


# The Quandary of the Quadricuspid Aortic Valve—The “Unlucky” 4-Leaf Clover: Case Report and Brief Clinical Review

Journal of Investigative Medicine High  
Impact Case Reports  
Volume 8: 1–5  
© 2020 American Federation for  
Medical Research  
DOI: 10.1177/2324709620921626  
journals.sagepub.com/home/hic  


**Rajeev Virender Seecheran, MBBS<sup>1</sup>, Valmiki Krishna Seecheran, MBBS<sup>1</sup>, Sangeeta Anjali Persad, MBBS<sup>1</sup>, Fidel Rampersad, MBBS, DM, FRCR<sup>2</sup>, Paramanand Maharaj, MBBS, FRCR<sup>2</sup>, Shari Khan, MBBS, MRCP<sup>1</sup>, and Naveen Anand Seecheran, MBBS, MSc, FACP, FACC, FESC, FSCAI<sup>2</sup> **

## Abstract

The quadricuspid aortic valve is an exceedingly rare congenital valvular anomaly, characterized by a tetrad of leaflets that typically presents with aortic regurgitation. Almost one third of cases are associated with coexisting cardiac defects with one fifth warranting surgical intervention. In this article, we describe the first documented-in-Caribbean case and present a brief clinical review of its pathophysiology, diagnosis, and management.

## Keywords

quadricuspid aortic valve, QAV, aortic regurgitation, AR, congenital valvular disease, congenital heart disease

## Introduction

The quadricuspid aortic valve (QAV) is an exceedingly rare congenital heart defect with an estimated incidence of ~0.0003% in autopsy series and <1% for those receiving aortic valve replacements (AVRs) for aortic regurgitation (AR).<sup>1</sup> The valvulopathy is characterized by the presence of 4 cusps, instead of the usual 3 found generally in the aortic valve.<sup>2</sup> It was initially reported in 1862 by Balinton, and to date, there have been marginally over 200 reported cases worldwide, alluding to its rarity.<sup>3</sup> Almost one third of cases are associated with coexisting cardiac defects with one fifth warranting surgical intervention.<sup>1</sup>

The embryopathological basis is not fully elucidated; however, it is postulated to derive from gestational anomalous septation of the conotruncus or endocardial cushions.<sup>4,5</sup> There is a marginal male predominance, and the mean age of incident diagnosis is ~51 years.<sup>6</sup>

The most common complication of QAV is AR, and it translates clinically depending on the degree of AR and whether any coexisting cardiac associations are present.<sup>7,8</sup> Mechanically, it is caused by inadequate coaptation of the fourth dysplastic cusp from progressive fibrosis, at the end of systole at the aortic annulus, resulting in an aperture and resultant backflow of blood.<sup>8,9</sup> Significant AR typically occurs in the fifth to sixth decades, necessitating operative repair or even replacement.<sup>1</sup>

With the advent of frequently accessible imaging studies such as echocardiography, computed tomography (CT), and magnetic resonance imaging, more cases are being incidentally detected; however, due to its rarity, it remains somewhat an enigmatic valvular defect, as the natural course and characteristics are not well-established.<sup>1</sup>

## Case Report

A 36-year-old South Asian male with no significant medical history or pertinent family history presented to the emergency department at the academic medical center with atypical chest pain and dyspnea. His vital signs indicated systolic blood pressures of 150s mm Hg (nearly equivalent in all

<sup>1</sup>North Central Regional Health Authority, Mt. Hope, Trinidad and Tobago

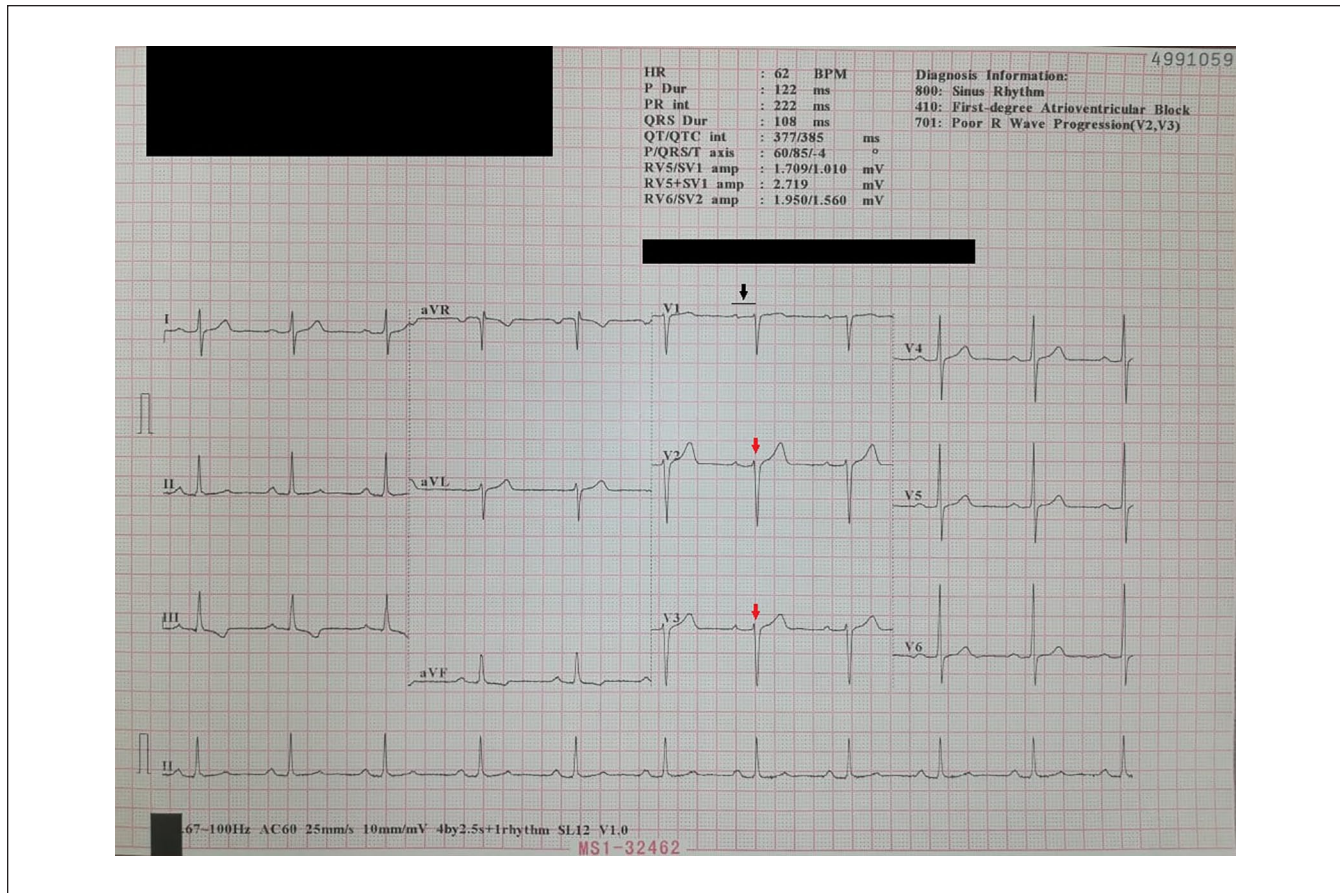
<sup>2</sup>University of the West Indies, St. Augustine, Trinidad and Tobago

Received March 22, 2020. Revised March 26, 2020. Accepted April 1, 2020.

### Corresponding Author:

Naveen Anand Seecheran, MBBS, MSc, FACP, FACC, FESC, FSCAI, Department of Clinical Medical Sciences, The University of the West Indies, 2nd Floor, Building #67, Eric Williams Medical Sciences Complex, Mt. Hope, Trinidad, West Indies.  
Email: nseecheran@gmail.com



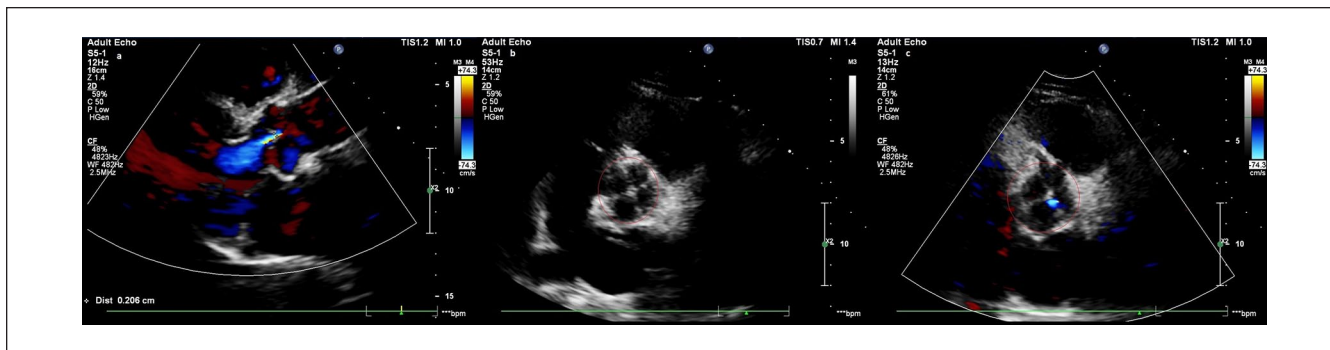


**Figure 1.** The patient's electrocardiogram. The black arrow indicated the first-degree atrioventricular block. The red arrows indicate the poor R-wave progression.

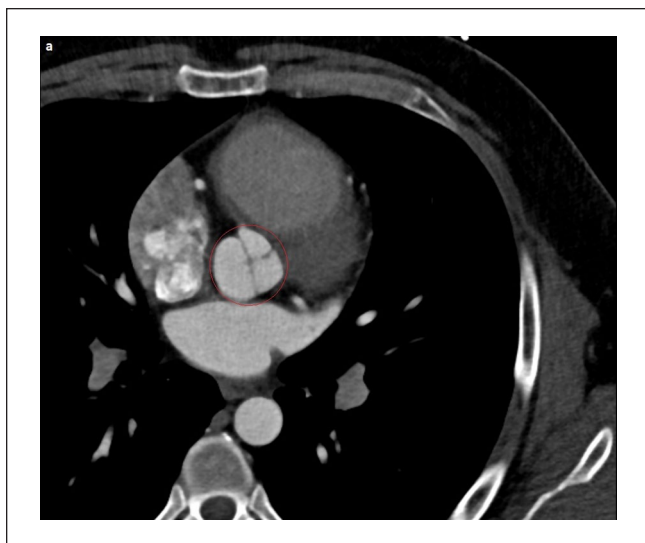
extremities), regular heart rate of 105 beats per minute, and respiratory rate of 18 breaths per minute, with an oxygen saturation of 98% on room air. His physical examination revealed a grade 1/6 diastolic murmur at the right upper sternal border without an elevated jugular venous pulse, crackles, or edema. A 12-lead electrocardiogram revealed sinus rhythm with a first-degree atrioventricular block and poor R-wave progression (see Figure 1). Pertinent diagnostic laboratory investigations included a D-dimer 121 ng/dL (normal  $\leq 500$  ng/mL), pro-brain natriuretic peptide 245 pg/mL (normal  $\leq 300$  pg/mL), cardiac biomarkers, CK-MB 18 U/L (normal  $< 20$  U/L), and troponin I 0.08 ng/mL (normal = 0.0-0.15 ng/mL). Routine investigations, such as a complete blood count, comprehensive metabolic panel, glycosylated hemoglobin, fasting lipid panel, and thyroid cascade, were normal. He was initiated on an optimal, guideline-directed acute coronary syndrome protocol with aspirin, ticagrelor, and enoxaparin, and subsequently admitted for further hospitalization.

Two-dimensional transthoracic echocardiography (2D-TTE) demonstrated a QAV with trivial to mild AR (see Figure 2a-c). Hurwitz and Roberts initially classified QAV morphology, with 7 permutations (A to G) predicated on the

cuspid dimensions, the most common being that of B—3 equal-sized cusps and 1 smaller cusp.<sup>2</sup> Subsequently, Nakamura et al derived a less complicated system with 4 subtypes, based on the position of the supernumerary cusp as follows: type I, the supernumerary cusp between the left and right coronary cusps; type II, the supernumerary cusp between the right and noncoronary cusps; type III, the supernumerary cusp between the left and noncoronary cusps; and type IV, unidentified supernumerary cusp as of 2 equal-sized smaller cusps.<sup>10</sup> Our patient displayed a Hurwitz-Roberts class A and Nakamura type I architecture. There was preserved left ventricular (LV) systolic function (ejection fraction of 65%), and no regional wall motion abnormalities with impaired and nonspecific diastolic dysfunction. A cardiac CT angiogram also revealed nonobstructive coronary artery disease with a calcium score of 0 and QAV (see Figure 3). Also, a transesophageal echocardiogram confirmed the valve defect with the following flow dynamic parameters (see Supplemental Videos 1 and 2 [available online] and Table 1). The QAV was noted to be structurally intact on all 3 imaging modalities (2D-TTE, cardiac CT angiogram, and 2D/3D-transesophageal echocardiogram) with no evidence of accelerated sclerosis, fibrosis, leaflet thickening, subvalvular



**Figure 2.** Two-dimensional transthoracic echocardiography series. (a) Parasternal long-axis view indicates the width of the central regurgitant jet, deemed trivial-mild. (b) A cross-sectional view of the aortic valve reveals the quadricuspid architecture enclosed by the red circumference. This is consistent with Hurwitz-Roberts class A and Nakamura type I morphology. (c) A cross-sectional view of the aortic valve reveals the central to mild trivial aortic regurgitant jet.



**Figure 3.** Cardiac computed tomography cross-sectional view revealing the Hurwitz-Roberts class A and Nakamura type I morphology quadricuspid aortic valve.

**Table I.** Two-Dimensional, 3-Dimensional Transesophageal Echocardiogram Flow Dynamic Parameters Across the Quadricuspid Aortic Valve.

Flow Dynamic Parameter	Value
<b>Aortic valve</b>	
Aortic valve area	3.23 cm <sup>2</sup>
Velocity (mean)	96 cm/s
Mean gradient	5 mm Hg
Velocity time integral	28.2 cm
Deceleration rate	1.5 m/s <sup>2</sup>
Pressure half-time	546 ms
<b>Left ventricular outflow tract</b>	
Velocity (mean)	85.7 cm/s
Mean gradient	3 mm Hg
Velocity time integral	24.1 cm

calcification, or associated cardiac defects. He was instituted on a daily low-dose cardiovascular regimen, similar to above, excluding the antithrombotic therapies. The patient’s ensuing 2-day hospitalization course was uneventful, and he was subsequently discharged with instructions for routine follow-up in 1 month.

**Discussion**

Valve dysfunction usually manifests in the fourth decade, where it continues to deteriorate to a significant level in the following 10 to 20 years based on trajectories provided by natural history data.<sup>1,11</sup> The functional status of the QAV, AR, together with any associated disorders, is pivotal in determining its clinical expression. Patients can be asymptomatic or present with the entire range of cardiovascular symptomatology, including angina, dyspnea, and syncope with an expectant, audible decrescendo diastolic murmur at the left sternal border, the former and latter of which our patient both displayed.

Quadricuspid aortic valve is usually an isolated anomaly, but other congenital cardiac associations can be present in up to one third of patients, such as coronary artery and ostia abnormalities; atrial and ventricular septal defects; mitral valvulopathies; and complex cyanotic congenital heart disease, such as tetralogy of Fallot, transposition of the great arteries, and hypertrophic cardiomyopathy as well as a myriad of other conditions.<sup>11,12</sup> Recently, a study indicated that aortic dilatation >4 cm could occur in approximately one third of patients, of which nearly one fifth were classified as moderate and attributed to the elastic disruption of the aortic ring.<sup>6</sup> LV hypertrophy, bundle branch blocks, and atrial fibrillation can also be coincident.<sup>8,13</sup> Our patient did not have any overt associations on further imaging; however, his electrocardiogram did reveal a first-degree atrioventricular block, which has not been previously linked.

Almost half of QAV cases are diagnosed by 2D-TTE, with one fifth and one sixth being detected during surgery

and autopsy, respectively.<sup>6</sup> Cardiac CT may accurately delineate the morphology and subtype of QAV, as well as the valve's inability to coapt with resultant regurgitant severity adequately.<sup>14</sup> It also provides other vital information such as the location of coronary ostia, the presence of obstructive coronary artery disease, and aortic dimensions. Cardiac magnetic resonance imaging is rapidly gaining traction as a diagnostic modality in acquiring other architectural and functional data, which may prove useful in the presurgical planning phase, as these patients may have coincident cardiac abnormalities.<sup>15</sup>

The patient presented with atypical chest pain, dyspnea, and was also hypertensive. As a result, he was initiated with optimal, guideline-directed angiotensin-receptor, neprilysin inhibition,  $\beta$ -blockade, and mineralocorticoid receptor antagonist (MRA) for his trivial to mild AR, which he hemodynamically tolerated without issues.<sup>16,17</sup>

The typical method of treatment is through surgery, such as aortic valve reconstruction surgery and AVR, usually with a synthetic valve.<sup>18</sup> AVR is often not an ideal strategy in young patients for several reasons, including valve thrombosis, durability, prosthetic valve endocarditis, and bleeding complications.<sup>18</sup> As a result, aortic valve repair may be a preferred alternative as it may allow complete coaptation and prolong overall durability.<sup>19</sup> Generally, the surgical procedure is usually predicated on the disease severity, condition of QAV, and surgeon's preference.<sup>20</sup> Since the advent of transcatheter heart valves, there has been a steadily increasing scope in which they can be clinically applicable. These include valve-in-valve treatment for failing bio-prostheses, treatment of bicuspid aortic valves in younger patients with complex anatomical features, and for native pure AR; however, these techniques have not been evaluated in QAV.<sup>21</sup>

Quadricuspid aortic valve can accentuate the risk of native valve endocarditis due to the supernumerary cusp. Consequently, antibiotic prophylaxis can be quite controversial with experts advocating both for and against strategies based on valve morphology and degree of AR.<sup>11,22</sup> Our patient did have an upcoming dental hygiene appointment, for which we recommended penicillin prophylaxis as he did not have any known drug allergies.

In a recent study evaluating the prognosis of AR, baseline trivial/mild AR was noted in almost one fifth of patients; mild-to-moderate AR in less than half; and moderate AR, almost 40%. The 10-year incidence of progression to equal or more than moderate-severe AR was 12%, 30%, and 53%, respectively. Patients who progressed underwent faster chamber remodeling with regard to effective regurgitant orifice area, annular and sinotubular junction dimensions, experienced a functional class decline, and more aortic valve/aortic surgery, which was associated with adverse consequences.<sup>23</sup>

The consequence of diagnosing QAV lies in the fact that the majority of these patients will require surgery for AR before incipient LV dysfunction with heart failure occurs. Although there are no formal guidelines in managing these

patients, it is prudent to routinely follow-up for ascertaining symptomatology with surveillance imaging.

The patient was advised to continue his optimal, guideline-directed medical therapy with low-dose valsartan, and sacubitril,  $\beta$ -blocker, MRA, and high-intensity statin. Additionally, it was recommended that he undergo echocardiographic surveillance every 6 months for his trivial-mild AR to determine any progression and decrement in LV ejection fraction. He was also informed of the likely need for mechanical valve AVR within the next decade and was in consensus with the management strategy, risk-benefit analysis, and attendant complications.

## Conclusion

We describe an exceedingly rare case of a QAV with trivial-mild AR with a brief clinical review. The clinician should be cognizant of the QAV as a congenital valvular defect, which may require increased imaging surveillance strategies, pharmacotherapeutic management with regard to AR-related heart failure, antibiotic prophylaxis consideration, and tentative operative intervention.

## Authors' Note

All procedures performed in studies involving human participants were in accordance with the Ethical Standards of the Institutional and National Research Committee, and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. All available data can be obtained by contacting the corresponding author.

## Author Contributions

RVS, VKS, SAP, FR, PM, SK, and NAS all contributed equally in writing the manuscript. All authors read and approved the final manuscript.

## Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

## Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

## Informed Consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

## ORCID iD

Naveen Anand Seecheran  <https://orcid.org/0000-0002-7779-0181>

## Supplemental Material

Supplemental material for this article is available online.

## References

1. Tsang MYC, Abudiab MM, Ammash NM, et al. Quadricuspid aortic valve: characteristics, associated structural cardiovascular abnormalities, and clinical outcomes. *Circulation*. 2016;133:312-319.
2. Hurwitz LE, Roberts WC. Quadricuspid semilunar valve. *Am J Cardiol*. 1973;31:623-626.
3. *The Lancet*. London: Saturday, July 26, 1862. *Lancet*. 1862;80:94-96. doi:10.1016/S0140-6736(01)13011-4
4. Savino K, Quintavalle E, Ambrosio G. Quadricuspid aortic valve: a case report and review of the literature. *J Cardiovasc Echogr*. 2015;25:72-76.
5. Tutarel O. The quadricuspid aortic valve. *Wien Klin Wochenschr*. 2003;115:212. doi:10.1007/bf03040314
6. Godefroid O, Colles P, Vercauteren S, Louagie Y, Marchandise B. Quadricuspid aortic valve: a rare etiology of aortic regurgitation. *Eur J Echocardiogr*. 2006;7:168-170.
7. Tsugu T, Murata M, Endo J, et al. Long-term outcomes in 3 cases of quadricuspid aortic valve, using a new classification system: a case series and literature review. *Echocardiography*. 2019;36:595-597.
8. Jagannath AD, Johri AM, Liberthson R, et al. Quadricuspid aortic valve: a report of 12 cases and a review of the literature. *Echocardiography*. 2011;28:1035-1040.
9. Zhu J, Zhang J, Wu S, Zhang Y, Ding F, Mei J. Congenital quadricuspid aortic valve associated with aortic insufficiency and mitral regurgitation. *J Cardiothorac Surg*. 2013;8:87. doi:10.1186/1749-8090-8-87
10. Nakamura Y, Taniguchi I, Saiki M, Morimoto K, Yamaga T. Quadricuspid aortic valve associated with aortic stenosis and regurgitation. *Jpn J Thorac Cardiovasc Surg*. 2001;49:714-716.
11. Janssens U, Klues HG, Hanrath P. Successful thrombolysis of right atrial and ventricle thrombi in a patient with peripartum cardiomyopathy and extensive thromboembolism. *Heart*. 1997;78:515-516.
12. Suzuki Y, Daitoku K, Minakawa M, Fukui K, Fukuda I. Congenital quadricuspid aortic valve with tetralogy of Fallot and pulmonary atresia. *Jpn J Thorac Cardiovasc Surg*. 2006;54:44-46.
13. Douglas H, Moore M, Purvis J. Comprehensive assessment of a quadricuspid aortic valve and coronary arteries by multidetector cardiac CT. *Heart*. 2012;98:1838.
14. Karlsberg DW, Elad Y, Kass RM, Karlsberg RP. Quadricuspid aortic valve defined by echocardiography and cardiac computed tomography. *Clin Med Insights Cardiol*. 2012;6:41-44.
15. Pouleur AC, le Polain de Waroux JB, Pasquet A, et al. Successful repair of a quadricuspid aortic valve illustrated by transoesophageal echocardiography, 64-slice multidetector computed tomography, and cardiac magnetic resonance. *Eur Heart J*. 2007;28:2769.
16. von Lueder TG, Kotecha D, Atar D, Hopper I. Neurohormonal blockade in heart failure. *Cardiac Fail Rev*. 2017;3:19-24.
17. Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2017;135:e1159-e1195. doi:10.1161/cir.0000000000000503
18. Song MG, Yang HS, Lee DH, Shin JK, Chee HK, Kim JS. Mid-term results in patients having tricuspidization of the quadricuspid aortic valve. *J Cardiothorac Surg*. 2014;9:29.
19. Schmidt KI, Jeserich M, Aicher D, Schäfers HJ. Tricuspidization of the quadricuspid aortic valve. *Ann Thorac Surg*. 2008;85:1087-1089.
20. Idrees JJ, Roselli EE, Arafat A, et al. Outcomes after repair or replacement of dysfunctional quadricuspid aortic valve. *J Thorac Cardiovasc Surg*. 2015;150:79-82.
21. Arias EA, Bhan A, Lim ZY, Mullen M. TAVI for pure native aortic regurgitation: are we there yet? *Interv Cardiol*. 2019;14:26-30.
22. Takeda N, Ohtaki E, Kasegawa H, Tobaru T, Sumiyoshi T. Infective endocarditis associated with quadricuspid aortic valve. *Jpn Heart J*. 2003;44:441-445.
23. Yang LT, Enriquez-Sarano M, Michelena HI, et al. Predictors of progression in patients with stage B aortic regurgitation. *J Am Coll Cardiol*. 2019;74:2480-2492.