

CASE REPORT

## Quadricuspid aortic valve – 10-year case series and literature review<sup>☆</sup>

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### KEYWORDS

Quadricuspid aortic valve;  
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### Abstract

**Introduction:** Quadricuspid aortic valve is a rare malformation, with an estimated incidence of 0.003 to 0.043% of all congenital heart disease. It usually appears as an isolated congenital anomaly, but may also be associated with other malformations, the most common being coronary artery anomalies. Current technology enables noninvasive diagnosis in most cases. This entity's natural history is progression to valve regurgitation, which is rare before adulthood.

**Objective:** Case review of quadricuspid aortic valve patients diagnosed in the last 10 years in a tertiary pediatric cardiology center.

**Methods:** Retrospective chart review of patients diagnosed with quadricuspid aortic valve between January 2000 and December 2009.

**Results:** Over the past 10 years, four cases of quadricuspid aortic valve were diagnosed in children aged between 6 months and 8 years, two male. In three cases, the four leaflets were of similar size, which is the most common finding. Two of the valves functioned normally and two had minimal regurgitation. All patients had associated cardiac malformations (one atrial and two ventricular septal defects, one supravalvular aortic stenosis and one quadricuspid pulmonary valve). One patient was also diagnosed with Williams syndrome. During a median follow-up of 2 years (0-9), all patients remained asymptomatic and none required medical or surgical treatment of the aortic valve.

**Conclusion:** Diagnosis of quadricuspid aortic valve is rare, especially in children, since most patients are asymptomatic and have normally functioning valves. In this study, half the patients had minimal aortic regurgitation. Contrary to what is described in the literature, all patients had concomitant cardiac malformations. We provide the first description of this entity's association with Williams syndrome. Clinical follow-up should be maintained in these patients in order to promptly detect the onset or worsening of functional alterations and to enable appropriate therapeutic intervention.

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**PALAVRAS-CHAVE**

Válvula aórtica  
quadricúspide;  
Cardiopatía  
congenital

**Válvula aórtica quadricúspide – Casuística de 10 anos e revisão da literatura****Resumo**

**Introdução:** A válvula aórtica quadricúspide é uma malformação rara, com uma incidência estimada de 0,003 a 0,043% de todas as cardiopatias congénitas. Surge habitualmente como uma anomalia congénita isolada, podendo igualmente estar associada a outras malformações, sendo as mais frequentes as anomalias das artérias coronárias. A tecnologia actual permite o diagnóstico não invasivo na grande maioria das situações. A sua história natural é a evolução para a insuficiência, rara antes da idade adulta.

**Objectivos:** Revisão dos casos de válvula aórtica quadricúspide diagnosticados nos últimos 10 anos num centro terciário de Cardiologia Pediátrica.

**Material e Métodos:** Revisão retrospectiva do processo clínico dos doentes aos quais foi detectada uma válvula aórtica quadricúspide, entre Janeiro de 2000 e Dezembro de 2009.

**Resultados:** Nos últimos 10 anos, foram diagnosticados quatro casos de válvula aórtica quadricúspide, em crianças com idades compreendidas entre os 6 meses e os 8 anos, duas do sexo masculino. Em três casos, os quatro folhetos eram de dimensões semelhantes, que é o achado mais frequente. Duas das válvulas eram normofuncionantes e duas apresentavam insuficiência mínima. Todos os doentes apresentavam outras malformações cardíacas associadas (uma comunicação interauricular, duas comunicações interventriculares, uma estenose supra-valvular aórtica e uma válvula pulmonar quadricúspide). Um doente tinha também o diagnóstico de Síndrome de Williams. Com um tempo de seguimento mediano de 2 anos [0 – 9], todos os doentes se mantiveram assintomáticos e não requereram tratamento médico ou cirúrgico para a válvula aórtica.

**Conclusão:** O diagnóstico de válvula aórtica quadricúspide é raro, sobretudo em idade pediátrica, quando a maioria dos doentes são assintomáticos e apresentam válvulas normofuncionantes. Nesta casuística, metade apresentava insuficiência aórtica mínima. Ao contrário do que está descrito na literatura, todos os doentes apresentavam malformações cardíacas concomitantes. Descrevemos pela primeira vez a associação com a Síndrome de Williams. Estes doentes deverão manter seguimento em ambulatório, de forma a detectar atempadamente o aparecimento ou agravamento de alterações funcionais e permitir uma intervenção terapêutica oportuna.

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**Introduction**

Quadricuspid aortic valve is a rare cardiac malformation, with an estimated incidence of 0.003<sup>1</sup> to 0.043%<sup>2</sup> of all congenital heart disease. It usually appears as an isolated congenital anomaly,<sup>1-3</sup> but may also be associated with other malformations, the most common being coronary artery anomalies.<sup>4,5</sup>

Technological advances enable noninvasive diagnosis in most cases.

There have been 200 cases described in the literature, most in adults. The largest review published to date included 184 patients, aged between 2 and 84 years, with a slight male predominance.<sup>5</sup> The few case series of children are generally small.<sup>6</sup>

Prompt detection of this malformation is important since it frequently evolves to aortic regurgitation,<sup>6,7</sup> which, while rare during childhood or adolescence, can manifest in adulthood and may require surgical treatment.<sup>1,8</sup>

**Objective**

Case review of quadricuspid aortic valve patients diagnosed in the last 10 years in a tertiary pediatric cardiology center.

**Methods**

We performed a retrospective chart review of patients diagnosed with quadricuspid aortic valve between January 2000 and December 2009.

**Case reports****Case 1**

A female patient was diagnosed with ostium secundum atrial septal defect (ASD) by transthoracic echocardiography (TTE), no other structural anomalies being detected. At age 8, she underwent cardiac catheterization for percutaneous ASD closure, which revealed a type A quadricuspid aortic valve, with minimal central regurgitation.

The patient is currently asymptomatic, with mild aortic regurgitation (Figure 1).

**Case 2**

A female patient was followed in pediatric cardiology from the age of one month for subaortic perimembranous ventricular septal defect (VSD).

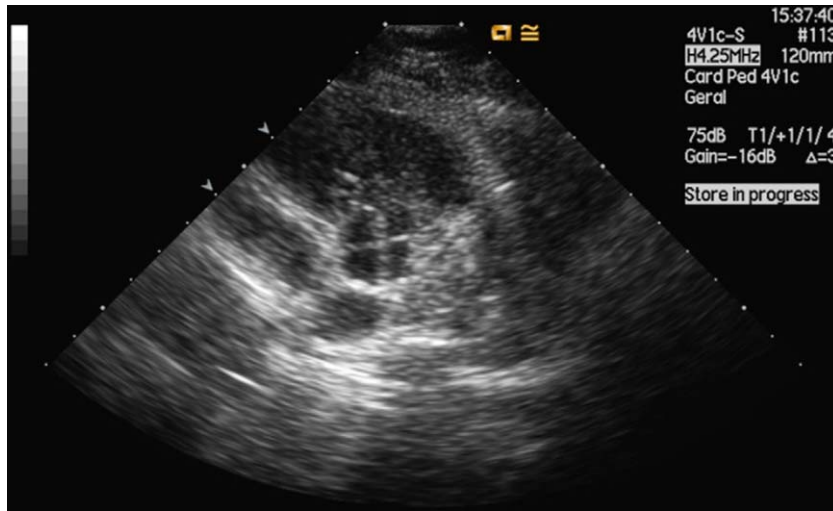


Figure 1 Type A quadricuspid aortic valve.

At age 6 months, routine TTE showed a restrictive perimembranous VSD, partially closed by tricuspid tissue, and type A quadricuspid aortic valve was diagnosed, with normal valve function.

The patient remains asymptomatic and continues to be monitored as an outpatient.

**Case 3**

A male patient, with a diagnosis of Williams syndrome, was followed in the pediatric cardiology outpatient clinic from the age of 4 months for subaortic perimembranous VSD, which closed spontaneously during the third year of life, and mild pulmonary infundibular stenosis (peak gradient 15 mmHg).

At age 7, TEE performed under sedation for worsening fatigue revealed severe supralvalvular aortic stenosis (peak

gradient 87 mmHg, mean 43 mmHg) and type A quadricuspid aortic valve, with minimal regurgitation. These findings were confirmed by transesophageal echocardiography.

The patient subsequently underwent surgical correction by supralvalvular aortoplasty with an autologous pericardial patch (Figure 2).

The patient continues to be monitored in the pediatric cardiology clinic and is asymptomatic. The most recent TTE showed no residual lesions or significant sequelae, and minimal aortic valve regurgitation (Figure 3).

**Case 4**

A male patient was referred to the pediatric cardiology clinic at the age of 6 for a heart murmur. TTE revealed a type F asymmetric quadricuspid aortic valve with normal function,

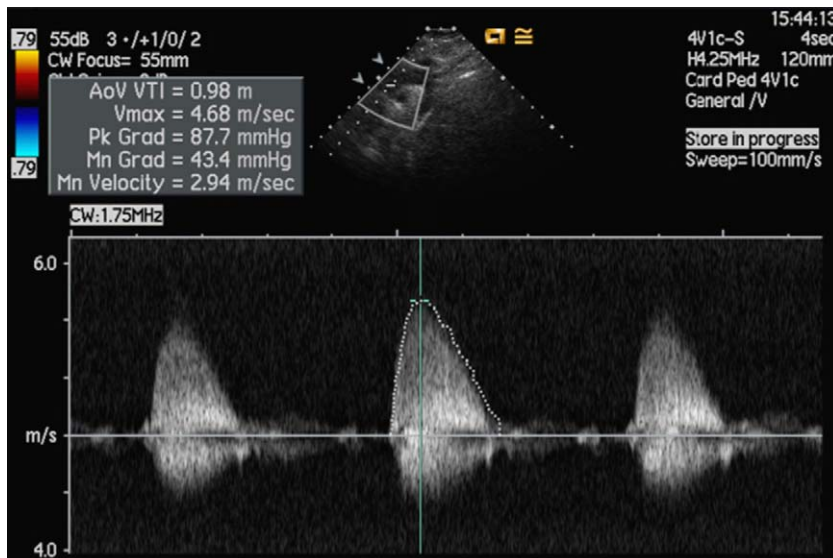


Figure 2 Supralvalvular aortic stenosis.

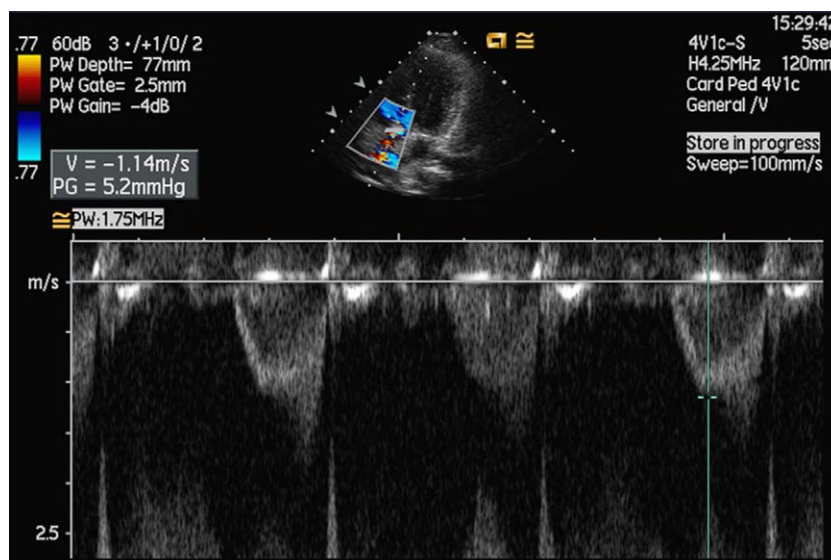


Figure 3 Aortic valve gradient estimated by pulsed wave Doppler after surgical correction.

and a quadricuspid pulmonary valve with minimal stenosis (gradient 15 mmHg).

The patient continues to be monitored in pediatric cardiology outpatient consultations and remains asymptomatic (Figure 4).

## Discussion

Quadricuspid aortic valve was first identified on autopsy by Balington<sup>9</sup> in 1862, the first *in vivo* description dating from 1968, by Robicsek et al.<sup>10</sup>

Systematic autopsy studies have estimated its incidence between 0.003<sup>1</sup> and 0.008%,<sup>11</sup> while a more recent echocardiographic review reported an incidence of 0.043%.<sup>2</sup>

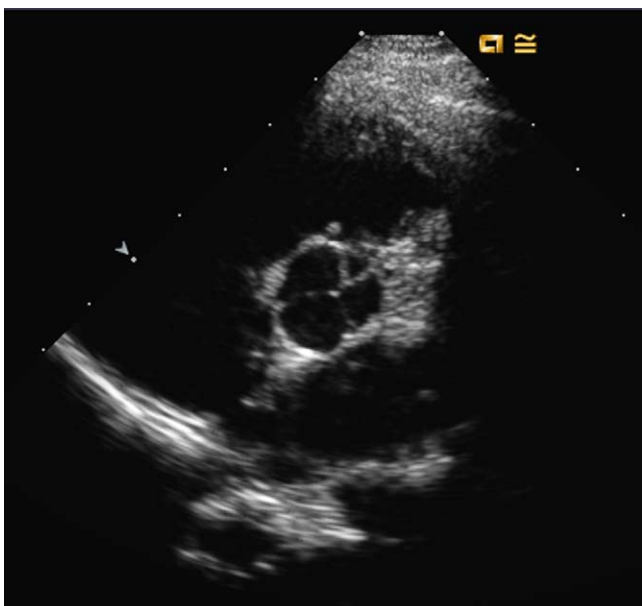


Figure 4 Type F quadricuspid aortic valve.

The embryology of quadricuspid aortic valves is unknown.<sup>12</sup> Both semilunar valves arise from mesenchymal ridges in the truncus arteriosus after it divides, with three swellings developing inside the vascular lumen between the fifth and ninth week of gestation.<sup>4</sup> Various pathophysiological mechanisms have been suggested that could alter the number of valve leaflets, including anomalous septation of the conotruncus, leading to asymmetric distribution of the swellings in each of the great arteries; abnormal proliferation of one or more mesenchymal ridges; or division of one of the valve leaflets during formation.<sup>4,11</sup>

Hurwitz and Roberts developed a system of classification<sup>1</sup> based on valve leaflet size (Table 1). According to their research, around 85% of cases are of type A, B or C.

In the last ten years, four cases of quadricuspid aortic valve have been diagnosed in the pediatric cardiology department of Hospital de Santa Marta, in children aged between 6 months and 8 years, two male and two female. In none of the cases presented was the reason for observation related to the valve abnormalities found.

In three cases, the four valve leaflets were of equal size (type A in Hurwitz and Roberts' classification), the most common finding in the literature.

Quadricuspid aortic valve usually appears as an isolated congenital anomaly,<sup>1,3,11</sup> but may also be associated with other malformations, including patent ductus arteriosus, ventricular septal defect, pulmonary valve stenosis,

Table 1 Hurwitz and Roberts' anatomical classification.

Type	Description
A	Four equal cusps
B	Three equal cusps and one smaller cusp
C	Two equal larger cusps and two equal smaller cusps
D	One large, two intermediate and one small cusp
E	Three equal cusps and one larger cusp
F	Two equal larger cusps and two unequal smaller cusps
G	Four unequal cusps

mitral valve malformation, left ventricular outflow tract obstruction (sub- or supra- valvular stenosis), coronary artery anomalies, hypertrophic cardiomyopathy and congenital atrioventricular block.<sup>13,14</sup> It has also been reported in association with Ehlers-Danlos syndrome.<sup>15</sup>

The most common malformations associated with quadricuspid aortic valve are coronary artery anomalies, found in around 10% of cases.<sup>4,5</sup> Various forms of presentation of such anomalies have been reported, including anomalous position of one of the coronary ostia,<sup>16,17</sup> single coronary ostium,<sup>18</sup> coronary-pulmonary artery fistula,<sup>19</sup> and occlusion of a coronary artery ostium by valve tissue,<sup>20</sup> which can be fatal.<sup>21</sup>

Interestingly, all the patients in our series had associated cardiac malformations, but none presented coronary artery anomalies. One patient had also been diagnosed with Williams syndrome, an association that has not previously been described in the literature.

Although quadricuspid aortic valve is a congenital malformation, diagnosis is usually late. The characteristic echocardiographic finding in short-axis view is an X-shaped commissure pattern during diastole and a rectangular appearance during systole.<sup>22</sup> Wider use of transesophageal echocardiography has made detection of quadricuspid aortic valve easier and hence more frequent.<sup>12</sup>

Unlike quadricuspid pulmonary valve, which is nine times more common, quadricuspid aortic valve tends to progress to regurgitation.<sup>6</sup> This functional alteration, caused by asymmetric distribution of transvalvular flow and incomplete leaflet coaptation, develops insidiously over decades and is rarely seen before adulthood. There have been cases of mixed valvular dysfunction but none of pure stenosis. No correlation has been found between valve morphology and function.<sup>12</sup>

In a recent review of all published cases, 66% presented severe, 8% moderate and 8% mild aortic regurgitation, and 13% had regurgitation and aortic stenosis. There was normal valve function in 10% of cases.<sup>7</sup>

In our series, normally functioning valves and minimal regurgitation were seen with equal frequency.

Surgical correction is usually performed between the fifth and sixth decades of life,<sup>1</sup> and only exceptionally in children.<sup>8</sup>

Some cases of infective endocarditis in patients with quadricuspid aortic valves have been reported,<sup>15,15,23</sup> but there is disagreement concerning prophylaxis against bacterial endocarditis, especially when the four cusps are of equal size and the valve has normal function.<sup>2,6,12</sup>

Patients with normally functioning quadricuspid aortic valves require regular clinical follow-up in order to promptly detect functional alterations and to enable appropriate therapeutic intervention.

In our series, with a median follow-up of two years (0-9), no patient required medical or surgical treatment to correct the aortic valve malformation.

## Conclusions

Diagnosis of quadricuspid aortic valve is rare, especially in children, since most patients are asymptomatic with normal valve function.

In our series, normally functioning aortic valves and minimal regurgitation were observed with equal frequency.

Contrary to what is described in the literature, all patients had concomitant cardiac malformations other than those traditionally associated with this entity. We provide the first description of an association with Williams syndrome.

Clinical follow-up should be maintained in these patients, in order to promptly detect the onset or worsening of functional alterations and to enable appropriate therapeutic intervention.

## Conflicts of interest

The authors have no conflicts of interest to declare.

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