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EDITORIAL COMMENT

Severe Calcific Aortic Stenosis

Left Ventricular Afterload and its Quantification*

Kirk L. Peterson, MD, FACC
San Diego, California

The physical forces that impede myocardial shortening (afterload) are highly relevant to pharmacologic, mechanical, and surgical treatments for left ventricular systolic dysfunction. The maintenance of a normal or near-normal afterload, matched appropriately to robust myocardial contractility and accompanied by adequate venous return and heart rate, together ensure the teleologic cardiac function of delivering oxygen and metabolic substrate to and from the periphery.

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QUANTIFICATION OF LEFT VENTRICULAR AFTERLOAD

Although the pathophysiologic role of afterload is recognized, its quantification is problematic because of the complexity of measuring either wall stress or the vascular load on the left ventricle. Mean aortic blood pressure often is used as a simplified parameter, but it fails to account for four integral factors of systolic load: 1) the patency of the left ventricular outflow tract; 2) the geometry of the left ventricle; 3) the functional integrity of the mitral valve; and 4) the frequency-dependent nature of the hydraulic load imposed by an arterial vasculature of variable compliance (and of the left atrium in the presence of mitral regurgitation). The first three deficiencies are met by calculation of midwall circumferential stress, a calculated estimate of the average wall force that resists a representative myofiber in its major vector of shortening. Wall stress changes constantly throughout ejection and varies directly with instantaneous left ventricular pressure and size and inversely with wall thickness. The calculation of instantaneous wall stress is possible in humans by using simultaneous left ventricular micromanometry and echocardiography; however, the technique is demanding technically and necessitates left heart catheterization (1). The fourth deficiency is addressed, in the absence of mitral regurgitation, by measuring the aortic input impedance spectrum, a function of phasic pressure-flow relations and one that accounts for peripheral resistance (the mean pressure difference across the circuit divided by the mean flow), aortic wall stiffness, inertial properties of blood, and reflected waves from the periphery. Simultaneous recording of high-fidelity ascending aortic flow velocity and pressure is required for the determination of this function in humans (2). Constancy of the ascending aortic cross-sectional area throughout systole, along with a relative flat, laminar flow profile, are assumed to convert measured velocity into instantaneous aortic flow.

AFTERLOAD IN VALVULAR AORTIC STENOSIS

When applying these mechanical and hydraulic principles to valvular aortic stenosis, quantifying ejection load becomes even more complex. The forces that resist left ventricular shortening represent the composite of a narrowed valve orifice at the outlet, left ventricular geometry, and the characteristics of the vasculature beyond the point of obstruction. In clinical parlance, valve obstruction often is quantified by the transvalvular mean and maximum instantaneous pressure gradients or velocities. Early on, Gorlin and Gorlin recognized the flow dependence of the measured pressure gradient and proposed calculation of valve orifice area based on the Torricelli model for nonturbulent fluid through a planar orifice. Although the Gorlin calculation of valve orifice has found long-lasting clinical applicability, the equation requires an empirical constant to account for blood viscosity, density, turbulence, and the ratio of the valve area to the vena contracta, which is the area of the narrowest part of the stream that passes through the orifice. Refinements to the constants of the original Gorlin equation for the aortic valve now have been proposed that allow mathematical correspondence with the continuity equation applied as part of a two-dimensional echocardiography/Doppler determination of orifice size (3).

A number of investigations have confirmed the "flow dependence" of the composite constant used in the Gorlin equation. In low-flow states, in particular, the valve orifice size may be underestimated, leading to a misleading conclusion of severe obstruction when, in fact, the low valve orifice calculation is due to depression of the cardiac output. Valve resistance, taken as the simple ratio of the pressure gradient divided by the cardiac output, also has been found useful for confirming the severity of obstruction before direct surgical inspection (4). However, in a Torricelli model of a constant flow state, valve resistance itself is linearly related to flow (5). Thus, neither the planar orifice nor the valve resistance is absolutely sufficient to account for all the hydraulic variables that are attendant to pulsatile flow through a deformed and narrowed valve and that give rise to high turbulence in the ascending aorta. Garcia et al. (6) have proposed an energy loss index that allows even greater correspondence with the true pressure gradient between the left ventricular cavity and the "recovery pressure" in the high ascending aorta. This novel assessment of valve orifice

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From the University of California, San Diego, San Diego, California.

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compromise represents a useful advance to the noninvasive estimation of the severity of aortic stenosis.

PERIPHERAL ARTERIAL VASCULATURE IN VALVULAR AORTIC STENOSIS

Just as mean aortic pressure is a deficient approach to measuring vascular load on the left ventricle, a preoccupation with only the pressure gradient and planar orifice size in valvular aortic stenosis also may be overly simplistic. In this issue of the *Journal*, Briand et al. (7) report a cohort of patients with aortic stenosis in whom the compliance of the systemic vasculature (stroke volume index divided by the pulse pressure at the brachial artery) appeared to be an independent predictor of depressed left ventricular systolic shortening (ejection fraction <50%) and diastolic dysfunction. When systemic compliance (directly equivalent to the characteristic impedance of the systemic vasculature) was summed with the energy loss index across the aortic valve, the net "valvulo-arterial impedance" (Z_{va}) was the only hemodynamic predictor of a depressed left ventricular ejection fraction. Although an increased systemic vascular resistance also was found in those patient groups with an elevated systemic arterial compliance, the former was not an independent predictor of left ventricular dysfunction in the multivariate analysis.

Although Briand et al. (7) have provided persuasive data on arterial compliance, the question arises whether Z_{va} represents the full vascular load in patients with valvular aortic stenosis. As stated previously, the most complete description of hydraulic load would be provided by the input impedance spectra of the systemic circulation. A simpler, yet comprehensive formulation of vascular load, as conceptualized by Sunagawa et al. (8), is provided by effective arterial elastance (E_a), or ascending aortic end-systolic pressure divided by the stroke volume. E_a is a steady-state arterial parameter that incorporates characteristic impedance (Z_o), resistance (R), arterial compliance (C), and cardiac cycle length (T). Segers et al. (9), using a mathematical heart-arterial interaction model, found that E_a was linearly related to R/T and stiffness (1/C) and that R/T contributed about three times more to E_a than 1/C. Chemla et al. (10) subsequently reported that the sensitivity of E_a to a change in R/T was 2.5 times higher than to a similar change in 1/C in both normotensive and hypertensive patients. One could hypothesize, therefore, that R/T might be a potent predictor of vascular load in aortic stenosis. It might better explain the counterintuitive-but-beneficial action of nitroprusside (predominantly an arteriolar vasodilator) on cardiac index in critically ill patients with left ventricular dysfunction and valvular aortic stenosis (11).

SYMPTOMS, CLINICAL OUTCOMES, AND THE SEVERITY OF VALVULAR AORTIC STENOSIS

Considering the complexity of measures of left ventricular afterload in aortic stenosis, it is not surprising that they correlate only generally with symptom development and actuarial survival. However, a number of other factors may explain this poor association. The disease is most prevalent in the elderly population, and the presence of other common types of comorbidity (operating independently of their action on arterial compliance), including coronary atherosclerosis, cerebral vascular disease, hypertension, diabetes mellitus, and chronic obstructive lung disease, strongly influence the development of symptoms and the ultimate rate of survival. Also of importance are the variable myocardial adaptations to chronic left ventricular pressure overload. Concentric hypertrophy of the chamber minimizes average wall stress and allows the maintenance of normal endocardial shortening despite the high intracavitary pressure. However, the increase in the ratio of wall thickness to minor axis radius is not completely salutary and contributes significantly to an increase in diastolic chamber and myocardial stiffness (12). Moreover, even in the face of large increases in wall thickness, severe aortic stenosis is associated frequently with an elevated midwall circumferential stress and reduced midwall shortening (1). In fact, if midwall measurements of circumferential shortening were assessed routinely by two-dimensional echocardiography, it is likely that afterload excess with associated depression of myocardial shortening would be detected more often in this valve lesion. It would then be possible to detect at an earlier time period incipient heart failure, which is known to be a powerful predictor of death in patients with severe aortic stenosis. Earlier detection of systolic left ventricular dysfunction would be all the more important because of the dramatic improvement in myocardial shortening that is observed clinically (and experimentally) after relief of the outflow tract obstruction.

Thus, it would be of interest whether left ventricular midwall circumferential stress would be superior to measures of vascular load in predicting left ventricular dysfunction and adverse clinical outcome. It may be relevant that Covell et al. (13) found (in an open-chest anesthetized animal) that alterations in characteristic impedance are reflected directly by alterations in ventricular performance but that these changes also are reflected by alterations in ventricular wall stress that more adequately predict reduced ventricular shortening associated with the change in load.

Irrespective of the physiologic construct invoked to quantify the forces that resist myocardial shortening, the paper by Briand et al. (7) highlights the vital role of both outflow obstruction and the peripheral circulation in the pathophysiology associated with valvular aortic stenosis. Their data support the notion that statin therapy may not only forestall the progression of valvular stenosis but also might mitigate vascular stiffening in the peripheral vasculature in these same patients. In time, what was once a strictly "surgical" disease may be effectively treated with modern pharmacologic agents that impact the progression of disease both at the aortic valve and within the downstream arterial vasculature.

Reprint requests and correspondence: Dr. Kirk L. Peterson, Department of Medicine, University of California, San Diego, 200 West Arbor Street, San Diego, California 92103-8411. E-mail: klpeterson@ucsd.edu.

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