Georg Ohm and the Changing Character of Aortic Stenosis
It’s Not Your Grandfather’s Oldsmobile

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Severe aortic stenosis (AS) untreated by aortic valve replacement is a fatal disease with a 3-year mortality rate of 75% once the classic symptoms of the disease ensue.1–4 Approximately 15% of AS patients present with syncope, which is an ominous occurrence.2 Indeed, a master cardiologist and my former mentor, Dr Lewis Dexter, quipped that sudden death in AS was simply prolonged syncope. Although exercise-induced arrhythmia and/or a pressure-induced vasodepressor response have been invoked to explain syncope in AS, the most commonly held theory invokes Ohm’s law. This well-known principle states that \( V=I\times R \), where \( V \) is voltage, \( I \) is current, and \( R \) is resistance. Applied to the circulation, the terms are substituted such that \( P=CO \times R \), where \( P \) is pressure, \( CO \) is cardiac output (L/min), and \( R \) is the vascular resistance in the area of interest. The Figure diagrams the circulation in the patient with AS as having 3 major resistors: \( R_1 \), the total pulmonary resistance made up of left ventricular (LV) filling pressure plus pulmonary vascular resistance that governs LV filling; \( R_2 \), the resistance offered by the aortic valve; and \( R_3 \), the systemic vascular resistance (SVR). Pressure at these 3 points in the circulation is determined by the product of \( CO \times R \). If resistance drops without a concomitant increase in output, pressure must also fall. In severe AS, it has been assumed that \( R_2 \) (valve resistance) exceeds \( R_3 \) (SVR) substantially. As such, a fall in SVR caused by exercise or by administration of a vasodilator would cause a fall in systemic pressure because \( R_2 \), the severely stenotic aortic valve, would block a compensatory increase in forward output causing systemic hypotension and syncope. Is this theory proven?

A study in this issue of Circulation addresses this issue. In a detailed hemodynamic analysis, Lindman et al5 present their findings on the effects of a single dose of sildenafil. The results were wonderfully complex and give enormous insight into the application of Ohm’s law to patients with AS. The patients in the study were well characterized. Their average valve area was 0.7 cm\(^2\), and their ejection fraction was normal. With the use of an assumed systolic ejection period of 0.33 seconds and the data provided in the study, estimated valve resistance (\( R_2 \)) was 370 dynes-s-cm\(^{-5}\) (valve resistance\(=1.33\times h\times SEP\times HR/CO\), where \( h \) is the mean gradient [mm Hg], \( SEP \) is the systolic ejection period [seconds], and \( HR \) is heart rate [bpm]). Although this figure is much lower than the calculated SVR of 2160 dynes-s-cm\(^{-5}\) (\( P/CO \times 80 \), where 80 is the factor that converts mm Hg to dynes/cm\(^2\) and CO in L/min to cm\(^3\)/s to yield dynes-s-cm\(^{-5}\)), the 2 resistances are not comparable because valve resistance occurs only during ejection whereas SVR assumes peripheral flow throughout the cardiac cycle. Still, sildenafil caused a significant increase in stroke volume despite a fall in LV filling pressure. Because sildenafil does not increase inotropy and preload certainly did not increase, the increase in stroke volume must have been predicated on a fall in afterload, leading to the inescapable conclusion that \( R_2 \) did not dominate resistance to outflow in this specific group of patients. The fall in SVR permitted an increase in stroke volume despite the stenotic aortic valve. Although there was a 14-mm Hg drop in mean arterial blood pressure from administration of the vasodilator, mean arterial blood pressure was still 94 mm Hg after drug. Although SVR fell more than blood pressure, the increase in stroke volume blunted the tendency toward hypotension. It is probable that the fall in pulmonary resistance also helped blunt the potential for underfilling of the left heart. Wedge pressure fell, but without the observed decrease in pulmonary vascular resistance (potentiating right heart output), the fall in wedge pressure may have been much greater, reducing preload, which might have precluded an increase in stroke volume.

Previous Use of Vasodilators in AS

The present study is not the first to report the use of vasodilators in AS. Indeed, there are several reports of the use of angiotensin-converting enzyme inhibitors in severe symptomatic disease.7–9 A recent study randomized patients with symptomatic AS to receive placebo or enalapril.7 For the most part, enalapril was well tolerated without causing hypotension while the drug improved symptoms and increased performance on a 6-minute walk. However, 3 patients with LV dysfunction suffered hypotension and had to be withdrawn. When Ikram and colleagues10 treated 35 patients with severe AS with sodium nitroprusside, they also found a variable response. Fourteen patients had an increase in CO and 24 had a decrease. The latter group had lower LV filling pressures and presumably had a significant reduction in preload, leading...
to the decreases in CO. Mean arterial pressure in the entire group fell from 99 to 80 mm Hg.

In another remarkable study, sodium nitroprusside was administered to AS patients with pulmonary edema during careful hemodynamic monitoring. The patients improved dramatically without induced hypotension. Although the drug reduced SVR, that change did not explain the outcome. Analysis of pressure-volume loops taken from the study patients indicated that nitroprusside increased contractility. The patients improved carefully hemodynamically. Analysis of pressure-volume loops taken from the study patients indicated that nitroprusside increased contractility. The patients improved carefully hemodynamically.

**AS: Then and Now**

Severe untreated AS has been recognized as a fatal disease for decades, but its demographics have changed dramatically over time. Forty years ago, rheumatic heart disease and congenital AS were the most common causes of AS, leading to severe disease at a relatively early age. Forty years ago, Doppler echocardiographic interrogation of the aortic valve was not yet used, so patients with AS were often not detected until the disease was much more severe than when detected today. Aortic valve areas of <0.5 cm² were often found for the first time during cardiac catheterization and the so-called Carabello sign was observed (I rarely observe it today). In that era, the proscription against the use of vasodilators in AS was strongly espoused. Today, however, atherosclerotic calcific disease is the major cause of AS, and disease is detected noninvasively earlier in its course. The change in etiology has shifted the age of symptom onset to about 2 decades later in life. Aging in turn brings about vascular changes that make systemic hypertension the rule rather than the exception. Thus, R₃ is greater today that it was 4 decades ago, and R₂ is less. As in the Lindman et al study, the presence of hypertension and relatively less severe obstruction to LV outflow may protect patients from clinical hypotension. Although Lindman et al reported a 14-mm Hg drop in mean arterial blood pressure, the mean arterial blood pressure was still 94 mm Hg, and indeed the patients were treated with anti-hypertensive therapy, use of diuretics, and occasional administration of nitroprusside to AS patients with pulmonary edema during careful hemodynamic monitoring.

**Figure.** Diagram of the circulation as an electric circuit. PAP indicates pulmonary artery pressure; CO, cardiac output; PR, pulmonary resistance; Ao, aortic; BP, systemic blood pressure; SVR, systemic vascular resistance; RV, right ventricle; R₁, total pulmonary resistance; LV, left ventricle; R₂, aortic valve resistance; and R₃, SVR.

**Phosphodiesterase 5 Inhibitors, AS, and Erectile Dysfunction: Can Vasodilators Be Used With Impunity in AS?**

The answer to this question is a resounding “no.” In a patient with a slightly tighter valve, less ventricular reserve, or a lower LV filling pressure or a patient whose untreated mean arterial blood pressure is 70 mm Hg instead of 104 mm Hg, the use of any vasodilator could cause hypotension and syncope. Furthermore, AS is a progressive disease, with R₂ becoming greater with time. Vasodilator therapy tolerated today may cause hypotension tomorrow when the stenosis is a little worse or the patient’s volume status has contracted from exercise, perspiration, etc. Although it is unlikely that sildenafil will be used in the near future to treat AS, the AS age group is also common to men with erectile dysfunction, the standard treatment of which includes sildenafil and other phosphodiesterase 5 inhibitors. Men on such therapy who also have AS should be apprised of the benefits and risks of such therapy and may wish to consider other erectile aids.

**Conclusions**

The safe use of vasodilators in some patients with severe AS is well documented, and the Lindman et al study adds to that literature, elegantly defining the hemodynamic changes accompanying sildenafil use. As noted, many patients with AS have a second fatal illness called hypertension that must also be treated, and the question about best therapy often arises. Worry that diuretics may decrease preload and that β-blockers may reduce the inotropic needed to drive blood past the stenotic valve raises the issue of vasodilator use. For symptomatic AS patients, the best course of action is, of course, aortic valve replacement. However, for the asymptomatic AS patient who requires antihypertensive therapy, we simply need to keep Ohm’s law in mind. Vasodilators can cause an increase in CO that helps offset the drop in SVR even in severe AS. Thus, vasodilators may be used with extreme caution to treat the hypertension that today commonly accompanies this common valve disease.

**Disclosures**

None.

**References**


KEY WORDS: Editorials aortic valve stenosis heart failure phosphodiesterase inhibitors