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EDITORIAL COMMENT

Aortic Stenosis

A 6-Decade Odyssey*

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The 1960s were the most exciting and challenging decade in the management of aortic stenosis (AS). The development of open-heart surgery in that period made possible aortic valve replacement (AVR), thereby prolonging and improving the lives of many patients with a debilitating and nearly always fatal condition. However, the early (30-day) mortality of the operation was high—10% to 15% in most centers—and dysfunction and/or thrombosis of the early prosthetic valves were troublesome.

An important task of cardiologists during that era was the selection of patients for referral for this operation. In 1963, the late John Ross, Jr and I were assigned this responsibility at the (then) National Heart Institute, which had a robust surgical program headed by Andrew G. Morrow. The task was challenging because of the limited information on the natural history of AS then available. We began by examining our patients with severe AS who declined to undergo AVR or for whom the procedure had been deferred, and then turned our attention to the literature. Our results are summarized in **Figure 1**, which showed that the survival of asymptomatic patients with severe AS, during what we referred to as the latent period in which obstruction was progressing, was similar to that of the general population. However, once serious symptoms (angina, syncope, and/or heart failure) developed, the patients "fell off a cliff" and had brief survival times.[1] These findings were confirmed, and for many years the practice in asymptomatic patients with moderate or severe AS became "watchful waiting" and referral for surgical treatment if and when any of these symptoms developed.

There have, of course, been immense changes in the diagnosis and management of patients with AS during the past 6 decades. With the aging of the population and the decline in rheumatic heart disease in high-income countries the most common cause of AS now is calcific aortic valve disease (CAVD), which has become the most frequent serious valvular disorder in adults and is steadily increasing in prevalence. Simultaneously, the risk of surgical AVR plummeted, and transcatheter AVR became successful in a growing fraction of patients. However, what has not changed is the importance of basing treatment on the balance between the risks of AVR and the natural history of AS.

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In this issue of the *Journal of the American College of Cardiology*, Généreux et al[2] in well-established cardiac centers have provided a valuable contemporary analysis of almost 600,000 adults who had echocardiograms that visualized the aortic valve. Of these, 70,778 (11.9%) had AS and were followed up for 4 years or until the time of AVR, using verified natural language processing. The investigators reported that many of the important baseline characteristics of these patients, including age, left ventricular ejection fraction, prior myocardial infarction, and atrial fibrillation, were similar along the spectrum of AS severity determined echocardiographically. However, the frequency of accompanying mitral and tricuspid valve disease and of aortic regurgitation rose progressively with the severity of the AS.

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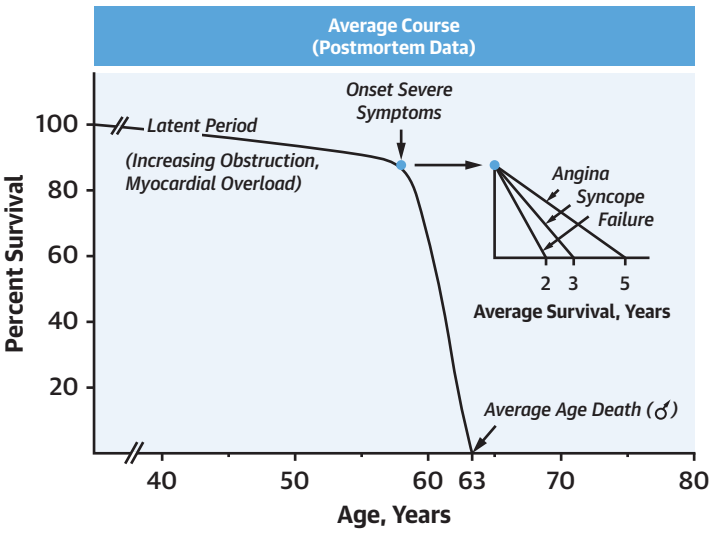
The adjusted 4-year mortality, 25.0% in patients with mild AS, rose progressively to 44.2% and 42.0% in those with moderately severe and severe AS, respectively. A key finding reported by Généreux et al[2] was that AVR was carried out in only 36.7% and 60.7% of those 2 subgroups. The specific reasons for withholding this guideline-recommended treatment[3] were not available to the investigators. Nonetheless, the percentage of patients not undergoing AVR was excessive, especially in the current era, in which both surgical and transcatheter AVR are effective and impose low risk. This large contemporary database reinforces the position that many patients with AS are currently undertreated even in experienced centers, a deficiency that, as Lindman et al[4] have pointed out, must be corrected.

The combination of echocardiographic assessment of the severity of obstruction and the patient's symptomatology remains the keystone in the selection of patients for AVR.[3] Patients with low-flow, low-gradient *severe* AS, irrespective of the presence of symptoms, may be candidates for AVR as well. Because of the concern that chronic pressure overload can result in irreversible myocardial damage,[5] there is growing interest in earlier AVR. Thus, asymptomatic patients with moderately severe and severe AS at high risk should also be considered.[6,7] They include patients with left ventricular dysfunction as reflected in an ejection fraction <55% or cardiac damage, which may be caused by left ventricular fibrosis that can be detected by cardiac magnetic resonance and accompanied by elevations of circulating natriuretic peptides and/or troponin. This population also includes asymptomatic patients who experience symptoms during a stress test, and patients with *very severe* obstruction, such as an aortic valve area ≤0.75 cm^2 or a *mean* transvalvular pressure gradient ≥50 mm Hg. Given that the quality of life after AVR varies inversely with the preoperative cardiac damage,[8] the procedure should be performed promptly once the decision to replace the AV has been made.

Looking forward, it is likely that artificial intelligence will enhance the early detection of asymptomatic patients with moderate or severe AS for whom aggressive follow-up care is indicated so that they can undergo AVR in a timely manner.[9] Also, in efforts to develop medical therapy, the pathogenesis of CAVD is undergoing increasing investigation.[10] An example is the observation that elevated levels of circulating lipoprotein(a) are an important risk factor for the development of CAVD. It is likely that prevention or reduction of this dyslipidemia will soon be possible, thereby reducing the incidence of CAVD. Other potential mechanisms that may be involved in the development and progression of CAVD include damage to endothelial cells, the recruitment of inflammatory cells, their release of cytokines, and the microcalcification of intracellular vesicles. Attacks on these could be helpful as well.

It has been exhilarating to have had a ringside seat observing the advances in the incidence, assessment, and management of AS since the time when John Ross and I began the study of this disorder in 1963,[1] and it is exciting to contemplate what will be possible in the future.

FIGURE 1 Valvular Aortic Stenosis in Adults



Average course of valvular aortic stenosis in adults. Data assembled from postmortem studies. Adapted with permission from Ross J Jr, Braunwald E. Aortic stenosis. *Circulation*. 1968;38(1s5):V61-V67. https://doi.org/10.1161/01.CIR.38.1S5.V-61

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