Clin. Cardiol. 25, 548–552 (2002)

Review

Quadricuspid Aortic Valves

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Summary: Quadricuspid aortic valves (QAV) are a rare but well recognized cause of significant aortic regurgitation. The first case was found reported in 1862. Since then there have been 110 reported cases of QAV and we report 4 more. Previously, these were diagnosed at the time of surgery or postmortem examination. With advances in echocardiography, including harmonic imaging, and also the advent of transesophageal echocardiography, more cases are being diagnosed prior to surgery. We describe four more cases, three diagnosed preoperatively and one at the time of surgery, and then review the previously reported cases. Of the 114 cases reported, 46 had the aortic valve replaced, most commonly in the 5th and 6th decade of life. Hurwitz and Roberts classified quadricuspid valves according to the size of the leaflets. It has previously been believed that QAVs with four equal sized leaflets were less likely to develop significant aortic regurgitation; however, on review of the available cases, this would not appear to be the case. The preoperative diagnosis of QAVs is important as they can be associated with abnormally placed coronary ostium. Of the 114 cases reported, there are 10 reports of abnormally placed ostia. There has been at least one reported case of death occurring because of obstruction of an abnormally placed right coronary ostium by a prosthetic aortic valve.

Key words: quadricuspid aortic valve, aortic regurgitation, transesophageal echocardiography, aortic valve replacement

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Received: January 9, 2002
Accepted: February 28, 2002

Introduction

Quadricuspid aortic valves are rare and most cases historically have been discovered incidentally at surgery or postmortem examination. With advances in echocardiography, more cases are now being discovered antemortem. We report four cases, three diagnosed during echocardiographic examination and one found unexpectedly during aortic valve replacement. We review the available literature and discuss the embryology, diagnosis, associated conditions, management, and correlation between morphology of the QAV and its function.

Case Report No. 1

A 54-year-old man was noted to have an ejection systolic murmur and hypertension at a routine medical examination and was referred for assessment.

On examination his blood pressure was 160/100 mmHg and auscultation revealed a 3/6 ejection systolic murmur and a 1/6 early diastolic murmur. A transthoracic echocardiogram (TTE) showed a dimensionally normal left ventricle with good function. The aortic valve appeared abnormal and possibly quadricuspid. There was a mild eccentric jet of aortic regurgitation. A transesophageal echocardiogram (TEE) was performed, which confirmed a quadricuspid aortic valve with four equal cusps visible on both the diastolic and systolic frames (Figs. 1 and 2). There was mild central aortic regurgitation but no significant aortic valve gradient.

The patient's hypertension was treated and he was given advice regarding endocarditis prophylaxis.

Case Report No. 2

A 26-year-old man was first noted to have significant aortic regurgitation in 1988. Repeat TTE showed a normal left ventricle and significant aortic regurgitation but did not visualize the number of valve leaflets. In 2000, the aortic valve was believed to be quadricuspid on TTE, and TEE was performed. This confirmed the findings of a quadricuspid valve with four

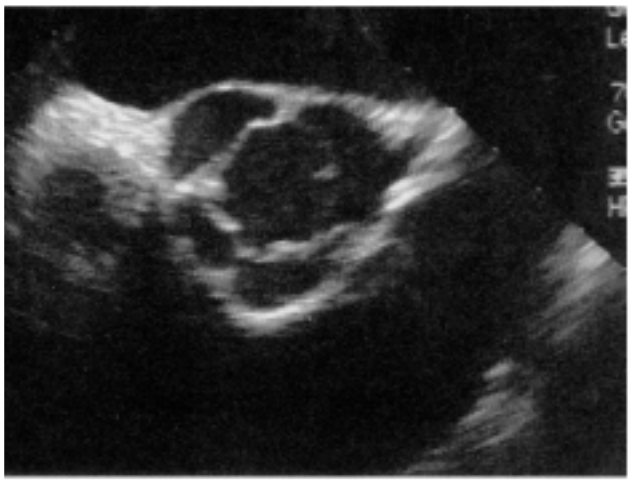

FIG. 1 Systolic transesophageal echocardiographic view of quadricuspid aortic valve in Case No. 1.

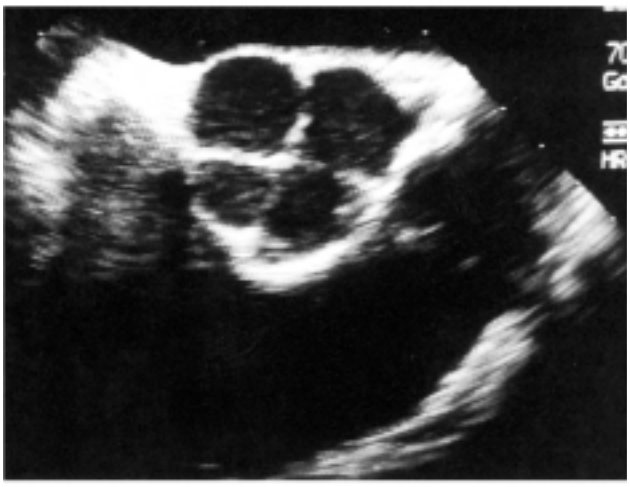

FIG. 2 Diastolic transesophageal echocardiographic view of quadricuspid aortic valve in Case No. 1.

equal leaflets, with moderate aortic regurgitation with central failure to co-apt. The left ventricle was normal and the aortic root was normal. He continues to be managed medically.

Case Report No. 3

A 72-year-old man with aortic regurgitation and chest pain underwent coronary angiography. Transthoracic echocardiography showed moderately severe aortic regurgitation but had not visualized the cusps well. The coronary arteries were normal, and there was moderately severe aortic regurgitation with mildly impaired left ventricular function. He underwent elective aortic valve replacement and at surgery the valve was noted to be quadricuspid.

Case Report No. 4

A 27-year-old man was referred with a 1-week history of dyspnea and intermittent palpitations. His resting 12-lead electrocardiogram showed voltage criteria for left ventricular hypertrophy. Clinical examination was unremarkable. Transthoracic echocardiography showed a QAV with four equal cusps, normal left ventricular dimensions and function, trivial central aortic regurgitation, and also mild pulmonary regurgitation. He is currently under routine medical review.

Incidence of Quadricuspid Aortic Valves

The bicuspid aortic valve is the most common aortic valve abnormality, occurring in approximately 2% of the population.[1] The next most frequent abnormality is the unicuspid aortic valve.[2] The truncal valve of truncus arteriosus is frequently quadricuspid[3] and will not be discussed further. The QAV is very rare. Simonds[4] failed to identify any cases of QAV in his own series of 6,252 autopsies, but in a pooled series of 25,666 autopsies he found 2 cases, an incidence of 0.008%. However, it is likely that QAVs may be overlooked if not specifically looked for. In one pathologic series evaluating the incidence of quadricuspid pulmonary valves, six cases had been overlooked at the original autopsy.[5] This would suggest that Simonds' autopsy incidence of QAVs is probably an underestimate. Feldman *et al.*[6] found a slightly higher echocardiographic incidence of 0.043% in 13,805 echocardiograms. Olson *et al.* observed an incidence of 1% of quadricuspid aortic valves on review of 225 patients undergoing surgery for pure aortic insufficiency.[7] In contrast, Turri *et al.*[8] failed to find a case of QAV on examination of 602 surgical specimens of aortic valves. Quadricuspid pulmonary valves are nine times more common than aortic valves.[5] There are also three reports of quinticuspid aortic valves.[4, 9, 10] To date, we were able to find 110 other cases of QAV in the literature. Of the cases reported, there was a slight male predominance, with a male to female ratio of 1.6:1; this is similar to the distribution of quadricuspid pulmonary valves.

Embryology

During Week 5 of normal embryogenesis, two mesenchymal ridges form in the cephalad portion of the truncus arteriosus. These truncoconal ridges fuse and descend in a spiral fashion into the ventricles forming the aorticopulmonary septum. At the junction of the conus and truncus, each semilunar valve is formed from three mesenchymal swellings. These swellings grow to form triangular-shaped valves. These loose swellings with their covering endothelium become excavated on their distal aspect to form the cusps. This process is well advanced by Week 6 and virtually complete by Week 9. The embryology of quadricuspid aortic valves remains unknown.

A variety of mechanisms have been suggested. These have included anomalous septation of the conotruncus,[4, 11, 12] excavation of one of the valve cushions,[4] and septation of a normal valve cushion as a result of an inflammatory episode.[13] Studies have suggested that QAVs may result from the division of one of the three mesenchymal ridges that normally give rise to three aortic valve cushions.[14, 15] They also demonstrated, at least in Syrian hamsters, that the division of the valve cushion starts at a very early stage of valve formation, when the conotruncal ridges begin to fuse.

Development of the aortic valve leaflets occurs temporally just after development of the coronary artery origins from the sinuses of Valsalva. One could speculate that a single developmental abnormality might result in a variety of abnormalities in the aortic root. Embryological studies have shown that position of the proximal coronary arteries is dependent upon where the coronary arteries grow into, rather than out of the aorta.[16] It is possible that these two groups of anomaly may therefore be embryologically related.

True QAVs must be distinguished from pseudo-QAVs resulting form bacterial endocarditis or rheumatic fever. To be considered a truly congenital malformation caused by abnormal embryogenesis, the malformation should contain a *corpus Arantii* on each cusp.[11]

Diagnosis

The first case was reported by Balington[17] in 1862. Quadricuspid aortic valves used to be diagnosed at autopsy or during aortic valve surgery. The first case diagnosed at aortography in the left anterior oblique view was reported by Peretz *et al.*[11] The advent of echocardiography has enhanced our ability to diagnose this condition; however, it may not be possible to visualize the aortic leaflets adequately with TTE. Preoperative diagnosis has become frequent with the advent of TEE. Using the transesophageal approach, a higher frequency transducer is used, and it is in closer proximity to the heart. There is no lung or chest wall tissue interposed between the transducer and the heart. Identification appears easier in the presence of four cusps of equal size. On the short axis view of the aortic valve in diastole, the commissural lines formed by the adjacent cusps result in an "X" configuration rather than the "Y" of the normal tricuspid aortic valve. Although the echocardiographic findings might suggest the size of the leaflets, they do not always correlate with the surgical findings. Transesophageal echocardiography has also demonstrated displacement of coronary ostium.[18] Recently, cinemagnetic resonance imaging has also been used for diagnosis[19] of a QAV. Of the 114 cases reported, 50 have been diagnosed by either TTE or TEE.

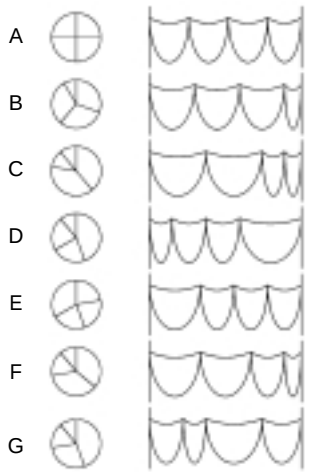

FIG. 3 Seven described anatomic variations of quadricuspid valves. Reprinted from Ref. No. 12 with permission. A = four equal cusps; B = three equal cusps, one smaller cusp; C = two equal larger cusps, two equal smaller cusps; D = one large, two intermediate, one small cusp; E = three equal cusps, one larger cusp; F = two equal larger cusps, two unequal smaller cusps; G = four unequal cusps.

Anatomic Variations

Hurwitz and Roberts[12] described the seven most common anatomic variations of quadricuspid semilunar valves (Fig. 3), depending on the size of the valve leaflets. Of the 97 cases in which comment of the size of the various leaflets has been made, the distribution of types is as in Table I. Over 85% of the reports are of type A, B, or C, that is, valves with four equal

TABLE I Valvular function and patient age according to valve classification of quadricuspid valve

Valve type	Number	% of total	Normal function	Average age	AR, no operation	Average age	AR, operation	Average age	Function unknown
A	31	32	4	41	12	52	12	56	3
B	40	41	13	44	7	51	17	56	3
C	14	15	2	23	0	—	10	55	2
D	3	3	0	—	2	52	1	67	0
E	2	2	0	—	0	—	0	—	2
F	2	2	0	—	0	—	2	41	0
G	5	5	1	82	0	—	4	59	0

Abbreviation: AR = aortic regurgitation.

cusps, three equal cusps with one smaller cusp, or two equal larger and two equal smaller cusps, respectively. As mentioned above, the echocardiographic findings may not always correlate with the surgical findings.

Function

Valvular regurgitation usually develops due to fibrous thickening with incomplete coaptation. With the unequal distribution of stress and abnormal leaflet coaptation, aortic regurgitation may occur. Aortic regurgitation is not often seen in young patients with QAVs. Aortic stenosis may be present but is rare. Of the cases reported, in which a functional assessment has been made, 73 had pure aortic regurgitation, 28 were normal, and in 7 cases there was evidence of mixed valvular dysfunction; in no case was there pure aortic stenosis.

It has previously been believed that valves with four equal leaflets, that is, type A, were more likely to function normally. In 28 of the 114 cases reported, the QAV was functioning normally. Of these, only 3 were type A and 13 were type B. As shown in Table I, of the 30 type A QAVs reported, 3 functioned normally (average age 41), 24 had significant regurgitation (average age 52), and 12 had required valve replacement due to regurgitation (average age 56). Compared with the other main group, type B, there is no significant difference in the average ages, but there are more normally functioning valves in the type B group. This would suggest that in fact QAVs with four equal leaflets are not more likely to function normally than do QAVs with unequal leaflets sizes, as was originally believed. Also, it appears that valvular function tends to deteriorate in adult life, often requiring surgery around the sixth decade. Of the 114 cases reported, 46 underwent valve replacement.

The risk of endocarditis is not clear. Some experts[6] believe the risk is low with valves with four equal cusps because of the lack of asymmetry or flow disturbance. There have been documented cases of endocarditis affecting a QAV.[20, 21, 22]

Associated Abnormalities

Anomalies of coronary artery origin and distribution represent < 1% of all congenital heart lesions.[23] From the point of view of the surgeon, it is important to be aware of any displacement of the coronary ostium to prevent ostial obstruction during fixing of the prosthetic ring. Obstruction of the coronary ostium by a prosthetic aortic valve has resulted in the death of a patient.[24] In 10 cases of QAV, abnormally placed coronary ostia have been found, 6 involving the right coronary artery and 4 the left. There has also been one case of a single coronary ostium.[25] Sudden death has been caused by complete isolation of the left coronary artery by an adherent cusp of a QAV.[26]

Quadricuspid aortic valves have been reported in association with other cardiac abnormalities, including nonobstructive cardiomyopathy,[27] pulmonary valve stenosis,[28] ventricular septal defect,[12] fibromuscular subaortic stenosis,[29] and supravalvular stenosis with left coronary artery atresia.[30]

Fenestrations of the aortic cusps in QAV are not regarded as congenital abnormalities, since increasing frequency of fenestration is seen with advancing age. Quadricuspid aortic valve has also been reported in association with Ehlers-Danlos syndrome.[31]

Management

Although the QAV is a congenital anomaly, regurgitation does not occur until adulthood. Therefore, if a quadricuspid valve is found on echocardiography, follow-up assessment is required as progress to severe regurgitation is to be expected. Valves with four equal leaflets are not less likely to develop significant aortic regurgitation. The average age reported for valve replacement is 54 years in the 46 cases of QAV operated on. However, the youngest patient undergoing valvular repair for a quadricuspid valve with significant regurgitation was only 5 years old.[30]

Aortic valve replacement for a QAV was performed as early as 1969[31] and is generally the treatment of choice for severe valvular regurgitation. In one case, a QAV was converted into a tricuspid valve by anastomosing the commissures of the right coronary and supranumery cusps, hence restoring coaptation.[29]

There are at least three confirmed cases of endocarditis affecting a QAV, and therefore endocarditis prophylaxis is advised.

Conclusion

Although an uncommon lesion, QAVs are a cause of significant aortic regurgitation, often requiring aortic valve replacement in the fifth and sixth decades. Previously it had been believed that QAVs with four equal cusps were less likely to require valve replacement, although that would appear to not be the case. There is a risk of infective endocarditis with QAVs, and patients should thus take prophylactic antibiotics for dental procedures and "dirty surgery."

In young patients who are investigated for aortic regurgitation, in whom TTE has failed to identify the number of valve leaflets, it may be advisable to perform a transesophageal echocardiogram. If this demonstrates a QAV, then the patient should be reviewed because of the common requirement for valve replacement in later life. If a QAV is found incidentally at the time of echocardiography for other reasons, then continued follow-up is recommended. Surgeons should be aware of the possibility of abnormally placed coronary ostia that occurs in about 10% of cases so as not to occlude the ostia by the prosthetic valve at the time of valve replacement.

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