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 present study is not the first to report the use of vasodilators in AS. Previous Use of Vasodilators in AS

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

From the Baylor College of Medicine, Veterans Affairs Medical Center, Houston, TX.

Correspondence to Blase A. Carabello, MD, Veterans Affairs Medical Center, Medical Service (111), 2002 Holcombe Blvd, Houston, TX 77030. E-mail blaseanthony.carabello@med.va.gov

(Circulation. 2012;125:2295–2297.)

© 2012 American Heart Association, Inc.

Circulation is available at http://circ.ahajournals.org

DOI: 10.1161/CIRCULATIONAHA.112.105825

The figures in the article show a hemodynamic analysis of the circulation in patients with AS. The figures demonstrate how the use of sildenafil affects the circulation, particularly in relation to the systemic vascular resistance (SVR) and the left ventricular (LV) filling pressure. The article discusses the use of sildenafil in AS, highlighting its potential effects on the circulation and the clinical implications.

The article also addresses the historical context of Ohm’s law in the context of aortic stenosis. It references Dr Lewis Dexter’s statement on the nature of sudden death in AS and discusses the current theories on the development of syncope in AS. The author, Blase A. Carabello, MD, provides a view on the current state of knowledge regarding the use of vasodilators in AS, emphasizing the importance of understanding the hemodynamic effects of these medications.

The article concludes with a summary of the findings and potential implications for clinical practice, including the need for further research on the use of sildenafil and other vasodilators in AS.

The article is a comprehensive review of the current understanding of Ohm’s law in the context of aortic stenosis, the hemodynamic effects of sildenafil, and the potential implications for clinical care.
to the decrease 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,12 a remarkable response for an agent not known to be a positive inotrope. It is likely that by reducing LV filling pressure, nitroprusside increased the pressure gradient driving subendocardial coronary blood flow, thus relieving subendocardial ischemia and improving the inotropic state.

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 catheterization3 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, R₂ is greater today that it was 4 decades ago, and R₃ is less. As in the Lindman et al study, the presence of hypertension and relatively lesser 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 hypertensive.

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 or 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 inotropism 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
Georg Ohm and the Changing Character of Aortic Stenosis: It's Not Your Grandfather's Oldsmobile
Blase A. Carabello

Circulation. 2012;125:2295-2297
doi: 10.1161/CIRCULATIONAHA.112.105825

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/125/19/2295

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/