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VALVULAR HEART DISEASE

CASE REPORT: CLINICAL CASE

Physiological Insights From Asymptomatic Severe Valvular Disease in a Highly Trained Athlete

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ABSTRACT

Parameters relied on as tools for prognostication in valvular disease can be confounded by athletic physiological remodeling. This case describes how cardiopulmonary exercise testing and multimodality imaging may be helpful in assessment of a 46-year-old female athlete with bicuspid aortic valve and subaortic membrane with associated asymptomatic severe mixed aortic valve disease. (JACC Case Rep. 2024;29:102551) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 46-year-old female medical practitioner was identified to have bicuspid aortic valve (BAV) and prominent subaortic membrane during routine echocardiographic screening after her father was diagnosed with symptomatic BAV. The patient was followed with serial echocardiograms, during which time the valvular pathology progressed from moderate to severe mixed aortic stenosis (AS)/aortic regurgitation (AR). She was referred to a tertiary sports cardiology center for expert evaluation and opinion.

Despite severe mixed aortic valve (AV) disease, the patient was asymptomatic. With detailed questioning, she described no change in exercise capacity, dyspnea, exertional chest pain, presyncope, syncope, or palpitations. Physical examination revealed an ejection systolic murmur and early diastolic murmur without signs of heart failure.

LEARNING OBJECTIVES

- To recognize that exercise-induced cardiac remodeling can mimic pathognomonic features of severe mixed aortic valve disease.
- To understand that CPET in combination with multimodality imaging may afford a potentially sensitive means of early LV decompensation in asymptomatic valvular disease.
- To understand the importance of shared decision making with patients.

PAST MEDICAL HISTORY

The patient had no other medical history and was taking no medications. She was an amateur endurance athlete, typically undertaking 12 to 18 hours of

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ABBREVIATIONS AND ACRONYMS

AR = aortic regurgitation

AS = aortic stenosis

AV = aortic valve

BAV = bicuspid aortic valve

CPET = cardiopulmonary exercise testing

LV = left ventricular

LVEF = left ventricular ejection fraction

TTE = transthoracic echocardiogram

high-intensity endurance exercise weekly—in a combination of running, swimming, and cycling. She had participated in 5 Ironman competitions since diagnosis.

DIFFERENTIAL DIAGNOSIS

Given the patient's history, differential diagnosis included asymptomatic severe mixed AV disease with or without indications for intervention.

INVESTIGATIONS

The patient underwent cardiopulmonary exercise testing (CPET) with stress transthoracic echocardiogram (TTE). Resting TTE showed normal left ventricular (LV) size (LV end-diastolic volume indexed for body surface area, 69 mL/m^2; normal <72 mL/m^2)[1] with normal LV systolic function (left ventricular ejection fraction [LVEF], 65%), normal global longitudinal strain (−20%), and moderate concentric increase in LV wall thickness. A subaortic membrane was visualized in the LV outflow tract with a peak velocity and gradient of 2.6 m/s and 26 mm Hg, respectively. A true BAV was associated with severe stenosis (maximum velocity, 5.4 m/s; peak gradient, 115 mm Hg; mean gradient, 70 mm Hg; AV area, 0.8 cm^2; indexed AV area, 0.4 cm^2/m^2; dimensionless index, 0.18). There was also moderate eccentric posteriorly directed AR. The ascending aorta was mildly dilated (42 mm) (**Table 1**, Videos 1 to 3).

CPET revealed a very high level of fitness (oxygen consumption/kg, 46 mL/kg/min, 157% predicted for age and sex) (**Figure 1**). Oxygen pulse incremented to 165% predicted. Systolic blood pressure increased to 180 mm Hg during exercise. Exercise ECG demonstrated monomorphic ventricular ectopics during high-intensity exercise, with no nonsustained ventricular tachycardia.

Poststress TTE demonstrated a peak velocity across the subaortic membrane and valve of 6.8 m/s (peak gradient, 185 mm Hg) and a mean gradient of 124 mm Hg. Combining the peak outflow gradient and systolic blood pressure, the implied peak ventricular pressure load could be estimated at 365 mm Hg (**Figure 2**).

Additional investigations included computed tomography coronary angiography, demonstrating normal coronaries and no coarctation. Cardiac magnetic resonance in 2018 and 2021 revealed increasing LV wall thickness and volumes (**Table 1**) with no fibrosis. Using volumetric comparisons of the LV and right ventricular stroke volumes, the AR was quantified and graded as severe.

MANAGEMENT

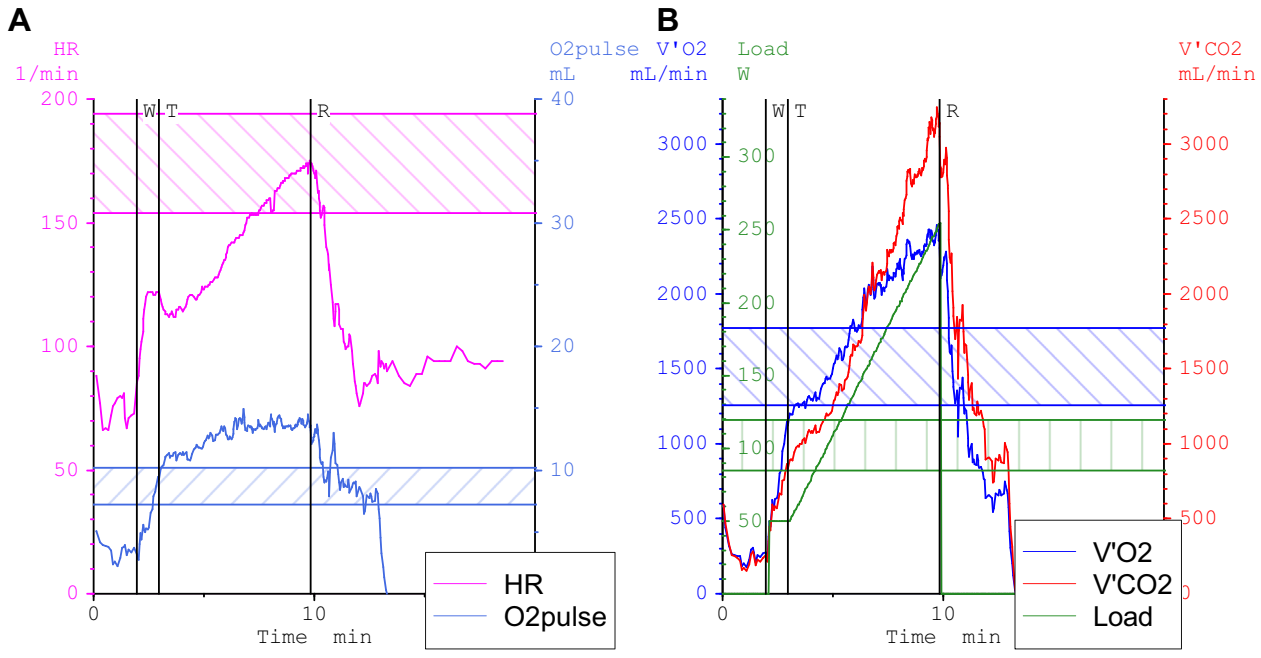
The patient remained asymptomatic and considered her fitness to be improving. After discussion at a

TABLE 1 Progression of Mixed Aortic Valve Disease by Multimodality Imaging

Year	TTE Resting SubAS + AV PG, mm Hg	TTE Resting SubAS + AV MG, mm Hg	TTE Poststress SubAS +AV PG, mm Hg	TTE Poststress SubAS + AV MG, mm Hg	TTE LVIDd, cm	TTE Aortic Regurgitation Severity	CMR LVEDVi, mL/m^2	CMR LVESVi, mL/m^2	CMR LVEF, %
Year 1	58	31				Moderate			
Year 3	69	38	81	47					
Year 4	79	38	-	-	4.8	Moderate			
Year 4	93	55	99	66					
Year 5	94	51			4.5	Moderate-Severe	118	29	76
Year 6	76	46	113	75					
Year 7	95	48			4.82	Moderate-Severe			
Year 8	86	58				Severe	130	47	64
Year 8	108	64			4.85	Severe			
Year 9	110	67	151	105		Severe			
Year 9	104	63			4.7	Severe			
Year 10	115	70	185	124	4.5	Moderate			

AV = aortic valve; CMR = cardiac magnetic resonance; LVEDVi = left ventricular end-diastolic volume indexed for body surface area; LVEF = left ventricular ejection fraction; LVESVi = left ventricular end systolic volume indexed for body surface area; LVIDd = left ventricular internal diameter end diastole; MG = mean gradient; PG = peak gradient; SubAS = subaortic stenosis; TTE = transthoracic echocardiogram.

FIGURE 1 Cardiopulmonary Exercise Test



Cross hatching represents mean predicted value for age/sex ± 15%. (A) The patient's oxygen pulse (oxygen consumption/heart rate, mL/beat), a surrogate of stroke volume, increments throughout exercise to 14.5 mL/beat (165% predicted), demonstrating supranormal values in the setting of superb cardiorespiratory fitness. Heart rate (beats/min) response is normal (100% predicted). (B) Demonstrating a high ventilatory threshold, oxygen consumption (mL/min) incrementing to 2,461 mL/min (46 mL/kg/min, 157% predicted), almost linear incrementation of carbon dioxide production (mL/min), and workload well exceeding mean predicted for age/sex (load [W]). HR = heart rate; VO_2 = oxygen consumption; VCO_2 = carbon dioxide production.

multidisciplinary cardiac meeting, and in conjunction with the patient, the decision was made to continue surveillance with close symptomatic monitoring in conjunction with multimodality imaging and CPET annually (**Figure 3**).

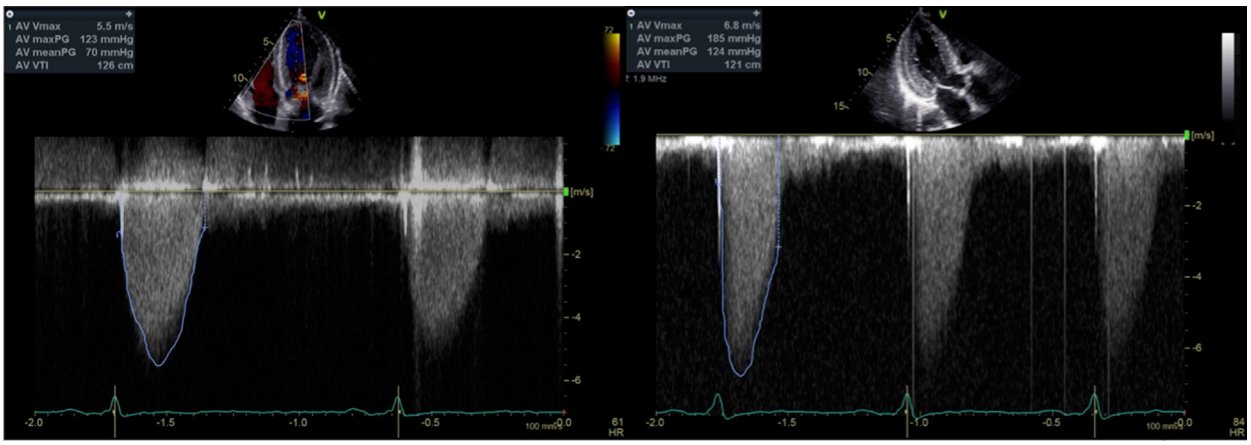
DISCUSSION

This case highlights the difficult management decisions in the nexus between severe valvular heart disease and athletic conditioning, creating issues for diagnosis, timing of intervention, and return-to-play advice.

In exercise-induced cardiac remodeling, LV dilation and LV hypertrophy are common.[2] These are also pathognomonic features of AR and AS, respectively.[3,4] Mildly reduced LVEF can also be seen in athletes[2] (although not in this case), whereas reduced LVEF in mixed AV disease alone would be an indication for intervention.[3,4] Many of the parameters relied on as tools for guiding the timing of intervention are confounded by athletic physiological remodeling. Furthermore, interobserver variability in TTE reinforces the importance of multimodality imaging for decision-making (**Table 1**).

Exercise testing aids the assessment of hemodynamic response in AV disease and can help identify patients with unrecognized symptoms or extreme hemodynamic changes, portending higher risk of exercise-related complications.[3] The transvalvular gradients demonstrated during exercise in this case are rarely seen, and it seems almost implausible that the patient would be asymptomatic, let alone have supranormal exercise capacity. There are scarce data in this unique situation. Referencing contemporary U.S. and European Guidelines for valvular heart disease,[3-5] the patient does not meet any Class I criteria for early intervention. The Class II indication of very severe AS (mean gradient ≥60 mm Hg or maximum velocity >5 m/s) is complicated by the fact that the gradient is a composite of flow acceleration through the subaortic membrane and AV. Similarly, she does

FIGURE 2 **Pre- and Post-Stress Aortic Signal Gradients**



A composite of flow through the subaortic membrane and aortic valve.

not meet any criteria for intervention for AR. Although her left ventricle is dilated, due at least in part to athletic remodeling, she has excellent contractile function with a normal LVEF and end-systolic LV dimensions.

Guidelines cannot be expected to cover all clinical scenarios and this case is unique. Although we closely follow the patient for symptoms, we think that there may be value in relying on physiological concepts to guide the difficult decision of early surgery in the asymptomatic state. On the basis that there is a strong association between increases in LV volumes and Vo_2max in women,[6] it would seem reasonable to hypothesize that adverse LV remodeling may be indicated by a simultaneous increase in LV volumes and reduction in Vo_2max. We argue that this would be a marker of LV decompensation due to the valvular pathology that could be used as rationale in shared decision-making to guide the patient toward early surgery. Currently, we have evidence of increasing LV volumes in the patient, but these are accompanied by performance improvements. The use of serial CPET will make follow-up more objective.

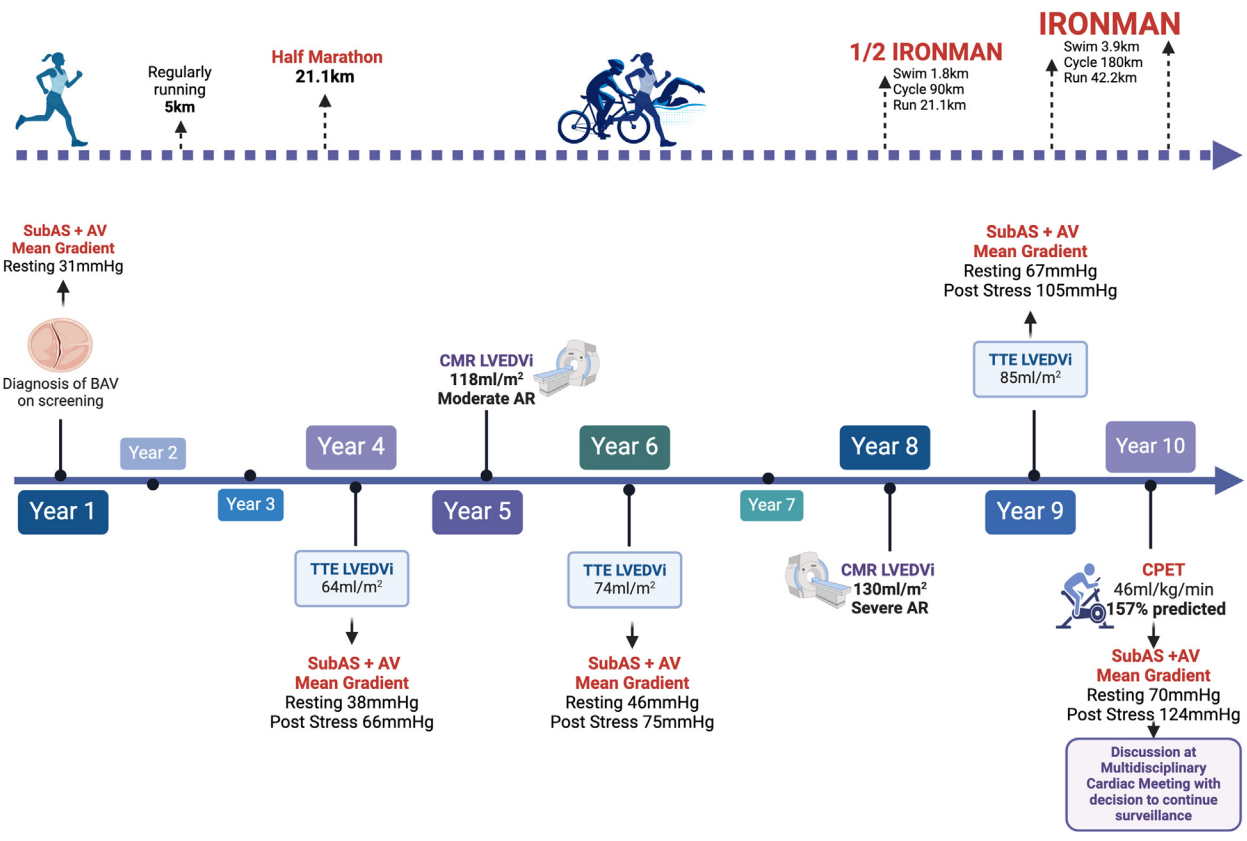
In this case, the patient's age influenced therapeutic options. A mechanical valve replacement represents a durable hemodynamic option but necessitates life-long anticoagulation. A bioprosthetic valve would require reoperation, and although percutaneous valve-in-valve treatment options for failing bioprosthetic valves are increasingly used, this would be unlikely to provide sufficient longevity. A Ross procedure may be the preferable option, but long-term valve survival is not guaranteed.[7]

Advising the patient in an evidence-based manner regarding her ongoing participation in sport is challenging. Guidelines are derived primarily from studies of valvular disease in nonathletic populations, with athlete-specific prospective data lacking.[8,9] Both U.S. and European guidelines for athletes with asymptomatic severe AS or AR advise against participation in competitive sports; however, these recommendations are based on consensus opinion only.[8,9] Subaortic membrane is reported to create a turbulent systolic jet which can cause damage to the AV leaflets resulting in progressive AR; however, the interaction with BAV and exercise remains unclear.[5] The risk of arrhythmias in mixed AV disease is reported to be infrequent in asymptomatic patients with normal LV function; therefore, the risk of early intervention in this case may exceed an active surveillance approach.[10-12] There are no recommendations regarding the impact of serial lesions as seen in this patient with a subaortic membrane and BAV. The patient has been made aware of these guidelines and in a shared decision-making process, has elected to continue to participate in endurance sport.

FOLLOW-UP

Risks associated with an active surveillance approach, including risks such as the emergence of symptoms, development of LV dysfunction, and modest increased risk of arrhythmia,[11,12] have been discussed with the patient and in shared decision-making with the patient, her lack of symptoms, lack of guideline-based indications for surgery, and the

FIGURE 3 Timeline of Events



Timeline of events since diagnosis to present, demonstrating increasing valvular gradients and left ventricular volumes with associated improving athletic performance. AR = aortic regurgitation; BAV = bicuspid aortic valve; CMR = cardiac magnetic resonance; CPET = cardiopulmonary exercise testing; LVEDVi = left ventricular end diastolic volume indexed for body surface area.

complexities of valve choice led her to prefer an active surveillance approach.

Follow up with annual CPET in combination with multimodality imaging and Holter monitoring may potentially mitigate risks of nonintervention through early detection of LV decompensation, subclinical symptoms or arrhythmias, and any reduction in exercise capacity.

CONCLUSIONS

Many of the parameters relied on as tools for prognostication in valvular disease are confounded by athletic physiological remodeling. Performing CPET in combination with multimodality imaging affords a potentially sensitive means of identifying early LV decompensation, subclinical symptoms, and arrhythmias, which may help in shared decision-making around timing of intervention. This case illustrates an extreme mismatch between the severity of the valvular disease and superb exercise capacity and the complexities of disaggregating the severity of coexistent pathologies in highly athletic patients, and highlights the importance of shared decision-making.

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KEY WORDS **bicuspid aortic valve, congenital valve disease, mixed aortic valve disease, multimodality imaging, sports cardiology, subaortic membrane**

APPENDIX **For supplemental videos, please see the online version of this paper.**