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Association for Academic Surgery

Clinical characteristics and surgical outcomes of dysfunctional quadricuspid aortic valve

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ARTICLE INFO

Article history:
Received 30 December 2017
Received in revised form
27 March 2018
Accepted 3 April 2018
Available online 1 May 2018

Keywords:
Aortic insufficiency
Aortic dilation
Outcomes
Quadricuspid aortic valve

ABSTRACT

Background: Quadricuspid aortic valve (QAV) is a rare and poorly understood congenital cardiac abnormality. This study aims to evaluate the clinical features and surgical outcomes of dysfunctional QAV.

Methods: From January 2011 to May 2017, 36 (mean age 50.7 ± 11.9 y, 19 males) of a total of 3855 patients who underwent aortic valve surgery were identified as having dysfunctional QAV (frequency 0.9%). All patients presented moderate or severe aortic regurgitation, and nine patients (25.0%) had concomitant aortic stenosis. The ascending aortic diameter was over 40 mm in seven patients (19.4%) and over 45 mm in two patients (5.6%). The most common QAV morphology was type B ($n = 12$, 33.3%) according to the Hurwitz-Roberts classification.

Results: All patients underwent aortic valve replacement and two required concomitant ascending aortic replacement. The mean follow-up time was 20.6 ± 14.2 mo. There was no early or late postoperative mortality or major complications. Pathological analysis of dilated ascending aorta demonstrated a relatively normal appearance. The ascending aorta did not grow after surgery (37.3 ± 4.1 mm *versus* 36.1 ± 2.5 mm, $P = 0.084$). Both the end-diastolic (58.1 ± 7.0 mm *versus* 50.0 ± 6.3 mm, $P < 0.001$) and end-systolic (37.7 ± 6.7 mm *versus* 32.8 ± 6.0 mm, $P < 0.001$) left ventricular dimensions were significantly decreased.

Conclusions: Aortic insufficiency is the predominant pathology in dysfunctional QAV patients. The incidence and extent of aortic dilation is not significant in QAV and not associated with aortic valve phenotypes. Short- and mid-term surgical outcomes were found to be satisfactory in this study.

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0022-4804/$ – see front matter
https://doi.org/10.1016/j.jss.2018.04.003

Introduction

Quadricuspid aortic valve (QAV) is a rare congenital malformation with an estimated incidence of 0.013%-0.043%.[1-5] Although most patients are asymptomatic, some require surgical intervention due to progressive aortic regurgitation (AR) or stenosis.[6-8] Unlike the bicuspid aortic valve (BAV), which has a well-documented association with ascending aortic aneurysm, QAV has not been widely studied, and the association between the morphology of QAV and ascending aorta dilation is unknown.[9-11] The surgical outcomes and ascending aorta behaviors are especially unclear in patients whose aortic valves require repair or replacement. This study aims to examine the characteristics of dysfunctional QAV and evaluate its surgical outcomes.

Methods

Patient population

From January 2011 to May 2017, a total of 3855 patients underwent aortic valve surgery at the Zhongshan Hospital of Fudan University. Among them, 827 patients (21.45%) had BAV, 36 patients (0.93%) had QAV, and five patients (0.13%) had unicuspid aortic valves. The diagnoses were made by transthoracic or transesophageal echocardiography and confirmed during surgery. Demographic and follow-up information was obtained from the Zhongshan Hospital Electronic Health Record System. The study was approved by the Ethics Committee of Zhongshan Hospital, Fudan University (approval number: B2017-324), with a waiver of informed consent.

Definitions of comorbidities

Hypertension was defined as systolic pressure $\geq$140 mm Hg or diastolic pressure $\geq$90 mm Hg.[12] Significant coronary artery disease was defined as >50% stenosis of the left main stem, >70% stenosis in a major coronary vessel, or 30%-70% stenosis with fractional flow reserve $\leq$0.8.[13] Diabetes mellitus was diagnosed according to American Diabetes Association criteria: (1) A1C $\geq$6.5%; (2) fasting plasma glucose $\geq$126 mg/dL; and (3) 2-h plasma glucose $\geq$200 mg/dL during an oral glucose tolerance test.[14] Chronic kidney disease was defined based on the presence of kidney damage or decreased kidney function lasting three or more months, irrespective of clinical diagnosis: (1) duration $\geq$ 3 mo, based on documentation or inference; (2) glomerular filtration rate <60 mL/min/1.73 m^2; and (3) kidney damage was defined by structural abnormalities or functional abnormalities other than decreased glomerular filtration rate.[15] The diagnosis of chronic obstructive pulmonary disease was based on patients' history, symptoms, and results of physical examinations, and each diagnosis was confirmed by spirometry, which indicated airflow obstruction in the absence of an alternative explanation for the symptoms or the airflow obstruction.[16]

Echocardiography

All echocardiographic images were collected in our echocardiography lab and reviewed by an experienced cardiologist with expertise in echocardiography. QAVs were classified into five subtypes based on leaflet size and distribution, as described by Hurwitz and Roberts.[17] Type A contains four equal-sized cusps; type B, three equal cusps and one small cusp; type C, two equal large cusps and two equal small cusps; type D, one large, two intermediate cusps and one small cusp; and type E, three equal cusps and one larger cusp (Fig. 1). We labeled any fused or unmeasurable cusps "undefined". The aortic root and ascending aortic diameters, as well as left ventricular data, were also evaluated and recorded using echocardiography.

Surgical indications

The indications for aortic valve replacement (AVR) were symptomatic patients with severe regurgitation, asymptomatic patients with severe regurgitation and left ventricular ejection fraction (LVEF) <50%, or asymptomatic patients with severe regurgitation, normal LVEF, and left ventricular end-systolic diameter (LVESD) >50 mm. The type of aortic prosthesis was determined by the patient's age, medical conditions, and willingness. The indication for concomitant ascending aortic replacement was patients' ascending aortic diameter $\geq$45 mm.

Pathological analysis

Ascending aorta with the diameter greater than 40 mm was routinely sampled if the patient underwent aortic valve procedure. We identified all the samples (paraffin blocks) of QAV patients and stained them with hematoxylin and eosin and with Masson and Elastica van Gieson. All samples and slides were prepared, treated, and analyzed in the central lab of our pathology department.

Follow-up and statistical analysis

Follow-up occurred via outpatient office visits. The follow-up time was defined as the interval between the date of the operation and the date of death from any cause or of the last follow-up. Categorical variables are summarized by frequencies and percentages, and continuous variables are summarized by median or mean $\pm$ standard deviation. The analysis of variance was used to access possible associations between various QAV subtypes. Preoperation and postoperation variables were analyzed using a paired *t*-test. Statistical analyses were performed with SPSS version 22 (IBM Corp, New York, NY), and *P* value less than 0.05 was considered significant.

Results

Patient characteristics

Of the 36 patients included, 19 (52.8%) were male. All patients had symptoms of heart failure at the time of diagnosis, and the majority were at the New York Heart Association Class II (n = 15, 41.7%) or Class III (n = 20, 55.6%). The mean age at