New Insights Into the Progression of Aortic Stenosis: Implications for Secondary Prevention

To the Editor:

Palta et al. suggest new insights into the progression of aortic stenosis. They report a series of 170 patients with “any degree” of aortic stenosis who underwent 2 echocardiograms >3 months apart. It is not indicated what proportion of patients with aortic stenosis were not included because they underwent only 1 examination. The selection criteria in this retrospective study may have introduced systematic and significant bias. Importantly, patients with severe or even moderate aortic stenosis may have been excluded because the initial severity or subsequent progression of the disease would have culminated in surgical correction or death before a second study was obtained. Consistent with this observation, the degree of aortic stenosis in patients in the study was mild (mean valve area, 1.17 cm²).

Data derived from Doppler estimation of blood flow velocities are restated as calculated aortic valve area (AVA), transvalvular gradient, and peak velocity. From these, it is concluded that the strongest association with rate of progression of aortic stenosis was the presence of mild disease on the first echocardiogram. However, as indicated above, patients with severe disease and rapid progression may have been excluded from the study.

The authors’ stated aim was to identify potentially modifiable risk factors for the purpose of secondary prevention. In patients with serum cholesterol >200 mg/dL versus those with ≤200 mg/dL, the annual reduction in AVA was 0.14±0.35 cm² versus 0.07±0.19 cm². The standard deviations exceed the means, indicating that this parameter was not normally distributed. The decrease in AVA should have been analyzed with nonparametric tests or with parametric tests using transformed data. The comparison as it stands is invalid. The same limitation applies to the distribution of serum creatinine in rapid versus slow progressors (1.7±1.7 versus 1.5±1.0 mg/dL). Furthermore, linear regression analysis cannot be applied to data that are not normally distributed. Therefore, the associations of decreasing AVA with serum calcium concentration and smoking are also invalid.

Although the identification of modifiable risk factors in aortic stenosis is an important goal, none of the conclusions from this study can be sustained by the presented statistical analyses.

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Response

We thank Drs Choudhury and Leyva for their interest in our article and appreciate their concerns and comments.

The 170 patients included in the study came from a parent group of 650 patients with “any degree” of aortic stenosis; the remaining patients did not meet the inclusion criteria. Because this is not a population-based study, there certainly would be referral bias. Such bias cannot be eliminated from any study originating from a tertiary care center. In addition, many of the patients with severe aortic stenosis or even those with moderate aortic stenosis undergoing other cardiac surgeries would naturally be eliminated from the study because of aortic valve replacement. Hence, this study is most relevant to patients with mild and moderate degrees of aortic stenosis in whom the potential benefit of retarding progression may be significant.

Many of the variables tested had a skewed distribution. For example, if the distribution of serum creatinine is examined in any population, there would be subjects with high serum creatinine skewing the distribution to the right, because the population mean would be <1 mg/dL. The same thing would be true in terms of annual reduction in aortic valve area, because some progress rapidly. This does not invalidate the t test or regression analysis if the number of subjects in the sample exceed 30. If the distribution is skewed and the sample size is <30 subjects, then nonparametric tests are more appropriate. A large sample size, like that in our study, tends to eliminate the effect of skewed distribution on the analysis. We performed the nonparametric tests as Drs Choudhury and Leyva suggested, and the results of the analysis were similar to those obtained originally.

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