aortic stenosis (AS) [2,3]. Consequently, a rise in the prevalence of AS in the community has been well documented [3–5]. This has become a growing concern, and there is a need to identify these patients in the community for optimal follow-up and management of AS.

The onset of clinical symptoms in patients with AS is strongly associated with a poor prognosis [6–8]. Once patients have developed symptoms, the risk of a cardiovascular event is significantly increased, and prompt surgical intervention is warranted [9]. Additionally, there is evidence that AS patients with severe symptoms are at risk of greater perioperative mortality and complications [10]. Therefore, early diagnosis in the asymptomatic phase in the community is important, not only for careful follow-up, but also for appropriate surgical intervention. Nevertheless, patients are often first diagnosed only after developing congestive heart failure, indicating that some patients with undiagnosed AS have a latent risk of cardiovascular events. However, there are few data on the symptom status or severity of

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AS when patients are first diagnosed, or on how the patients are detected in the community.

In the present study, we investigated when and how patients were first diagnosed with AS in our hospital.

Materials and methods

Study patients

We performed a retrospective chart review of all cases of AS diagnosed in the Juntendo University Hospital echocardiographic database, and screened 189 consecutive patients who had been diagnosed between 1989 and 2009. Cases were identified by a review of all echocardiographic reports. All patients who had been found to have an increased peak aortic valve (AV) velocity ($\geq$2.5 m/s by continuous wave Doppler ultrasound) were assessed for inclusion in the study. Patients were excluded if they had previous AV replacement or infectious endocarditis. Before using any of the information from the chart review, we obtained approval from the institutional ethics committee of Juntendo University Hospital.

Patient demographic data

We collected demographic and clinical data and other information on each patient at the time of first diagnosis and during follow-up from the medical records, which were then reviewed by experienced cardiologists. We also examined the reason why asymptomatic patients visited or were referred to our hospital. The presence of symptoms (angina, dyspnea, syncope, pre-syncope, or congestive heart failure) at the time of the initial clinical and echocardiographic evaluations was determined. We also recorded if any of the following cardiovascular risk factors were present: diabetes mellitus (overnight fasting serum glucose > 126 mg/dl on at least two occasions, or medically treated); systemic hypertension (blood pressure > 140/90 mmHg, or medically treated); hypercholesterolemia (serum total cholesterol > 220 mg/dl, or medically treated); and a regular smoking habit. The presence of coronary artery disease (CAD) was defined as a past history of CAD, which was previously established if they had >50% diameter stenosis based on coronary angiography or computed tomography. The patients were classified as Symptomatic if they had voluntarily visited or been referred to our hospital because of clinical symptoms, or Asymptomatic if they had been referred to our hospital for suspected AS or any cardiovascular disease by objective findings, such as a cardiac murmur by auscultation, abnormal electrocardiography, or abnormal echocardiography.

Information on cardiac events during the follow-up period was obtained by mailed questionnaires, reviews of medical records, and scripted telephone interviews. Cardiac events were defined as AV replacement or cardiac death.

Echocardiographic study

Doppler echocardiography was performed using commercially available echocardiographic machines. All patients underwent a comprehensive examination that included 2-dimensional (2D) and Doppler echocardiography by an experienced sonographer or cardiologist. The peak AV velocity and mean AV pressure gradient were derived from transaortic flow recorded with continuous–wave Doppler using a multi-window approach. The aortic valve area (AVA) was calculated using the continuity equation [11]. Then, the severity of AS was assessed according to the current guideline [9]. Significant aortic regurgitation (AR) was defined as a moderate or greater grade of AR based on the presence of a color Doppler jet width $\geq$25% of the left ventricular (LV) outflow tract [9]. The LV

end-diastolic volume (EDV) and end-systolic volume (ESV) were measured by the method of disks using 2D images obtained from both the apical 4- and 2-chamber views. The LV ejection fraction was calculated using the following equation: $100 \times (EDV - ESV)/EDV$ [12]. LV mass was calculated using diastolic measurements of LV internal diameter and wall thickness on 2D echocardiography, according to the formula recommended by the American Society of Echocardiography: LV mass (g) = $0.8 \times \{1.04[(IVST + LVID + PWT)^3 - (LVID)^3]\} + 6$ g (IVST: interventricular septal wall thickness; LVID, LV internal diameter; PWT, posterior wall thickness) [12]. Then, LV mass index was calculated as LV mass/body surface area.

Statistical analysis

Data are presented as mean $\pm$ standard deviation for continuous variables, or as a number with percentage for categorical variables. Differences between groups were analyzed by Student's t-test or Mann–Whitney U-test for continuous variables, and by the Chi-square test for categorical variables. The Kaplan–Meier method was used for cumulative survival analysis, with the log-rank test for assessing statistical differences between curves. Two-tailed p-values < 0.05 were considered statistically significant. All statistical analyses were performed using SPSS 17.0 software (SPSS Inc., Chicago, IL, USA).

Results

Of the 198 patients, 82 (41.6%) had voluntarily visited or been referred to our hospital after developing clinical symptoms (Symptomatic group) (Fig. 1). Thus, two of every five AS patients had never been diagnosed until they had developed symptoms. On the other hand, 116 asymptomatic patients (58.4%) had been referred to our hospital suspected of having AS or other cardiovascular disease by objective findings during an annual or occasional health checkup (e.g. cardiac murmur by auscultation, abnormal electrocardiography, or echocardiography) (Asymptomatic group). The most common initial finding that led to the diagnosis of AS was a cardiac murmur on auscultation, indicating that auscultation plays an important role in finding AS patients in the community. The cause of the AS was sclerotic change in 171 patients, rheumatic disease in 11, bicuspid valve in 5, and congenital abnormality in 1.

Table 1 shows a comparison of demographic data at baseline between the 2 groups. The Asymptomatic group had a greater proportion of males than the Symptomatic group, suggesting that male AS patients tend to be diagnosed by objective findings rather than by symptoms. The Symptomatic group had decreased LV ejection fraction and AVA, and increased LVESV and LV mass index compared with the Asymptomatic group, suggesting that the Symptomatic group was first diagnosed at a more advanced stage
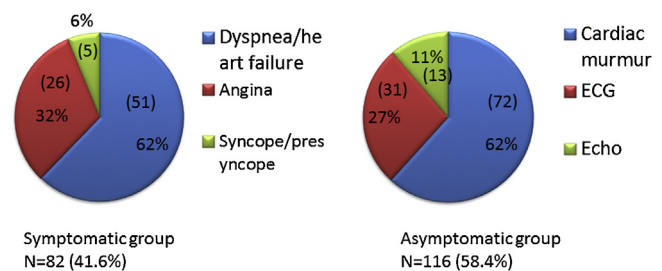

Fig. 1. How was aortic stenosis (AS) first diagnosed? These data show that 41.6% of AS patients were first diagnosed after developing clinical symptoms. Auscultation remains an important tool for detecting asymptomatic patients with AS in the community. ECG, electrocardiography.