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EDITORIAL COMMENT

Comparison of Long-Term Risk of Thoracic Aortic Aneurysm and Dissection in Patients With Bicuspid Aortic Valve and Marfan Syndrome After Aortic Valve Replacement*

Himanshu J. Patel, MD

Bicuspid aortic valve (BAV) syndrome is a heterogeneous inheritable condition estimated to occur in 0.5% to 2% of the general population (1). Its phenotypic expression ranges from a "true" bicuspid valve associated with 2 sinuses of Valsalva to a "functional" bicuspid valve, in which 3 sinuses of Valsalva exist but 2 of the aortic cusps have varying degrees of fusion. The latter type results in fusion of a combination of any 2 of the 3 cusps, with a resulting asymmetric sinus of Valsalva. Associated lesions also can include coarctation of the aorta and ventricular septal defects.

BAV syndrome is often associated with an aortopathy, which is expressed in 1 of 4 ways: root, ascending and proximal arch aorta dilation, normal root with only ascending and arch aorta dilation, and either root or ascending aorta dilation alone (2). On the basis of pathological findings of medial degeneration also commonly seen in Marfan syndrome (MFS), an assumption regarding the virulent nature of BAV aortopathy led to recommendations for surgery that resembled those for Marfan syndrome (i.e., aneurysm diameter threshold of 5.0 cm) (3). Important differences do exist, as is evidenced by the dismal natural history of untreated MFS root aneurysm (4). In contrast to the average age of death of 32 years in patients with MFS who do not undergo prophylactic root replacement, BAV displays a spectrum of clinical presentation ranging from indolence to acute dissection. Recognition of these differences led to the newer guideline recommendations for elective thoracic aneurysmectomy for BAV syndrome (now 5.5 cm) (5).

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In this issue of the *Journal*, Itagaki et al. (6) have reported a timely study, describing the comparative late risks for aneurysm and dissection in patients with BAVs and MFS. The source of the data was the Statewide Planning and Research Cooperative System, an administrative database on every hospitalization and emergency department visit in New York State. Using coding diagnoses, they identified patients who underwent primary aortic valve replacement with an associated BAV (n = 2,079) or MFS (n = 73) and compared late aortic outcomes in these 2 groups with a control group of patients (n = 11,053) treated for rheumatic aortic valve disease. Those patients with a history of or undergoing concomitant aortic repair, or a history of other valvular or coronary artery surgery, were excluded. Other patients with genetic syndromes or inflammatory diseases that could potentially affect aortic growth were also excluded.

Their unique findings are as follows:

1. The control group had a significantly (and surprisingly) high rate of operative mortality at 6.2%. In contrast, the operative mortality reported for BAV or MFS patients was <3%.

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From the Department of Cardiac Surgery, University of Michigan Hospitals, Ann Arbor, Michigan. Dr. Patel has reported that he has no relationships relevant to the contents of this paper to disclose. Kim Eagle, MD, served as Guest Editor for this paper.

2. The 15-year cumulative incidence of aortic dissection was higher in MFS (5.5%), and the incidence in BAV patients (0.55%) was not different than the control patients.
3. The 15-year cumulative incidence of thoracic aneurysms was much higher in the MFS (10.8%) and BAV (4.8%) patients than in the control group (1.4%).
4. The 15-year cumulative incidence of thoracic aortic repair was again higher in the MFS (10.4%) or BAV (2.5%) patients than in control patients (0.5%). Indications for repair included aortic dissection in 30.8% of patients, with a mortality rate of 30.0%. In contrast, the mortality rate for aortic aneurysmectomy on late follow-up was 10.8%.

The novel findings in this study describe the intermediate risk imposed by the presence of BAVs, which appears to lie somewhere between MFS patients and those from the general population. These data importantly identified a relatively low risk of aortic-related complications at late follow-up in all groups of patients. The important caveat, however, is that the study group excluded a large number of patients who underwent concomitant aortic repair. Presumably, this excluded patients with smaller aneurysms that, if left alone, may have altered this natural history to favor higher risks of aortic complications.

Although this study is an important addition to the current published data, several limitations exist. Administrative databases have inherent data validity limitations and are not as clinically robust, although they do provide large sample sizes. Exclusion of a large number of patients at the outset of the study, as described previously, may have biased the conclusions against identifying aortic events in both MFS and BAV patients.

All of these issues, when taken together with the fundamental lack of knowledge regarding BAV syndrome, suggests that there is a need for a prospectively-collected, clinically-robust database to further evaluate the natural history and genetic underpinnings of this complex, heterogeneous pathology.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Himanshu J. Patel, Department of Cardiac Surgery, University of Michigan Hospitals, 1500 East Medical Center Drive, 5144 Frankel Cardiovascular Center, SPC #5864, Ann Arbor, Michigan 48109-5864. E-mail: hjpatel@med.umich.edu.

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KEY WORDS aneurysm, aortic dissection, bicuspid valve, Marfan syndrome