Prevalence and Prognosis of Aortic Valve Disease in Subjects Older than 85 Years of Age

David Leibowitz, MD[a,c,*], Jochanan Stessman, MD[a,b], Jeremy M. Jacobs, MBBS[a,b], Irit Stessman-Lande, BMedSci[c], and Dan Gilon, MD[c]

Although degenerative aortic valve disease is common with increasing age, limited data exist regarding prevalence and prognosis of aortic valve disease among the oldest old. Subjects were recruited from the Jerusalem Longitudinal Cohort Study. Echocardiography was performed at home in 498 randomly selected subjects. Subjects were divided into 3 groups; normal subjects, subjects with valve calcium but without stenosis (AVC), and subjects with aortic stenosis (AS). Survival status at 5-year follow-up was assessed via the centralized population registry. AVC was noted in 55% of the study subjects and AS was seen in 8.2%. There were no significant differences between the 3 groups in any of the clinical parameters examined including risk factors for atherosclerotic heart disease. Of the 498 subjects, 107 (21%) had died at the time of 5-year follow-up. Five-year mortality was similar among the normal (17%) and AVC (20%) subjects but was significantly higher among the subjects with AS (46%; p <0.0001). AS was associated with a nearly fourfold increased likelihood of mortality (hazard ratio 3.7, 95% confidence interval 1.4 to 9.3). In conclusion, among subjects ≥85 years of age, the prevalence of AS is higher than previously reported and not associated with traditional vascular risk factors. AS but not AVC alone was independently predictive of 5-year mortality. **(Am J Cardiol 2013;112:395−399)**

Degenerative aortic valve disease (AVD) with calcification of the valve leaflets is common with increasing age.[1,2] Studies have suggested that this is due to an active inflammatory process with pathologic changes and risk factors similar to atherosclerosis.[3,4] Given the aging of the population, there is an increasing burden of AVD in the general population.[5,6] People aged ≥85 years (the "oldest old") are the world's most rapidly growing age group, yet data regarding prevalence of and risk factors for AVD in very elderly patients are sparse.[7] Whereas in younger subjects AVD has been associated with increased mortality, the impact of AVD on mortality among the oldest old remains unclear.[8,9] Given the development of nonsurgical methods for the treatment of AVD, this question has important clinical implications.

Existing studies of echocardiography in the oldest old have been performed in the hospital or clinic setting, possibly contributing to a biased study population in this age group because subjects find it harder to leave their homes.[10] The introduction of portable echocardiography machines has made it possible to study patients in their homes and therefore offers a more representative population of the oldest old. The objectives of this study were to (1) examine the prevalence of both AV calcification and stenosis in a community-dwelling, age-homogenous population of subjects born in the years 1920 and 1921, (2) assess risk factors for occurrence of AVD in this elderly population, and (3) examine the impact of AVD on 5-year mortality.

Methods

Subjects were recruited from the Jerusalem Longitudinal Cohort Study that was initiated in 1990 and has followed an age-homogenous cohort of West Jerusalem residents born between January 1920 and December 1921. The methodology has been described elsewhere in detail.[11,12] The present study examines data from the third most recent phase of data collection, which took place during 2005−2006. Subjects were interviewed and examined in their homes on 2 occasions. The institutional ethics committee approved the study design, and written informed consent was obtained from all participants.

The study sample, which formed approximately one-third of the total birth cohort, was randomly chosen from the total sample of people born in 1920 and 1921 and living in Jerusalem (n = 1,222). Subjects in the study group, those who declined to participate, and those baseline cohort members not enrolled had near identical mortality- and disease-specific hospital morbidity, demonstrating the representative nature of the initial study group. Survival status at 5-year follow-up was assessed via the centralized population registry. Follow-up was available for all study subjects. Echocardiography was performed in 498 randomly selected subjects, evenly distributed between new recruits and subjects participating from previous phases.

Diagnosis of ischemic heart disease was based on a history of hospitalization for acute coronary syndrome, coronary catheterization with evidence of significant

[a]Jerusalem Institute of Aging Research, [b]Department of Geriatrics and Rehabilitation, and [c]Heart Institute, Hadassah-Hebrew University Medical Center and Hebrew University Hadassah Medical School, Mount Scopus, Jerusalem, Israel. Manuscript received January 17, 2013; revised manuscript received and accepted March 24, 2013.

Drs Leibowitz and Stessman contributed equally to this work.

See page 398 for disclosure information.

*Corresponding author: Tel: 972-2-5844530; fax: 972-2-5844113.
E-mail address: oleibo@hadassah.org.il (D. Leibowitz).

0002-9149/13/$ - see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.amjcard.2013.03.044

Table 1
Clinical characteristics of the study population

Variable	Total Population (n = 498)	Normal (n = 183)	AVC (n = 274)	AS (n = 41)
Total		36.8%	55%	8.2%
Men	46.8%	50.3%	44.5%	46.3%
Low education	48.6%	47.5%	54%	51.2%
Low SES	26.2%	22.8%	29.4%	20%
Not married	48.2%	48.3%	48%	48.8%
Not physically active	70.1%	70.6%	70.1%	68.3%
Poor self-rated health	68.7%	68.4%	69.6%	65%
Depression	32.7%	27.2%	35.2%	40%
Difficulty in ADLs	28.9%	27%	30%	29.3%
Renal disease	10.1%	12.1%	9.2%	7.3%
Diabetes mellitus	19%	20.3%	19.6%	9.8%
Ischemic heart disease	36.4%	36.8%	36.2%	36.6%
Heart failure	11.1%	11.5%	10.3%	14.6%
Hypertension	71.2%	72%	72%	63.4%
Dementia	17.6%	15.7%	18.4%	20%
Never smoked	59.3%	57.5%	58.5%	73.2%

No significant differences between groups.
ADLs = activities of daily living; SES = socioeconomic status.

coronary artery disease, myocardial infarction on electrocardiogram, a history typical for angina pectoris on exertion, or previous coronary artery bypass grafting surgery. Hypertension was defined as treatment with antihypertensive medications or blood pressure >140 mm Hg systolic or 90 mm Hg diastolic on examination. Hyperlipidemia was defined as use of cholesterol-lowering medications. Diagnosis of diabetes mellitus was a composite of hypoglycemic medications, personal history, or a medical record diagnosis. Congestive heart failure was based on hospital discharge diagnosis and according to examining research physician diagnosis at the time of examination at home.

Self-rated health was assessed according to the question how do you rate your general health? Responses were good or poor. A cognitive assessment was performed according to a standardized Mini-Mental State Examination with cognitive impairment defined as ≤24 out of 30.[13] Dependence in functional status was defined as requiring the help of another person in ≥1 of the following activities of daily living: eating, dressing, bathing, personal hygiene, toileting, and transfer.[14]

Four hundred ninety-eight subjects had standard 2-dimensional and Doppler echocardiography at their place of residence with a portable echocardiograph (Vivid I, GE Healthcare, Haifa, Israel). All subjects underwent standard 2-dimensional and Doppler echocardiography with measurements according to the recommendations of the European Association of Echocardiography and American Society of Echocardiography.[15] Measurements were performed for 3 consecutive cardiac cycles and averaged. Left ventricular (LV) mass was calculated according to a necropsy validated formula of LV mass (grams) = 0.8 × (1.04 × ((septal thickness + LV internal diameter + posterior wall thickness)^3−(LV internal diameter)^3)) + 0.6 and indexed to body surface area.[16] Left atrial (LA) volumes were calculated at end-systole from the apical 4-chamber view using the area-length method.[17]

Ejection fraction was calculated by averaging measurements of end-diastolic and end-systolic volumes from the apical 4-chamber view using the area-length method for 3 consecutive beats. In patients with atrial fibrillation (n = 25), measurements were averaged for 5 consecutive beats. Peak systolic mitral annular function (s wave) was measured as an additional index of systolic function.

Diastolic parameters were measured from the apical 4-chamber view using pulsed-wave Doppler at the level of the mitral annulus (e and a waves) and tissue Doppler imaging (e′ and a′ waves) of the septal and lateral myocardial walls. The ratio of E/e′ using the average of septal and lateral tissue velocities obtained was calculated as an index of diastolic function.[18] Patients with atrial fibrillation were excluded from analyses of a wave velocities.

Two-dimensional assessment of the aortic valve was performed in parasternal long- and short-axis views. Patients who underwent aortic valve replacement (n = 5) were excluded from the study. Calcifications were defined as bright echoes >1 mm in size on ≥1 cusps.[19] The maximal velocity across the aortic valve was measured with continuous Doppler from apical views. Aortic stenosis was defined as reduced systolic opening on 2-dimensional imaging with a velocity of at least 2.5 m/s across the valve.[3,4,8] For the purpose of analysis, subjects were divided into 3 groups: normal control subjects, subjects with valve calcification but without stenosis, and subjects with AS.

Descriptive statistics were performed and percentages were calculated as appropriate. Because cardiac data was normally distributed, results are described as means and standard deviations. For continuous variables differences between means were calculated using 1-way analysis of variance and multiple comparisons was performed using Tukey's method. p values were performed as appropriate. Categorical variables were examined using chi-square tests. Cumulative survival was assessed by Kaplan-Meier analysis and log-rank test for statistical significance. To detect significant difference in mortality, 144 events were necessary. Adjusted and unadjusted Cox proportional hazard models were performed. Models were adjusted for gender, physical activity, diabetes, ischemic heart disease, congestive heart failure, hypertension, renal disease, LA volume, LV mass, and E:e′; further adjustment was made for AS as a dummy variable where "normal" was the reference group. All p values were 2-tailed, and $p < 0.05$ was considered significant. The data storage and analysis was performed using SAS version 9.1e (SAS Institute, Inc., Cary, North Carolina).

Results

Aortic valve calcium was noted in 55% of the study subjects, and aortic stenosis was seen in 8.2%. Clinical characteristics of the subjects are depicted in Table 1. There were no significant differences between the 3 groups in any of the clinical parameters examined including risk factors for atherosclerotic heart disease. Echocardiographic