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Original article

The aortic stenosis complex: aortic valve, atherosclerosis, aortopathy

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ABSTRACT

Background: Aortic stenosis may be related to coronary atherosclerosis in patients with tricuspid aortic valve, while aortic dilatation often is present in patients with bicuspid aortic valve. We sought to define associations among aortic stenosis, coronary atherosclerosis, and thoracic aortic aneurysm in patients with tricuspid or bicuspid aortic valve undergoing surgery for aortic stenosis in a large referral medical center.

Methods: Two hundred seventy patients with severe aortic stenosis (tricuspid 175, bicuspid 95) undergoing surgical aortic valve replacement (AVR) were studied.

Results: Coronary artery bypass grafting (CABG) surgery plus AVR was required more often in tricuspid compared to bicuspid aortic valve [62.2% versus 26.3%; $p < 0.0001$; odds ratio 4.5, confidence interval (CI) 2.5–8.3]. The incidence of coronary atherosclerosis requiring CABG in bicuspid aortic valve (26.3%) was greater than that expected in the general population for similar age. Thoracic aorta surgery due to aortic aneurysm plus AVR was performed more often in bicuspid compared to tricuspid aortic valve (27.3% versus 3.4%; $p < 0.0001$; odds ratio 7.7, CI 3.0–22.1). The incidence of ascending aorta aneurysm requiring surgery, however, was not more common in tricuspid aortic valve (3.4%) to that expected in the general population for similar age.

Conclusion: Incidence of coronary atherosclerosis is high in patients with aortic stenosis, both in those with tricuspid and bicuspid aortic valve. Incidence of ascending aortic aneurysm is high in patients with bicuspid, but not those with tricuspid aortic valve. These findings should be taken into consideration in the evaluation and management of patients with the aortic stenosis complex.

Introduction

Traditionally, it was thought that calcific aortic stenosis in patients with a tricuspid aortic valve was related to valve degeneration due to aging caused by several years of mechanical stress and biologic response to such injury. Recent developments, however, suggest that calcific aortic stenosis in patients with a tricuspid aortic valve may be related to coronary atherosclerosis, and that the initiating pathogenetic mechanisms are similar in both disorders [1–3].

Bicuspid aortic valve is familial and present in approximately 2% of live births [4,5]. Patients with a bicuspid aortic valve typically develop aortic stenosis at a younger age, usually before the age of 65 years, compared to aortic stenosis in patients with a tricuspid aortic valve, which more often develops after the age of 70 years [6,7]. Aortic stenosis in patients with a bicuspid aortic valve, which often is associated with aortic dilatation with the potential for dissection, may also be related to atherosclerosis [5,8–10].

Although associations between aortic stenosis in patients with a tricuspid aortic valve and coronary atherosclerosis, and aortic dilatation in patients with a bicuspid aortic have been suggested, the incidence of atherosclerosis in patients with a bicuspid aortic valve and aortic dilatation in those with a tricuspid aortic valve have not been well defined. Furthermore, these interrelationshipsin patients requiring aortic valve surgery for aortic stenosis are not well known. The present study was undertaken to investigate associations between aortic stenosis and coronary atherosclerosis, and between aortic stenosis and thoracic aortic aneurysm, in patients with tricuspid and bicuspid aortic valve who had surgical aortic valve replacement in a large tertiary-care referral medical center.

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Methods

Study population

Medical records from The Ohio State University Wexner Medical Center (Columbus, OH, USA), a large referral center, were reviewed from January 2002 to June 2008. The study was approved by The Ohio State University Institutional Review Board. A total of 270 patients who had open-heart surgery for single aortic valve replacement due to severe aortic stenosis were identified. In these patients, aortic valve area was less than 1.0 cm^2 or less than 0.6 cm^2/m^2; 175 patients had tricuspid and 95 had bicuspid aortic valve (Fig. 1). One hundred and nine patients with a tricuspid aortic valve and aortic stenosis (62.2%), and 25 (26.3%) patients with a bicuspid aortic valve and aortic stenosis, had concomitant coronary artery bypass grafting (CABG) surgery for significant coronary artery disease; significant coronary artery disease was defined as a 70% stenosis or greater in at least one major coronary artery as determined by selective coronary arteriography.

Six patients (3.4%) with a tricuspid aortic valve and aortic stenosis, and 26 patients (27.3%) with a bicuspid aortic valve and aortic stenosis, had concomitant surgery for thoracic aortic aneurysm. Aortic dilatation requiring surgery was considered when the diameter of the ascending aorta was equal to or greater than 5.0 cm as determined by aortography and/or echocardiography. The number of aortic valve leaflets, tricuspid or bicuspid, was confirmed in all patients preoperatively by echocardiogram and by the surgeon in the operating room; the presence of tricuspid or bicuspid aortic valve was also confirmed by pathologic examination. In-hospital surgical mortality and length-of-stay were also determined. Hospital length-of-stay included only patients who survived hospitalization. Due to the wide range in hospital length-of-stay with potential outliers, both median and mean values are presented.

Statistical analysis

Descriptive data are expressed as either mean ± standard deviation or as a median with a low and high range. The association of significant coronary artery disease or significant dilatation of the thoracic aorta in relation to tricuspid or bicuspid aortic valve was determined using logistic regression analysis adjusting for age and gender. The Student's *t*-test was used to detect differences between means of age and log transformed hospital length-of-stay for patients with tricuspid or bicuspid aortic valve. To define if there was a statistically significant difference in gender, traditional risk factors, and in-hospital surgical mortality between groups a Fisher's exact test or a Chi-square test was performed where appropriate. Wilcoxon rank-sum test was used to determine difference in median length-of-stay between groups. A p-value <0.05 was considered statistically significant.

Results

Patients with a bicuspid aortic valve were on average 9 years younger than patients with a tricuspid aortic valve at the time of aortic valve replacement, 62 ± 13 years and 71 ± 10 years, respectively ($p < 0.0001$); however, there was some overlap in which several patients with a bicuspid aortic valve and aortic stenosis were older than 70 years, and several patients with a tricuspid aortic valve and aortic stenosis were younger than 60 years. There was a predominance of males in the entire cohort; however, this was more pronounced among those with a bicuspid (71.6%) compared to those with a tricuspid (55.4%) aortic valve ($p < 0.05$). In tricuspid and bicuspid aortic valve, history of arterial hypertension (87% versus 70%, respectively; $p = 0.001$) and diabetes mellitus (47% versus 31%, respectively; $p = 0.016$) were greater in patients with a tricuspid aortic valve, while history of hyperlipidemia (60% versus 61%, respectively) and smoking (48% versus 53%, respectively) were not statistically different between the two groups.

Individual patients with aortic stenosis (tricuspid or bicuspid aortic valve) requiring aortic valve replacement with or without concomitant CABG surgery are shown in Fig. 2. In order to better compare the frequency of coronary artery disease in different ages between tricuspid and bicuspid aortic valve, patients were divided into six subgroups as shown in Fig. 3. Although the frequency of coronary artery disease increases with age, incidence of coronary artery disease at any age was higher in patients with tricuspid compared with bicuspid aortic valve.

The overall incidence of significant coronary artery disease requiring CABG at the time of aortic valve replacement was significantly greater in patients with a tricuspid compared to those with a bicuspid aortic valve, 109 out of 175 (62.2%) versus 25 out of 95 (26.3%), respectively ($p < 0.0001$; Fig. 4A); odds ratio 4.5 with a confidence interval (CI) 2.5–8.3 ($p < 0.0001$; Fig. 4B) adjusted for age ($p = 0.0088$) and gender ($p = 0.0005$). The incidence of coronary artery disease requiring CABG, however, in patients with a bicuspid aortic valve and aortic stenosis appears to be greater to that expected in a population of the United States of America (USA) with similar age [11].

The incidence of significant ascending aortic aneurysm requiring thoracic aortic surgery in relation to age is shown in Fig. 5. It can

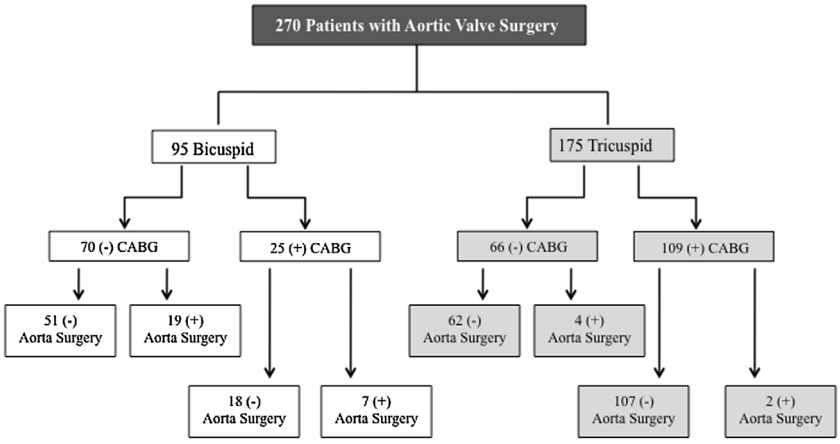

Fig. 1. Aortic stenosis in patients with tricuspid or bicuspid aortic valve who had surgical aortic valve replacement with or without concomitant coronary artery bypass grafting (CABG) surgery and/or thoracic aorta surgery; (−) indicates no surgery, (+) indicates surgery.