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Editorial Comment

Percutaneous Aortic Balloon Valvuloplasty: Relief of Obstruction to Outflow Or Inflow?*

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Percutaneous aortic balloon valvuloplasty usually results in only a modest improvement in valve hemodynamics (1,2) with a high short-term restenosis rate (3). Nonetheless, patients who undergo this procedure usually have an initial improvement in symptoms and many demonstrate sustained symptomatic benefit at follow-up despite documented valve restenosis (2,3). There has consistently been a lack of relation between recurrent symptoms and the conventional variables used to evaluate aortic stenosis in patients after aortic valvuloplasty. Such variables include measurements of outflow obstruction (valve gradient and valve area) as well as systolic ejection indexes (cardiac output and ejection fraction). It has been suggested that there is a "critical" level of obstruction that, when exceeded, produces symptoms (3,4). Perhaps the commonly used hydraulic and continuity methods to determine valve area may not be able to determine this level, which may vary from patient to patient. However, other reasons for this observed symptomatic improvement may be present that are not measured in daily clinical practice.

Left ventricular diastolic function in aortic stenosis. In the presence of long-term pressure overload, systolic function is usually well preserved. The increase in systolic wall stress produced by the stenotic aortic valve leads to parallel replication of sarcomeres and concentric hypertrophy, which tends to normalize wall tension (5). However, there are adverse pathophysiologic effects of this hypertrophy on diastolic filling of the ventricle that result in increased diastolic pressures as well as diffuse subendocardial ischemia (6–8). Both of these factors contribute to symptoms in patients with aortic stenosis, that is, symptoms due to diastolic abnormalities of the left ventricle.

The mechanism of left ventricular diastolic dysfunction in pressure overload hypertrophy is multifactorial and many aspects remain controversial. Excess afterload, myocardial ischemia and intrinsic abnormalities of the hypertrophied myocardium all play a role in producing these diastolic abnormalities. Impairment of left ventricular relaxation is often present in patients with aortic stenosis. This has been attributed to afterload mismatch that slows relaxation in both the isolated cardiac muscle preparation and the intact canine model (9,10). There is also evidence that other factors (extent of hypertrophy, abnormalities of calcium regulation or ischemia) account for abnormalities of relaxation (11,12). Chamber stiffness is increased, producing higher diastolic pressures during filling. This increase in chamber stiffness may be due to an increase in muscle mass in some patients; in others, enhanced myocardial elastic stiffness may be present (13,14). Early diastolic filling (peak filling rate) has been reported to be depressed in patients with aortic stenosis (15,16). However, early left ventricular filling is determined by a complex interplay between the static and dynamic properties of the left atrium and ventricle. Thus, early filling is not uniform from patient to patient but varies according to the degree of hypertrophy, systolic function and left atrial driving pressures (17).

Relating abnormal diastolic function to symptoms. Abnormalities of diastolic function play an important role in almost all diseases of the heart (7,18,19). However, there has not been extensive experience in the evaluation of diastolic dysfunction in clinical situations for several reasons: 1) Diastole is a series of complex, interrelated events and measurement of these events is difficult. High fidelity pressure measurements and pressure-volume or stress-strain relations are currently used to provide indexes of these diastolic events, but there remain many limitations to even these invasive, time-consuming procedures (20). 2) There is such a diverse spectrum of diastolic abnormalities in any one disease state that a large number of patients must be studied to establish any reasonable conclusion about the overall contribution of diastolic abnormalities to pathophysiology. 3) Finally, all measures of diastolic variables are highly dependent on many factors other than intrinsic myocardial disease, such as loading conditions, heart rhythm and rate, and age (8,18,19). Because of these factors, it has been difficult to directly relate abnormalities of diastolic function with symptoms or prognosis in various diseases.

The present study. In this issue of the Journal, Sheikh et al. (21) were able to demonstrate a relation between abnormalities of diastolic function and symptoms. The follow-up of patients after an intervention (such as percutaneous aortic

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balloon valvuloplasty) in a disease with a large component of diastolic function abnormality (such as aortic stenosis with left ventricular hypertrophy) is an ideal situation for evaluating these relations because each patient serves as his or her own control. The finding that diastolic function worsens immediately after balloon valvuloplasty with prolongation of relaxation has been supported by others (22,23) and probably reflects transient myocardial ischemia, which is produced during balloon inflation (24). At short-term follow-up patients who remained asymptomatic had improved myocardial relaxation and chamber stiffness, as opposed to those who developed recurrent symptoms. This sustained symptomatic improvement was not related to more conventional measurements used clinically in the evaluation of aortic stenosis, such as ejection fraction, aortic valve gradient or aortic valve area.

Many questions still need to be answered concerning these data. All relations were based on symptomatic status, which is a subjective end point. Because of the critically ill nature of the patients who underwent valvuloplasty, only 53% of the total group had follow-up studies, so a bias may be present in the results. There was no correction for body surface area in any measured variable except for left ventricular mass. Thus, major questions remain as to which underlying pathophysiologic mechanisms caused these changes in diastolic variables and why some patients improved when others did not. Although regression of left ventricular hypertrophy has been proposed, other mechanisms such as changes in afterload or increased coronary flow reserve may have contributed to improvement in diastolic variables in patients with symptomatic improvement. Other factors, such as changes in preload, myocardial ischemia, coexistent valvular regurgitation or contrast load, could also affect these diastolic variables. The changes in peak filling rates are not fully explained because the symptomatic patients in this study were those with the lower peak filling rates. This is in discordance with the findings of others (17,25) who showed that it is patients with the most severe hypertrophy and higher filling pressures who have higher rates of peak filling in early diastole.

Clinical implications. Despite these limitations, these findings have raised important questions not only about the mechanism of percutaneous aortic balloon valvuloplasty, but also about the underlying pathophysiologic processes that contribute to symptoms in patients with aortic stenosis. They support the hypothesis that abnormalities of diastolic performance may be an important and perhaps the primary cause of symptoms in patients with aortic stenosis. Although diastolic performance has been implicated in the past, understanding of its influence was based mainly on extrapolation from intricate analyses of a small number of patients at one point in time. As a greater understanding of the diastolic filling process develops, it is hoped that more noninvasive approaches can be used to measure abnormalities of diastolic filling. This should allow evaluation of large numbers of patients with different disease states in serial fashion to further define the role of diastolic function in heart disease.

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