Time to Treat Hypertension in Patients With Aortic Stenosis

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Historically, patients with aortic stenosis (AS) rarely had concurrent systemic hypertension (HTN). Now, echocardiography allows early diagnosis, calcific remodeling has replaced rheumatic heart disease as the most prevalent cause of AS in the developed world, and the population of adults with AS is older, paralleling the demographic shift in the age of our population. In combination, these trends mean that HTN is a more common comorbidity in patients with AS and is coexistent for a longer period of time before aortic valve replacement. In studies involving younger patients with AS, the prevalence of HTN is 30% to 40%, whereas in recent series involving older patients at high risk for aortic valve replacement, the prevalence of HTN is 75% or higher.4,5

In patients with AS, increased systemic vascular load, resulting from increased vascular stiffness, resistance, pressure, or a combination of these factors, adds to the load on the left ventricle (LV) from the stenotic valve and is associated with increased hypertrophic remodeling, impaired LV function, and worse clinical outcomes. As Carabello pointed out, the resistance of the valve and the resistance of the systemic vasculature—in effect, 2 resistors in series—both contribute to pressure overload on the LV. In comparison with decades ago, patients managed with AS today tend to have lower valvular resistance and higher peripheral resistance. Whether aggressive treatment of increased systemic vascular load will improve outcomes and whether specific targeting of stiffness or resistance matters is an area of active investigation.

Despite the recognition that HTN is an important medical problem that requires effective treatment to minimize cardiovascular morbidity and mortality, there has been reluctance to treat (or at least adequately treat) HTN in patients with AS. This reluctance stems from the now outdated notion that obstruction at the valve level is the overwhelmingly dominant cause of increased LV load and that, in the face of this fixed afterload, cardiac output cannot be augmented. This faulty reasoning underlies the traditional teaching that vasodilators are contraindicated in AS because they would decrease systemic vascular resistance without a compensatory increase in cardiac output, thus precipitating hypotension.

However, a growing body of literature has reported that a high percentage of patients with significant AS do take antihypertensive and vasoactive medications without evident adverse effects. Additionally, careful hemodynamic studies in patients with severe AS treated with single doses of vasodilating medications (captopril, nitroprusside, and sildenafil) have demonstrated the safety, tolerability, and, indeed, hemodynamic benefit of vasodilation in patients with severe symptomatic AS. Those studies demonstrated that the particular vasodilating medications used result in a decrease in systemic vascular resistance and pulmonary capillary wedge pressure combined with an increase in stroke volume, but no change in heart rate. Pulmonary vascular hemodynamics also improve with a decrease in pulmonary artery pressure and pulmonary vascular resistance. Treatment with sildenafil provides relatively greater effects on the pulmonary vasculature in comparison with the effect on unloading the LV, which could have additional benefits for patients with AS and pulmonary hypertension.

In this issue of Circulation, Eleid et al report an elegant invasive hemodynamic analysis of patients with significant AS to whom a vasodilator was administered. In this study, 18 symptomatic patients with systemic HTN (systolic blood pressure >140 mm Hg) and severe low-gradient AS with preserved ejection fraction (EF) (aortic valve area [AVA] ≤1.0 cm$^2$ or indexed AVA ≤0.6 cm$^2$/m$^2$; mean gradient <40 mm Hg; and EF >50%) were compared with 6 symptomatic patients with low-gradient severe AS and reduced EF (≤50%). The administration of nitroprusside had a balanced effect on the pulmonary and systemic circulations with similar decreases in pulmonary and systemic vascular resistance and pressure (=35%–40%). They also observed a 40% decrease in LV end-diastolic pressure and a trend toward a =10% increase in stroke volume and cardiac index with no change in heart rate. These data extend our understanding of the response to vasodilation of patients with AS, particularly in the subgroup of patients with low-gradient AS with a preserved EF.

Of note, the patients with preserved EF included in this study had a very elevated systemic blood pressure with an average aortic systolic pressure of 176 mm Hg and mean aortic pressure of 115 mm Hg. In future studies, it would be of interest to compare the hemodynamics in patients with chronically elevated ambulatory blood pressures versus patients with an acute elevation in blood pressure attributable to holding cardiac/antihypertensive medications on the day of the catheterization or the adrenergic stimulation from the procedure itself.

Interestingly, the administration of nitroprusside in hypertensive patients was associated with a modest but significant increase in mean transvalvar gradient from 27 to 29 mm Hg and an increase in AVA from 0.86±0.11 to 1.02±0.16 cm$^2$. The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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Somewhat analogous to the use of dobutamine to clarify pseudo versus truly severe AS in patients with a small AVA, low gradient, and a preserved EF, they demonstrate that nitroprusside can increase flow and provide insight into the true severity of the AS. However, cut points for determining truly severe AS based on a change in AVA and gradient with pharmacological intervention are not uniform across studies and require further investigation. Even so, the current data provide further support for the concept that systemic HTN can influence the evaluation of AS severity.

Clinical Implications
In managing patients with AS, it is important to recognize the high prevalence of coexistent systemic HTN, its harmful effects on LV remodeling and function, and its adverse impact on clinical outcomes. Moreover, when determining the severity of AS and making decisions about the timing of valve replacement, it is important to recognize that systemic HTN can influence the assessment of AS severity (generally causing overestimation of severity; Figure). After valve replacement is performed, there may be a greater tendency toward systemic HTN because of the increased flow from the relief of valvular afterload, which may mitigate the expected favorable effects of LV unloading with valve replacement and limit symptomatic improvement. For all these reasons, both before and after valve replacement, treatment of systemic HTN should be an important objective of medical therapy.

When managing a symptomatic patient with uncontrolled systemic HTN (at the time of the echocardiogram) and a small AVA, low gradient, and preserved EF, it is reasonable to redo the echocardiogram when the patient is normotensive, particularly if the measurements of AS severity are borderline between moderate and severe. It also is prudent to reassess symptoms once the patient is consistently normotensive. When managing an asymptomatic patient with uncontrolled systemic HTN and a small AVA, low gradient, and preserved EF, effective HTN treatment may mitigate the deleterious effects on the LV of increased systemic vascular load and potentially delay symptom onset. Although LV outflow obstruction at the level of the valve is the sine qua non of AS, increased systemic vascular load—identified most readily as systemic HTN—is often coexistent with AS and contributes to the pressure overload, hypertrophic remodeling, and dysfunction of the LV, which underlies much of the morbidity and mortality of the disease. As such, we must remember to treat the patient (including HTN and other cardiovascular comorbidities) and not have a myopic focus on the valve alone to provide the best clinical outcomes.

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References


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