Quadricuspid Aortic Valve
Characteristics, Associated Structural Cardiovascular Abnormalities, and Clinical Outcomes

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Background—Quadricuspid aortic valve (QAV) is a rare congenital cardiac defect. This study sought to determine QAV frequency in a large echocardiography database, to characterize associated cardiovascular abnormalities, and to describe long-term outcomes.

Methods and Results—Fifty patients (mean±SD age, 43.5±21.8 years at the time of the index diagnosis; female sex, 52%) received a diagnosis of QAV between January 1, 1975, and March 14, 2014 (frequency, 0.006%). The QAV was type A in 32% and type B in 32% (Hurwitz and Roberts classification). Aortic dilatation was present in 29% of the patients, and 26% had moderate or severe aortic valve regurgitation at the index diagnosis. Stenosis affected only 8% of the valves and was mild. Other findings, including abnormalities of other cardiac valves, septal defects, persistent left superior vena cava, and patent ductus arteriosus, were present in 32% of patients. During a mean±SD follow-up of 4.8±5.6 years, 8 patients underwent aortic valve surgery, with severe aortic valve regurgitation being the surgical indication in 7 patients. One patient with mild to moderate aortic valve regurgitation underwent aortic valve repair for obstruction of the left coronary ostium by the accessory cusp of QAV. No infective endocarditis or aortic dissection was found. Overall survival was 91.5% and 87.7% at 5 and 10 years.

Conclusions—Aortic dilatation and other structural cardiac abnormalities were relatively common among patients with QAV. Aortic valve regurgitation was the predominant hemodynamic abnormality and the indication for aortic valve surgery in most patients who received surgery. Long-term survival was excellent. (Circulation. 2016;133:312-319. DOI: 10.1161/CIRCULATIONAHA.115.017743.)

Key Words: aortic valve ▶ aortic valve insufficiency ▶ echocardiography ▶ survival

Quadricuspid aortic valve (QAV) is a rare congenital cardiac defect with an estimated frequency of <0.05%.1–4 In a previous study from the Mayo Clinic, in which the archived 2-dimensional echocardiography database between 1982 and 1988 was reviewed, 8 cases of QAV were identified from >60,000 individual patient examinations.2 Because of its rarity, the characteristics, natural history, and long-term outcomes of QAV are poorly defined.

Clinical Perspective on p 319

Most reports of QAV represent single-center experiences with small numbers of cases.2–6 These reports have shown that it is frequently associated with progressive aortic valve regurgitation (AR), whereas aortic valve stenosis and ascending aortic enlargement are uncommon.3,4 Nearly one-half of patients with QAV require a surgical procedure for their aortic valve disease.4 Options for QAV include aortic valve repair and aortic valve replacement,5,6 but data on long-term clinical and surgical outcomes are lacking. This investigation of patients with QAV sought to determine the characteristics of QAV in a large echocardiography database, including associated structural and hemodynamic cardiovascular abnormalities, and to describe the long-term outcomes.

Methods

Study Group
This investigation was approved by the Mayo Clinic Institutional Review Board. We searched the echocardiography database of all patients seen between January 1, 1975, and March 14, 2014, for those with a QAV diagnosis through transthoracic or transesophageal procedures performed at any of the echocardiography laboratories of the Mayo Clinic. Echocardiographic images were reviewed, and the QAV diagnosis was confirmed in each case by 2 echocardiographers (including M.Y.C.T.) independently. Thirteen patients with a quadricuspid aortic or truncal valve in the presence of other conotruncal anomalies (eg, tetralogy of Fallot, pulmonary atresia, truncus arteriosus) were excluded.1–3 Pathological and cardiovascular surgical

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databases were searched to ensure that all patients with a QAV diagnosis were included in the study. Demographic information was obtained through medical record review.

From echocardiographic short-axis images or review of pathological specimens, QAVs were classified into 7 subtypes based on leaflet size and distribution, as described by Hurwitz and Roberts10 (Figures 1 and 2). This classification system was originally developed for differentiating various subtypes of quadricuspid pulmonary valve, which is more common than QAV.10 According to this classification system, type A contains 4 equal-sized cusps; type B, 3 equal cusps and 1 small cusp; type C, 2 equal large and 2 equal small cusps; type D, 1 large, 2 intermediate, and 1 small cusp; type E, 3 equal and 1 larger cusp; type F, 2 equal larger and 2 unequal smaller cusps; and type G, 4 unequal cusps.

**Echocardiography**

All patients had undergone comprehensive 2-dimensional and Doppler echocardiography performed with commercially available ultrasonography equipment in accordance with the American Society of Echocardiography guidelines.11,12 Aortic stenosis was defined as 2-dimensional evidence of restricted aortic cusp motion and a peak aortic velocity >2.0 m/s. Aortic valve area was calculated by the continuity equation with the time-velocity integrals of the left ventricular outflow tract and aortic valve. Severity of AR was graded after integration of the available qualitative and quantitative parameters.13

Dimensions of the aortic root (aortic sinuses of Valsalva) and tubular ascending aorta were measured from the parasternal long-axis window at end diastole and compared with reference ranges for the patient’s age and body surface area.12,14 Aortic dilatation was classified as mild when its dimension was <5 mm above the upper limit of the reference range and as moderate when its dimension was 5 to 10 mm above the upper limit of the reference range or between 45 and 50 mm.15–17

**Clinical Outcomes**

Time 0 represented the time when the index diagnosis of QAV was made either through echocardiography or through surgical or pathological examination if not diagnosed preoperatively. To characterize the natural history of changes in AR and aortic dimensions, we identified the patients monitored through serial echocardiography at least 1 year after the index study. Subsequent need for aortic valve repair or replacement and the occurrence of cardiovascular events were obtained through review of the patient’s medical record.

Information on vital status was obtained from the US Social Security Death Index. For all-cause mortality, the records of patients not known to be deceased were censored at the time the US Social Security Death Index was interrogated. For survival free of cardiovascular events or aortic valve surgery, medical records of patients not known to have any of the listed characteristics were censored at the time of the last documented clinical follow-up.

**Statistical Analysis**

Data were presented as mean±SD or number (percentage) of patients. The Pearson χ² test was used to examine possible associations between various clinical characteristics. Overall survival was estimated with the Kaplan–Meier method and compared with the use of the log-rank test. Overall survival of patients with QAV was compared with an otherwise healthy population matched for age and sex on the basis of data from the Olmsted County, Minnesota, general population database. Statistical analyses were performed with SPSS version 20 (IBM Corp), and values of P<0.05 were considered significant.

**Results**

**Demographic Characteristics**

Between January 1, 1975, and August 31, 2001, transthoracic echocardiography was performed on 357,228 patients at the Mayo Clinic, and 21 patients received the diagnosis of QAV (frequency, 0.0059%). From September 1, 2001, through March 14, 2014, a total of 431,505 patients underwent transthoracic echocardiography, of which 28 patients had a diagnosis of QAV (frequency, 0.0065%). Among these 49 patients with QAV diagnosed on the basis of echocardiographic findings, 7 had QAV first identified through transesophageal echocardiography.
For a 50th patient, severe regurgitation of a trileaflet aortic valve and mild aortic root dilatation had been diagnosed previously with echocardiography. At aortic valve surgery, the patient was found to have a QA V. Retrospective review of this patient’s preoperative echocardiographic images showed type F QA V. The diagnosis of QA V was confirmed with transesophageal echocardiography or surgical or anatomic examination in 18 patients (36%). For the 50 patients, mean±SD age at diagnosis was 43.5±21.8 years (range, 2 days–84 years), and 52% were female (Table 1).

Aortic Valve
Classification according to subtypes of QA V is shown in Table 1 and the Table I in the online-only Data Supplement, and selected images from echocardiography or pathological specimens of various QA V subtypes are shown in Figures 1 and 2. Classification was not possible for 1 patient who did not have retrievable echocardiographic images; her diagnosis of QA V was confirmed with transesophageal echocardiography. A majority (64%) of our study cohort had type A (32%) or type B (32%) QA V.

Functional status of QA V in relation to valve subtypes is shown in Table 2. AR of any degree was present in 45 patients (90%), of whom 13 (26%) had moderate or severe AR, at the time of index diagnosis of QA V. Only 4 patients (8%) had aortic stenosis, which was mild in all 4.

Among 13 patients who underwent follow-up echocardiography without intervening aortic valve surgery, 3 (23%) were noted to have had progression of AR during a mean±SD follow-up of 5.5±3.7 years. The degree of AR increased from mild (grade I/IV) to moderate (grade II/IV) in 1 patient with type B QA V during 14 years of follow-up; the AR of 2 other patients (1 patient with type A and a 1 patient with type B QA V) worsened from moderate-severe (grade III/IV) to severe (grade IV/IV) during 2 and 5 years of follow-up, respectively. No significant association was found between changes in AR severity and QA V subtypes (P=0.34).

Ascending Aorta
At the time of index diagnosis of QA V, 48 of our 50 patients (96%) had an adequate assessment of the ascending aorta, with visualization of the sinus of Valsalva and the proximal to mid tubular ascending aorta. Aortic dilatation was present in 14 of the 48 patients (29%) and involved the aortic root in 5 (36%), the tubular ascending aorta in 5 (36%), and both the aortic root and tubular ascending aorta in 4 (29%). Eleven of these 14 patients (79%) had mild aortic dilatation; the other 3 had moderate dilatation. No significant association was detected between aortic dilatation at the index diagnosis and a documented history of hypertension (P=0.12). Among the 14 patients with aortic dilatation at the index diagnosis of QA V, 9 had moderate or greater AR. Only 4 of the 34 patients without aortic dilatation had moderate or greater AR, suggesting that aortic dilatation was associated with the presence of moderate or greater AR (P<0.001).

Changes in aortic dimensions were assessed by serial echocardiography in 20 patients (55% male), 7 of whom had undergone aortic valve surgery. Aortic dimensions (aortic root or tubular ascending aorta) increased over time in 10 patients (50%) by ≥2 mm during a mean±SD follow-up of 6.2±4.3 years, but 9 of these 10 patients had only a mild increase of ≤5 mm in aortic size. One patient’s ascending aortic diameter enlarged by 15 mm in the 17 years between the index diagnosis and the surgical aortic valve replacement and graft replacement of the ascending aorta. No significant association was found between changes in aortic dimension over time and QA V subtypes (P=0.64) or history of hypertension (P=0.64).
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Associated Cardiac Disorders
Other structural cardiac abnormalities were present in 16 patients (32%; Table 3). No echocardiographic evidence of aortic coarctation was noted. Four of the 50 patients had undergone coronary artery assessment with invasive angiography or computed tomography, and no coronary anomalies were identified.

Family History of Congenital Heart Disease
Information on family history was available for 47 of the 50 patients (94%). One patient reported the diagnosis of a ventricular septal defect in his son; otherwise, no reported family history of QAV or other types of congenital heart disease was reported.

Clinical Outcomes
The mean±SD duration of clinical follow-up at our institution was 4.8±5.6 years (range, 0–23 years). Overall survival for the entire cohort was 91.5% and 87.7% at the 5- and 10-year follow-up, respectively (Figure 3A). Survival free of surgery or death was 73.9% at the 5-year follow-up (Figure 3B). No infective endocarditis or aortic dissection was documented.

During the follow-up period, 8 of the 50 patients (16%) underwent aortic valve surgery (6 replacements and 2 repairs). The mean±SD duration between the index diagnosis of QAV and aortic valve surgery was 4.3±6.2 years (range, 0–17 years). The indication for aortic valve surgery was severe AR for all but 1 patient (age, 16 years) with mild to moderate AR and occlusion of the left coronary ostium by the small fourth cusp of QAV and collateralization from the right coronary artery. Aortic valve repair for this patient consisted of surgical excision of the small fourth cusp and resuspension of the other cusps. Adequate perfusion of the left coronary system was documented postoperatively.

One of the 8 patients with aortic valve replacement underwent concurrent replacement of the ascending aorta 17 years after the initial diagnosis. Histopathological examination of the excised ascending aorta showed intimal

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### Table 1. Characteristics of the Study Population at the Time of the Index Diagnosis of QAV

<table>
<thead>
<tr>
<th>Baseline Characteristics*</th>
<th>Patients Who Did Not Receive AV Operation (n=42)</th>
<th>Patients Who Had AV Operation (n=8)</th>
<th>Total (N=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis, mean (SD), y</td>
<td>45.2 (21.7)</td>
<td>34.8 (21.6)</td>
<td>43.5 (21.8)</td>
</tr>
<tr>
<td>Male sex</td>
<td>18 (43)</td>
<td>6 (75)</td>
<td>24 (48)</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>15 (36)</td>
<td>2 (25)</td>
<td>17 (34)</td>
</tr>
<tr>
<td>Subtype at index QAV diagnosis with echocardiography, n (%)†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>13 (31)</td>
<td>3 (38)</td>
<td>16 (32)</td>
</tr>
<tr>
<td>B</td>
<td>14 (33)</td>
<td>2 (25)</td>
<td>16 (32)</td>
</tr>
<tr>
<td>C</td>
<td>7 (17)</td>
<td>1 (13)</td>
<td>8 (16)</td>
</tr>
<tr>
<td>D</td>
<td>3 (7)</td>
<td>1 (13)</td>
<td>4 (8)</td>
</tr>
<tr>
<td>E</td>
<td>1 (2)</td>
<td>0 (0)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>F</td>
<td>3 (7)</td>
<td>1 (13)</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (2)</td>
<td>0 (0)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Aortic dilatation (n=48)</td>
<td>9/40 (23)</td>
<td>5/8 (63)</td>
<td>14 (29)</td>
</tr>
<tr>
<td>Site of aortic dilatation (n=48)‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic root</td>
<td>4/40 (10)</td>
<td>1/8 (13)</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Tubular ascending aorta</td>
<td>4/40 (10)</td>
<td>1/8 (13)</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Both</td>
<td>1/40 (3)</td>
<td>3/8 (38)</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>5 (12)</td>
<td>0 (0)</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Trivial-mild</td>
<td>26 (62)</td>
<td>0 (0)</td>
<td>26 (52)</td>
</tr>
<tr>
<td>Mild-moderate</td>
<td>5 (12)</td>
<td>1 (13)</td>
<td>6 (12)</td>
</tr>
<tr>
<td>Moderate</td>
<td>3 (7)</td>
<td>2 (25)</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Moderate-severe</td>
<td>2 (5)</td>
<td>3 (38)</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Severe</td>
<td>1 (2)</td>
<td>2 (25)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Moderate or severe AR</td>
<td>6 (14)</td>
<td>7 (88)</td>
<td>13 (26)</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>4 (10)</td>
<td>0 (0)</td>
<td>4 (8)</td>
</tr>
<tr>
<td>LVEDD, mean (SD), mm</td>
<td>49 (8)</td>
<td>58 (9)</td>
<td>50 (9)</td>
</tr>
<tr>
<td>LVEF, mean (SD), %</td>
<td>62 (7)</td>
<td>54 (8)</td>
<td>60 (8)</td>
</tr>
<tr>
<td>Confirmation of QAV with TEE or surgical examination</td>
<td>10 (24)</td>
<td>8 (100)</td>
<td>18 (36)</td>
</tr>
</tbody>
</table>

AR indicates aortic regurgitation; AV, aortic valve; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; QAV, quadricuspid aortic valve; and TEE, transesophageal echocardiography.

*Values are presented as number (percentage) of patients unless specified otherwise.
†No patient had QAV of subtype G.
‡Assessment was not possible in 2 patients.
thickening and focal medial degeneration but no evidence of tear or dissection. Among the 8 patients who underwent aortic valve surgery, 3 patients had type A QAV, 2 patients had type B, and 1 patient each had type C, type D, and type F. No other patient underwent concomitant repair of other structural cardiac lesions at the time of aortic valve surgery.

Among these 8 patients, no death occurred during a mean±SD postoperative follow-up of 12.4±7.2 years (Figure 4A). The patients were monitored at our institution for a mean±SD of 6.1±4.9 years after their operations. One patient had progressive AR and received a reoperation with a Ross procedure, consisting of replacement of the aortic valve and aortic root with a pulmonary autograft and a pulmonary valve replacement with a homograft at 4 years after the initial operation. Another patient had a transient ischemic attack 5 years after her surgery. One patient survived a cardiac arrest 7 years after his initial operation, but no specific cause of arrest was identified. No other patients had cardiovascular events requiring hospitalization at our institution.

Patients without aortic valve surgery (n=42) were monitored at our institution for a mean±SD period of 3.8±4.4 years (range, 0–16 years). Among the patients, QAV showed type A pattern in 13, type B in 14, and the other subtypes in 15. Development of atrial fibrillation in 2 patients was the only documented cardiovascular event during follow-up. Seven patients died during a mean±SD follow-up of 10.8±8.7 years. Overall survival was 89.9% and 84.9% at the 5- and 10-year follow-up, respectively (Figure I in the online-only Data Supplement). The cause of death was determined in 4 of the 7 patients who died and was unrelated to cardiovascular issues. No significant difference was found in overall survival between the postsurgical group and the nonsurgical group (P=0.15 by the log-rank test; Figure 4A). No significant difference occurred in overall survival of our patients with QAV versus an otherwise healthy population matched for age and sex (P=0.99 by the log-rank test; Figure 4B).

**Discussion**

**Frequency of QAV**

Previous studies have found the frequency of QAV to be 0.01% to 0.04% on the basis of echocardiographic or autopsy data.\(^1\)\(^-\)\(^3\)\(^,\)\(^10\)\(^,\)\(^18\) In the present study, QAV occurred in 0.006% of patients undergoing a comprehensive echocardiographic study at the Mayo Clinic. Only patients with unequivocal evidence of QAV were included in our study, and these patients were identified from a larger population than in previous studies. Consequently, we consider our results representative of a more accurate estimate.

**Demographic Characteristics**

**Sex**

In our study population, 52% were female (male-to-female ratio, 1:1.08), but 75% of the patients who subsequently

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### Table 2. Functional Status of QAV Subtypes in the Study Population

<table>
<thead>
<tr>
<th>QAV Subtype*</th>
<th>Functionally Normal AV,† n</th>
<th>AR Only (With Moderate or Greater AR), n</th>
<th>Aortic Stenosis Only, n</th>
<th>Both AR and Stenosis, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (n=16)</td>
<td>0</td>
<td>16 (6)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>B (n=16)</td>
<td>2</td>
<td>12 (3)</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>C (n=8)</td>
<td>2</td>
<td>5 (2)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>D (n=4)</td>
<td>0</td>
<td>3 (0)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>E (n=1)</td>
<td>0</td>
<td>1 (0)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>F (n=4)</td>
<td>0</td>
<td>4 (2)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

AR, aortic regurgitation; AV, aortic valve; and QAV, quadricuspid aortic valve.

*No patient had QAV subtype G.

†Functionally normal aortic valve is defined as the absence of aortic regurgitation or stenosis detected with echocardiography at the time of the index QAV diagnosis.

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### Table 3. Presence of Other Structural Cardiac Lesions in Patients With a QAV

<table>
<thead>
<tr>
<th>Other Structural Cardiac Lesions</th>
<th>Patients Who Did Not Receive AV Operation (n=42), n (%)</th>
<th>Patients Who Had AV Operation (n=8), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>28 (67)</td>
<td>6 (75)</td>
</tr>
<tr>
<td>Bowing, prolapse, or myxomatous changes of MV</td>
<td>8 (19)</td>
<td>1 (13)</td>
</tr>
<tr>
<td>TV prolapse</td>
<td>1 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pulmonary valve stenosis</td>
<td>1 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>ASD</td>
<td>1 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>VSD</td>
<td>2 (5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>ASD and persistent left SVC</td>
<td>0 (0)</td>
<td>1 (13)</td>
</tr>
<tr>
<td>Pulmonary valve stenosis, ASD, and PDA</td>
<td>1 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Coronary anomaly</td>
<td>0 (0)</td>
<td>1 (13)*</td>
</tr>
</tbody>
</table>

ASD indicates atrial septal defect; AV, aortic valve; MV, mitral valve; PDA, patent ductus arteriosus; QAV, quadricuspid aortic valve; SVC, superior vena cava; TV, tricuspid valve; and VSD, ventricular septal defect.

*This patient’s left coronary ostium was occluded by a small accessory AV cusp.
underwent aortic valve surgery were male. We speculate that the male preponderance reported in previous literature^3^ might be a result of the inclusion of only patients who had undergone aortic valve surgery.

**Age**

In this study, the mean±SD age at diagnosis of QA V was 44±22 years, similar to previous reports. Patients who subsequently underwent aortic valve surgery were ≈10 years younger at the time of diagnosis than those without surgery.

**Aortic Valve Characteristics**

**Subtypes**

Previous studies have demonstrated that the 3 commonest QA V subtypes are types A, B, and C. In addition, AR is the predominant hemodynamic abnormality observed in patients with a QA V . The distribution of QA V subtypes and the associated hemodynamic abnormalities identified in our cohort were similar to other clinical and autopsy series.

**Regurgitation**

Progressive cusp fibrosis with subsequent failure of cusp coaptation over time has been suggested as the key mechanism in regurgitation. An association between QA V morphological characteristics and severity of AR was not observed in our 50 patients. Rather, various QA V subtypes were found in patients who initially presented with moderate or severe AR and among those who subsequently underwent aortic valve surgery.

To the best of our knowledge, the natural history of changes in AR and aortic dimensions over time has not been specifically examined among patients with QA V . In the present study, among the 13 patients monitored through serial echocardiography who did not receive an aortic valve surgery, 23% had progression of their AR.

**Stenosis**

In the present study, AR was the predominant hemodynamic abnormality observed in patients with QA V , whereas evidence of aortic stenosis was noted in only 8% of our patients. This observation is similar to findings reported by previous studies.

**Endocarditis**

Infective endocarditis associated with QA V has been reported in the literature, and bicuspid aortic valve is known to increase the risk of infection. However, there was no documented endocarditis in any of our patients with QA V during follow-up.

**Ascending Aortic Characterisitics**

Ascending aortic dilatation, common in patients with congenital bicuspid aortic valve, has been reported rarely in patients with QA V in the past. However, in our study cohort, echocardiography showed that 29% of patients had dilatation of the aortic root, tubular ascending aorta, or both at the time of the index diagnosis of QA V . In addition, this aortic dilatation was associated with poorer survival free of aortic valve surgery or death, although the enlargement was only mild in 79% of these patients. Interestingly, a recent report of
outcomes in patients who underwent surgery for a dysfunc-
tional QAV also suggests that 13 of 31 patients (42%) had an
ascending aortic diameter of ≥4 cm, and 7 patients underwent
concomitant repair of ascending aorta. The discrepancy in
the reported frequency of aortic dilatation may have arisen
from the use of different cutoff values for abnormal ascend-
ing aortic dimensions or from inadequate examination of the
ascending aorta by echocardiography.

Aortic dimensions were found to have increased over time in
10 of our 20 patients monitored with serial echocardiography, but
9 of these 10 patients showed a mild increase of only ≤5 mm in
their aortic diameters. Whereas aortic dilatation was not uncom-
mon at the time of index diagnosis of QAV, only 1 of 8 patients
who subsequently underwent aortic valve surgery received con-
comitant ascending aortic repair or replacement. Overall, our
data indicate that the severity of AR and aortic dimensions stayed
stable or progressed relatively slowly in most patients.

The current evidence is inadequate to determine whether
the aortic dilatation observed in patients with a QAV repre-
sents a genetically mediated aortopathy or is simply the result
of hemodynamic factors related to valvular dysfunction. QAV was not associated with ascending aortic dissection or
rupture in our series.

Types of Associated Cardiac Disorders
QAV is generally an isolated anomaly, although a few coexistent
cardiac disorders have been reported in some patients. These dis-
orders include anomalies of the origin and epicardial distribution
of coronary arteries, atrial septal defect, ventricular septal defect,
patent ductus arteriosus, discrete subaortic stenosis, congenital
pulmonary valve stenosis, mitral valve prolapse, and hypertro-
phic cardiomyopathy. In our study, coexisting structural
cardiac anomalies were present in 32% of the 50 patients.

Coronary Arteries
Other investigators have reported coronary anomalies, includ-
ing malformation and displacement of coronary ostia, in up to
10% of patients with a QAV. In contrast, the frequency of a
clinically significant abnormality of coronary ostia was only
2% in our study and involved a patient whose left coronary
ostium was occluded by a small accessory aortic valve cusp. It
is generally difficult to assess the coronary ostia with echocar-
diography in adults, which may explain the lower frequency
of such anomalies in our study.

Patient Outcomes
To the best of our knowledge, our study is the first to investigate
the long-term outcomes of patients with QAV. Only 8 of our 50
patients (16%) received aortic valve surgery during follow-up.
Five of these 8 patients had type A or B QAV. Similar find-
ings have been reported by other investigators. It is unclear
whether these specific subtypes of QAV predispose patients to
more severe AR or whether this is simply a reflection of the
preponderance of types A and B in patients with QAV.

All 8 surgical patients had regular postoperative follow-
up visits at our institution for a mean±SD period of 6.1±4.9
years. During this time, 1 patient who had initially undergone
an aortic valve repair later had aortic valve replacement for
progressive worsening of AR.

Complete heart block has been reported as a potential com-
plication for patients undergoing aortic valve surgery. None
of the patients in the present study had this complication.

Long-term outcome was favorable not only for patients
without aortic valve surgery but also for those who under-
went aortic valve repair or replacement. There was no sig-
nificant difference in long-term survival between patients who
had aortic valve surgery and those who did not. Importantly,
despite a structurally abnormal aortic valve and the presen-
ture of an enlarged ascending aorta in 29% of our patients,
no instances of infective endocarditis or aortic dissection
were documented. This outcome contrasts with the behavior
of bicuspid aortic valve, which is associated with an 8-fold
increase in the age-adjusted risk of aortic dissection compared
with that of the general population.

Limitations
Our analysis was limited by the relatively small size of our
study cohort and by its retrospective design, although it
reflects the analysis of a large database. QAV is a rare con-
genital anomaly, and it may not be easily identified on trans-
 thoracic echocardiography. The reported frequency of QAV
in our study may therefore represent an underestimation. In
addition, anatomic confirmation through surgical or pathol-
ogical examination was available in only the 8 patients who had
undergone an aortic valve surgery. Comparison of individual
cusp size for the purpose of classifying the aortic valve into
different subtypes can be challenging and may not correlate
well with surgical or pathological findings. In our study, how-
ever, the distribution of various subtypes of QAV was consist-
tent with that reported in previous studies.

In addition, the mean duration of clinical follow-up at
our center was 4.8 years, and it is possible that some patients
might have undergone aortic valve surgeries at another institu-
tion at a later time. Still, our study represents the first attempt
in the literature to examine the natural history and long-term
outcomes of patients with QAV.

Conclusions
QAV is a rare congenital cardiac anomaly, and our study pro-
vides important insights into its frequency, echocardiographic
characteristics, natural history, and long-term outcomes. AR
was the predominant hemodynamic abnormality, whereas aor-
tic stenosis was rare. Aortic dilatation was more prevalent than
has been reported previously. Nevertheless, a majority of our
patients had no or only mild progression of AR and aortic dil-
atation over time, and only 16% underwent aortic valve surgery
during a mean follow-up of almost 5 years. Long-term sur-
ival was excellent both without and with aortic valve surgery.

Disclosures
None.

References
AJ. Incidence, description and functional assessment of isolated quadri-
Quadricuspid aortic valve (QAV) is a rare congenital cardiac defect in which an aortic valve is made up of 4 aortic valve cusps instead of 3 semilunar cusps as observed in a normal aortic valve. Given its low estimated frequency (<0.05%), QAV characteristics, natural history, and long-term outcomes have remained poorly defined. The present study sought to provide insights into these domains by analyzing 50 patients with QAV (frequency, 0.006%) from a large echocardiography data-base. In contrast to the male preponderance of QAV reported by other investigators, the sex distribution was relatively equal. Aortic regurgitation was the predominant hemodynamic abnormality associated with QAV, and aortic stenosis was rare. Aortic dilatation (found in 4 equal-sized cusps) and type B (3 equal and 1 smaller cusp) were the most common subtypes. Aortic regurgitation was the surgical indication in all but 1 patient. No infective endocarditis or aortic dissection was documented in our cohort. Long-term outcome was favorable not only for patients who did not receive aortic valve surgery but also for those who underwent aortic valve surgery.
Quadricuspid Aortic Valve: Characteristics, Associated Structural Cardiovascular Abnormalities, and Clinical Outcomes

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Supplemental Table. Characteristics of the Study Population at Time of Index Diagnosis of QAV With and Without Cardiac Lesions

<table>
<thead>
<tr>
<th>Basic Characteristicsa</th>
<th>Patients With Isolated QAV (n=34)</th>
<th>Patients With QAV and Other Structural Cardiac Lesions (n=16)</th>
<th>Total (N=50)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis, mean (SD), y</td>
<td>47 (21)</td>
<td>36 (22)</td>
<td>44 (22)</td>
<td>.08</td>
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<tr>
<td>Male sex</td>
<td>14 (41)</td>
<td>10 (63)</td>
<td>24 (48)</td>
<td>.16</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>14 (41)</td>
<td>3 (19)</td>
<td>17 (34)</td>
<td>.12</td>
</tr>
<tr>
<td>Subtype at index QAV diagnosis with echocardiographyb</td>
<td>13 (38)</td>
<td>3 (19)</td>
<td>16 (32)</td>
<td>.11</td>
</tr>
<tr>
<td>A</td>
<td>13 (38)</td>
<td>3 (19)</td>
<td>16 (32)</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>13 (38)</td>
<td>3 (19)</td>
<td>16 (32)</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>4 (12)</td>
<td>4 (25)</td>
<td>8 (16)</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>2 (6)</td>
<td>2 (13)</td>
<td>4 (8)</td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>1 (3)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>1 (3)</td>
<td>3 (19)</td>
<td>4 (8)</td>
<td></td>
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</tbody>
</table>
Supplemental Table (continued)

<table>
<thead>
<tr>
<th>Basic Characteristics&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Patients With Isolated QAV (n=34)</th>
<th>Patients With QAV and Other Structural Cardiac Lesions (n=16)</th>
<th>Total (N=50)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown</td>
<td>0 (0)</td>
<td>1 (6)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Aortic dilatation (n=48)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>10/32 (31)</td>
<td>4/16 (25)</td>
<td>14/48 (29)</td>
<td>.55</td>
</tr>
<tr>
<td>Site of aortic dilatation (n=48)&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td>.53</td>
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<tr>
<td>Aortic root</td>
<td>4/32 (13)</td>
<td>1/16 (6)</td>
<td>5/48 (10)</td>
<td></td>
</tr>
<tr>
<td>Tubular ascending aorta</td>
<td>4/32 (13)</td>
<td>1/16 (6)</td>
<td>5/48 (10)</td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>2/32 (6)</td>
<td>2/16 (13)</td>
<td>4/48 (8)</td>
<td></td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>2 (6)</td>
<td>3 (19)</td>
<td>5 (10)</td>
<td></td>
</tr>
<tr>
<td>Trivial-mild</td>
<td>15 (44)</td>
<td>11 (69)</td>
<td>26 (52)</td>
<td></td>
</tr>
<tr>
<td>Mild-moderate</td>
<td>6 (18)</td>
<td>0 (0)</td>
<td>6 (12)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>4 (12)</td>
<td>1 (6)</td>
<td>5 (10)</td>
<td></td>
</tr>
<tr>
<td>Moderate-severe</td>
<td>4 (12)</td>
<td>1 (6)</td>
<td>5 (10)</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>3 (9)</td>
<td>0 (0)</td>
<td>3 (6)</td>
<td></td>
</tr>
</tbody>
</table>
### Supplemental Table (continued)

<table>
<thead>
<tr>
<th>Basic Characteristicsa</th>
<th>Patients With Isolated QAV (n=34)</th>
<th>Patients With QAV and Other Structural Cardiac Lesions (n=16)</th>
<th>Total (N=50)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate or severe aortic regurgitation</td>
<td>11 (32)</td>
<td>2 (13)</td>
<td>13 (26)</td>
<td>.14</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>3 (9)</td>
<td>1 (6)</td>
<td>4 (8)</td>
<td>.75</td>
</tr>
<tr>
<td>LVEDD, mean (SD), mm</td>
<td>51 (8)</td>
<td>48 (10)</td>
<td>50 (9)</td>
<td>.28</td>
</tr>
<tr>
<td>LVEF, mean (SD), %</td>
<td>61 (7)</td>
<td>60 (9)</td>
<td>60 (8)</td>
<td>.78</td>
</tr>
<tr>
<td>Confirmation of QAV with TEE or surgical examination</td>
<td>13 (38)</td>
<td>5 (31)</td>
<td>18 (36)</td>
<td>.47</td>
</tr>
</tbody>
</table>

Abbreviations: LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; QAV, quadricuspid aortic valve; TEE, transesophageal echocardiography.

a Values are presented as number (percentage) of patients unless specified otherwise.

b No patient had QAV of subtype G.

c Assessment was not possible in 2 patients.
**Supplemental Figure.** Kaplan-Meier Curves for Overall Survival of Patients With Isolated QAV and Patients With QAV and Other Structural Cardiac Lesions. There was no significant difference in overall survival between patients with isolated QAV and those with QAV and other structural cardiac lesions. QAV indicates quadricuspid aortic valve.