Role of Transesophageal Echocardiography in the Diagnosis of Coronary Ischemia in a Patient with History of Ross Procedure

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INTRODUCTION

Typical angina is most commonly a presenting symptom due to underlying coronary artery disease (CAD). However, when patients with a history of complex congenital surgeries that involve coronary manipulation present with angina, it can pose a unique diagnostic challenge. The Ross procedure is a complex operative procedure done in a select subgroup of patients that involves dissection of the aortic root, mobilization of the right and left main coronary arteries, harvesting of pulmonary autograft, implantation of the pulmonary autograft in the aortic position, coronary artery reimplantation, and pulmonary homograft implantation.[1] In this case report, we present a patient with a history of Ross procedure who developed anginal symptoms 25 years after the index surgery. The patient's stress test showed inducible ischemia; however, coronary angiography was negative for obstructive CAD. The additional workup, which included the invaluable use of a transesophageal echocardiogram (TEE), was instrumental and pivotal in formulating the diagnosis outlined below.

CASE PRESENTATION

A 44-year-old man with a history of bicuspid aortic valve (AV) that was repaired with a Ross procedure at the age of 19 years was referred to the adult cardiology noninvasive laboratory for evaluation of exertional dyspnea and chest pain. Prior to the onset of symptoms, the patient exercised regularly at the gym; however, over the last 6 months, the effort tolerance had steadily declined and in the 2 months prior to presentation, the patient started experiencing exertional chest pain, prompting them to stop aerobic exercises. The patient endorsed no other known medical history except for hypertension that was optimally controlled with an angiotensin-converting enzyme inhibitor and beta-blocker therapy. They denied ever using any tobacco but did endorse consuming three to four cans of beer daily. Vitals signs at presentation showed a blood pressure (BP) of 145/73 mm Hg and heart rate of 65 beats/minute. The patient was breathing on room air. Physical examination revealed a grade 2/6 harsh systolic ejection murmur at the left and right upper sternal borders. There was a 2/4 diastolic murmur heard in the same area. Lungs were clear to auscultation bilaterally. There was no pedal edema or jugular venous distension.

Given the presentation of typical chest pain, the patient underwent an exercise stress transthoracic echocardiogram (TTE) using the standard Bruce protocol. The electrocardiogram (ECG) at rest showed normal sinus rhythm with no ST-segment changes (Figure 1). At rest, the TTE revealed a left ventricular (LV) systolic/diastolic diameter of 5.2 cm/7.0 cm and septal/posterior thickness of 1.4 cm/1.2 cm (Figure 2) with an estimated LV ejection fraction (LVEF) of 55% to 60% (Video 1). There were no regional wall motion abnormalities. The right ventricle (RV) was dilated (basal diameter, 4.5 cm) and hypokinetic. The AV and aortic root were not well visualized. Aortic annulus measurement was 3.2 cm in peak systole. The LV outflow tract (LVOT) velocity-time integral was 35 cm. The peak aortic systolic velocity was 150 cm/sec, the peak aortic systolic gradient was 9 mm Hg, and the AV mean gradient was 4 mm Hg. Color-flow Doppler appeared to demonstrate only mild aortic regurgitation (AR). The pulmonary homograft was also not well visualized. Peak/mean transpulmonary gradient was 48 mm Hg/23 mm Hg. Pulmonary regurgitation pressure half-time was 218 ms.

The patient exercised for a total duration of 7 minutes and 18 seconds, achieving 10.0 metabolic equivalents, representing average functional capacity when standardized for age and sex. The patient achieved 86% of maximum predicted heart rate. The BP at rest was 145/73 mm Hg and the peak BP was 160/90 mm Hg. Exercise was terminated after the patient developed dyspnea and angina and the ECG showed frequent polymorphic ventricular complexes in couplets and triplets (Figure 1B). There were no ischemic ST changes. Immediate postexercise TTE showed further LV cavity dilation and decline in LVEF to 30% with global hypokinesis and severe hypokinesis of base to apical anterior and anterolateral wall, mid to apical anteroseptal wall, base to apical inferolateral wall, and apical wall segments (Videos 2 and 3). The clinical and echocardiographic findings raised concern for obstructive left main coronary artery (LMCA) or triple vessel disease, and the patient was scheduled for invasive coronary angiography.

The invasive coronary angiogram was technically challenging due to anatomical variation in this patient post–Ross procedure. Left coronary ostium could not be initially identified despite multiple attempts to engage. Hence, an aortogram was performed. Incidentally, the aortogram revealed AR (Video 4), which was not appreciated on the initial TTE. Subsequent engagement of the LMCA was then achieved, which did not demonstrate any significant obstructive epicardial CAD (Video 5).

Given the evidence of inducible ischemia in someone with a history of aortic root reconstruction/coronary reimplantation, further anatomic assessment was deemed necessary despite the apparently

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VIDEO HIGHLIGHTS

Video 1: Baseline two-dimensional TTE, apical 4-chamber view, demonstrates normal LV systolic function.

Video 2: Exercise stress echocardiogram with an ultrasound-enhancing agent, apical 4-chamber (*top*) and apical 2-chamber (*bottom*) views at rest (*left*) and poststress (*right*), demonstrates LV cavity dilation, decline in LVEF to 30%, and global hypokinesis with severe focal hypokinesis of the mid-distal, anterolateral, and apical segments.

Video 3: Exercise stress echocardiogram with an ultrasound-enhancing agent, apical long-axis (*top*) and parasternal short-axis (*bottom*) views at rest (*left*) and poststress (*right*), demonstrates LV cavity dilation, decline in LVEF to 30%, and global hypokinesis with severe focal hypokinesis of the mid-distal, anteroseptum inferolateral, and apical wall segments.

Video 4: Invasive contrast-enhanced cine-aortogram, anteroposterior display during panning of the entire aorta after power injection into the pigtail catheter (positioned in the dilated aortic root), demonstrates severe AR with rapid LV contrast opacification.

Video 5: Selective left coronary angiogram demonstrates the LMCA and branches without any significant obstructive epicardial CAD.

Video 6: Two-dimensional TEE, biplane midesophageal view, demonstrates malcoaptation of the AV cusps and asymmetric dilation of the neoaorta (5.0 cm). Sparse contrast is noted in the right heart.

Video 7: Two-dimensional TEE, midesophageal zoomed long-axis (130°) view without (*left*) and with (*right*) color-flow Doppler, demonstrates leaflet malcoaptation with severe eccentric AR directed anteriorly.

View the video content online at www.cvcasejournal.com.

normal coronary angiogram. Thus, we proceeded with cardiac computed tomography (CCT), which revealed a posterior origin of the LMCA, which coursed between the aorta and the right branch of the pulmonary artery. There was an acute angulation at the takeoff with an ostial kink resulting in 25% stenosis (Figure 3). The aortic root measured in end diastole was severely dilated with a diameter of 53.0 mm from cusp to cusp and 48.0 mm from cusp to commissure (Figure 4A). The pulmonary homograft placed at 19 years of age appeared stenotic with calcification and with poststenotic dilation of the main pulmonary artery (Figure 4B).

The CCT findings did not adequately explain the acute ischemic changes on stress TTE. Akin to the mechanism of ischemia in patients with anomalous left coronary artery arising from right coronary artery/right sinus that can predispose to sudden cardiac death due to its interarterial course, we hypothesized that with aortic dilation and rotation, the reimplanted LMCA had assumed a nonstandard position, compromising the left main ostium (with possible worsening during exercise). The left main ostium was rotated posteriorly and interposed between the aorta and the right pulmonary artery (RPA), making it vulnerable to stretch and compression during exercise stress, which could explain the inducible ischemia (left main distribution) during stress.

A TEE was pursued next, which further supported our hypothesis that compression and stretch of the left main coronary ostium and artery was the culprit for the stress test findings. The LMCA reimplantation site appeared high and displaced posteriorly (from asymmetric dilation of the neoaorta). The LMCA shaft was interposed between the aorta and RPA, with an acute takeoff and proximal narrowing of ostial lip, which showed cyclical dynamic compression. In measurements obtained from multiplanar reconstruction of three-dimensional zoom data, the LMCA midshaft segment measured 3.8 mm in diameter and the proximal LMCA measured 2.5 mm in diameter (Figure 5). There was moderate asymmetric dilation of the neoaorta (diameter, 5.0 cm at level of sinuses; Video 6) as expected in the Ross procedure, and there was normal caliber ascending aorta at 3.4 cm. The neo-AV was trileaflet and implanted high, with an elongated LVOT and asymmetric dilation of cusps with malcoaptation of aortic leaflets (Video 6, Figure 6). Severe AR with a very eccentric/anteriorly directed jet that dissipated after impinging on the anterior LVOT was noted (Video 7). Aortic regurgitation jet pressure half-time of 233 ms (severe regurgitation <200 ms; Figure 7) had to be measured from an off-axis, misaligned view due to significant jet eccentricity (Video 7). M-mode imaging across the aorta revealed prominent pulsatility with an aortic pulsatility index (API) of 43% (Figure 8). The diameter of the aorta in M mode at end systole (maximal diameter, Dmax) was 2.6 cm, and at end diastole (minimal diameter, Dmin) it was 1.8 cm. The API, calculated using the formula (Dmax – Dmin)/Dmin, was 43%. Sanchez *et al.*[2] demonstrated that severe AR, when assessed using M mode, is associated with a median API

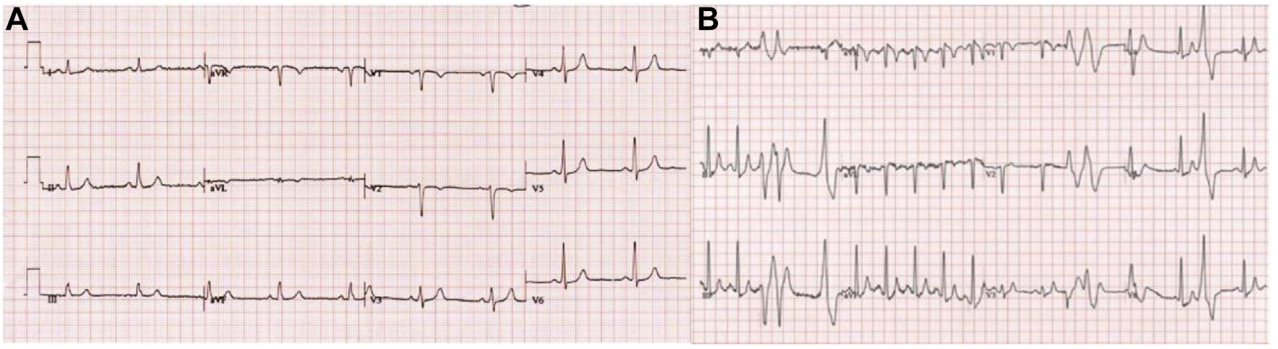

Figure 1 Twelve-lead ECG demonstrates normal sinus rhythm with no ST-segment changes at rest **(A)** and frequent polymorphic ventricular complexes in couplets and triplets at stress **(B)**.

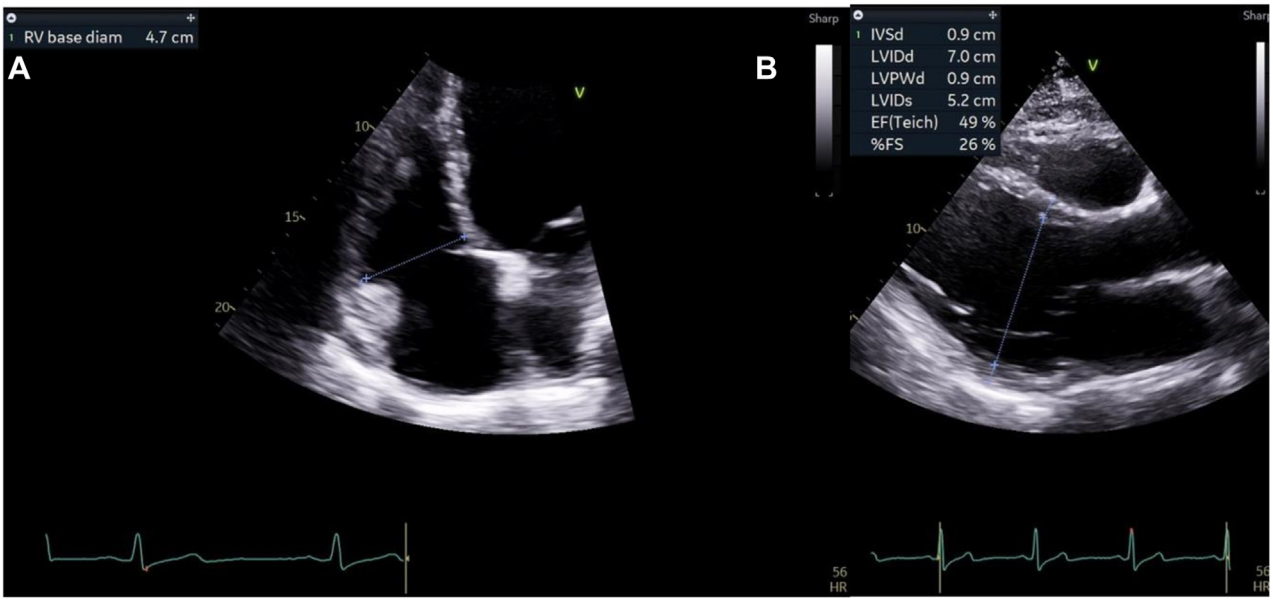

Figure 2 Baseline two-dimensional TTE, apical 4-chamber RV-focused **(A)** and parasternal long-axis **(B)** diastolic views, demonstrates biventricular dilation.

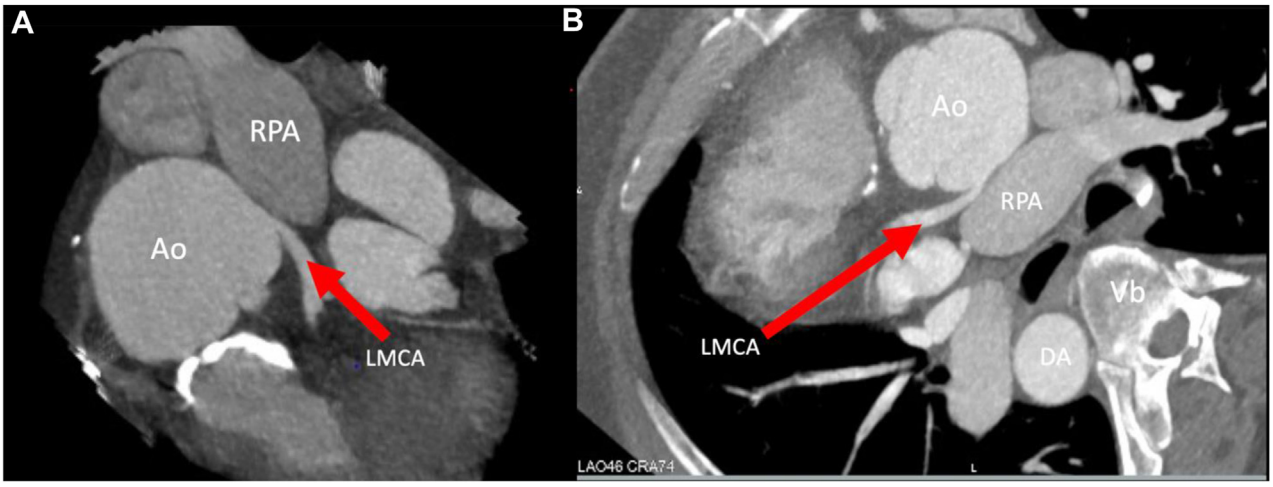

Figure 3 Cardiac computed tomography, multiplanar reconstruction, oblique axial displays focused on the heart **(A)** and showing the complete chest **(B)**, demonstrates the posterior rotation of the reimplanted LMCA (*arrow*) coursing between the RPA and the ascending aorta (Ao). *DA*, Descending aorta; *Vb*, vertebral body.

of 19.7%, compared to 3.8% in the control group. Holodiastolic flow reversals were also noted in the descending distal thoracic aorta (Figure 9). In aggregate, these findings are consistent with severe AR. The pulmonary homograft was poorly visualized. The peak transpulmonic gradient was 42.0 mm Hg, and mean PV gradient was 24.0 mm Hg. The severe AR demonstrated on the TEE was poorly profiled on the TTE. The likely reasons for this include jet eccentricity along with the cranially implanted AV in the reconstructed neoaorta. The TEE revealed an eccentric AR jet with rapid dissipation of jet velocity and momentum, leading to a poorly defined jet on color-flow Doppler and explaining challenges related to alignment of the continuous-wave cursor encountered with TTE. Color-flow Doppler area is determined by jet momentum (area $\times$ velocity^2). These challenges are illustrated in Figure 10.

After multidisciplinary discussions that included both adult and adult congenital cardiology teams, along with cardiothoracic surgery and cardiac imaging specialists, it was concluded that the angulation of the left main ostium and intra-arterial course/stretched LMCA were vulnerable to compression in their current anatomic location (plausibly exacerbated with exercise) and the likely proximate cause for the patient's angina and stress test findings. Given this hypothesis, the risk of sudden cardiac death, and the presence of severe AR, it was decided to proceed with surgical intervention. Revision of the Ross procedure was performed. Surgical exploration found a taut LMCA,

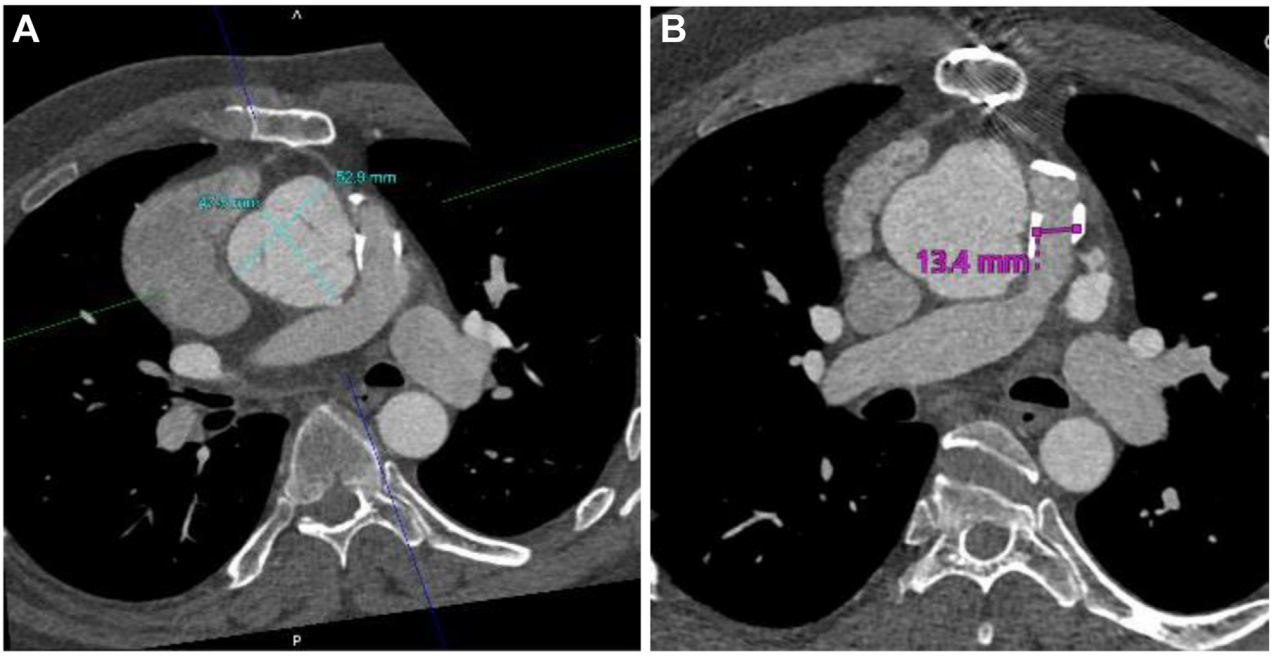

Figure 4 Cardiac computed tomography, multiplanar reconstruction, axial displays, demonstrates the aortic root dilation **(A)** and calcification with stenosis of the pulmonary homograft **(B)**.

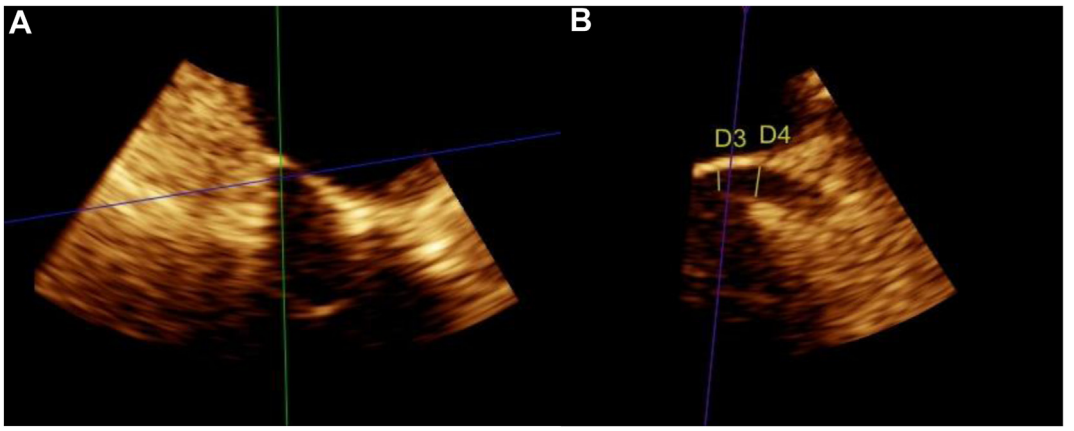

Figure 5 Three-dimensional TEE, biplane reconstruction, short-axis **(A)** and long-axis **(B)** views, demonstrates the narrowing of the ostium of the LMCA; the left main midshaft segment diameter (D4) is 3.8 mm, and the proximal left main (D3) diameter is 2.5 mm.

posteriorly displaced, with adhesions noted between the posterior aspect of the LMCA and the RPA. These adhesions were surgically dissected, and the LMCA ostium was reimplanted inferomedially, with restoration of considerable slack to the LMCA segment. The pulmonary autograft (neoaorta) was confirmed to be dilated and there was severe malcoaptation of the neoaortic leaflets. The valve was replaced with a 27/29 mm bileaflet mechanical AV composite. The pulmonary homograft was replaced with the 27 mm pericardial tissue valve composite graft.

The patient tolerated the procedure well and without complications. A TTE performed prior to discharge showed normal LVEF of 55%. The patient was regularly followed up in the dedicated adult congenital heart disease clinic at 3, 6, and 9 months after the procedure. At present, the patient is functionally back to baseline, being physically active with no symptoms of exertional angina or dyspnea, and there have been no hospital readmissions postprocedure.

DISCUSSION

Symptomatic coronary ischemia is not a commonly reported immediate or late complication of the Ross procedure. The Ross procedure involves replacing the AV with a pulmonary autograft and the pulmonary valve with a homograft.[3] In addition, it is a more complex operation than an AV replacement with a prosthetic valve as it involves dissection of the aortic root, mobilization of the coronary arteries, and coronary artery reimplantation.[1] Although the procedure is reported to result in improved life expectancy and quality of life, it is not a commonly adopted procedure most likely due to the perioperative mortality associated with the procedure.[4,5] According to the Society of Thoracic Surgeons National Database, less than 0.5% of the AV procedures performed between 1994 and 2010 were Ross procedures.[4] Aboud *et al.*[6] analyzed a total of 2,444 adult patients in the Ross Registry between 1988 and 2018 and found that

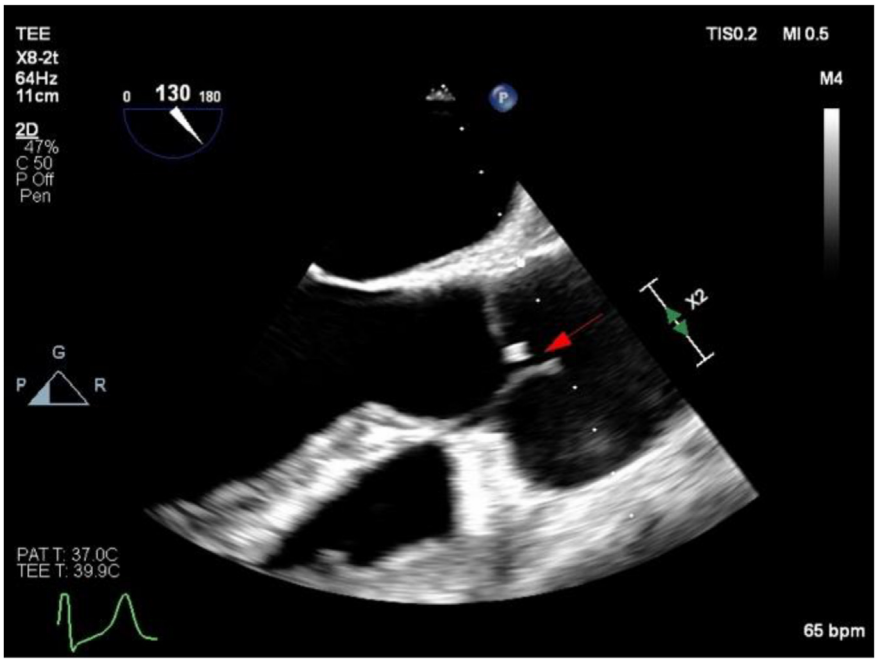

Figure 6 Two-dimensional TEE, midesophageal long-axis (130°) view, demonstrates malcoaptation of the AV cusps.

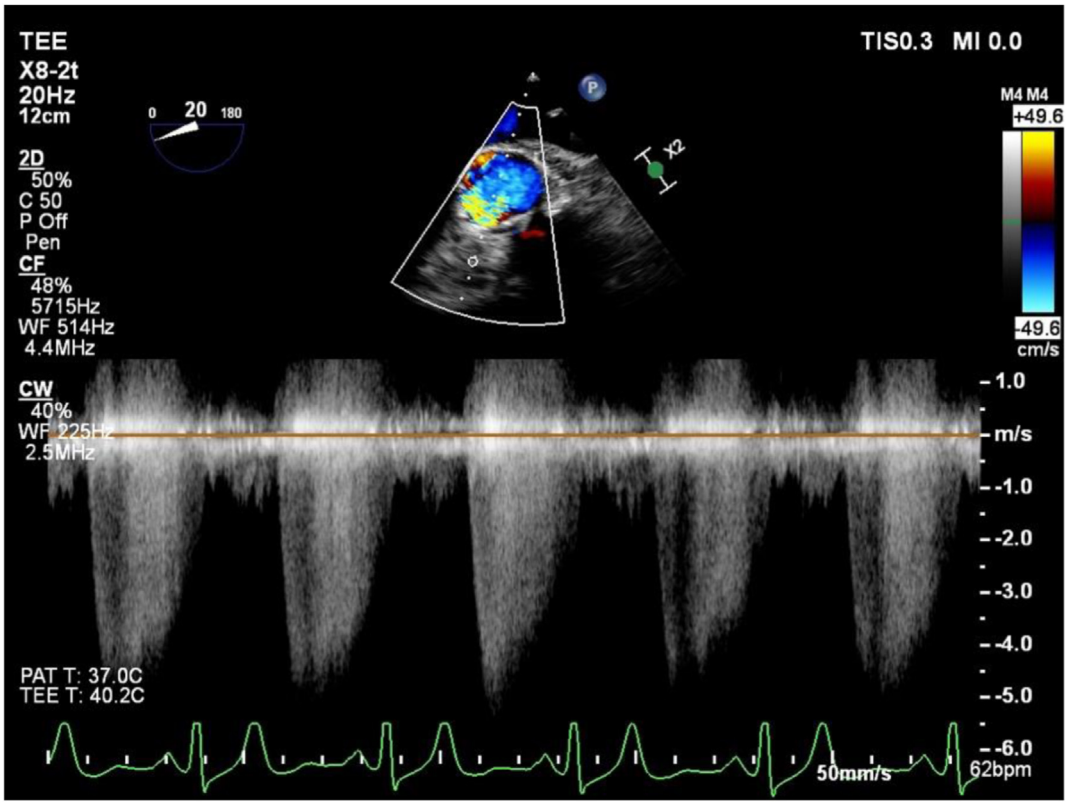

Figure 7 Two-dimensional TEE-guided, continuous-wave Doppler spectrum, midesophageal AV short-axis (20°) view, obtained off-axis due to severe jet eccentricity, demonstrates pressure half-time. Note the peak early AR jet velocity of approximately 4.5 m/sec, suggesting adequate Doppler signal quality.

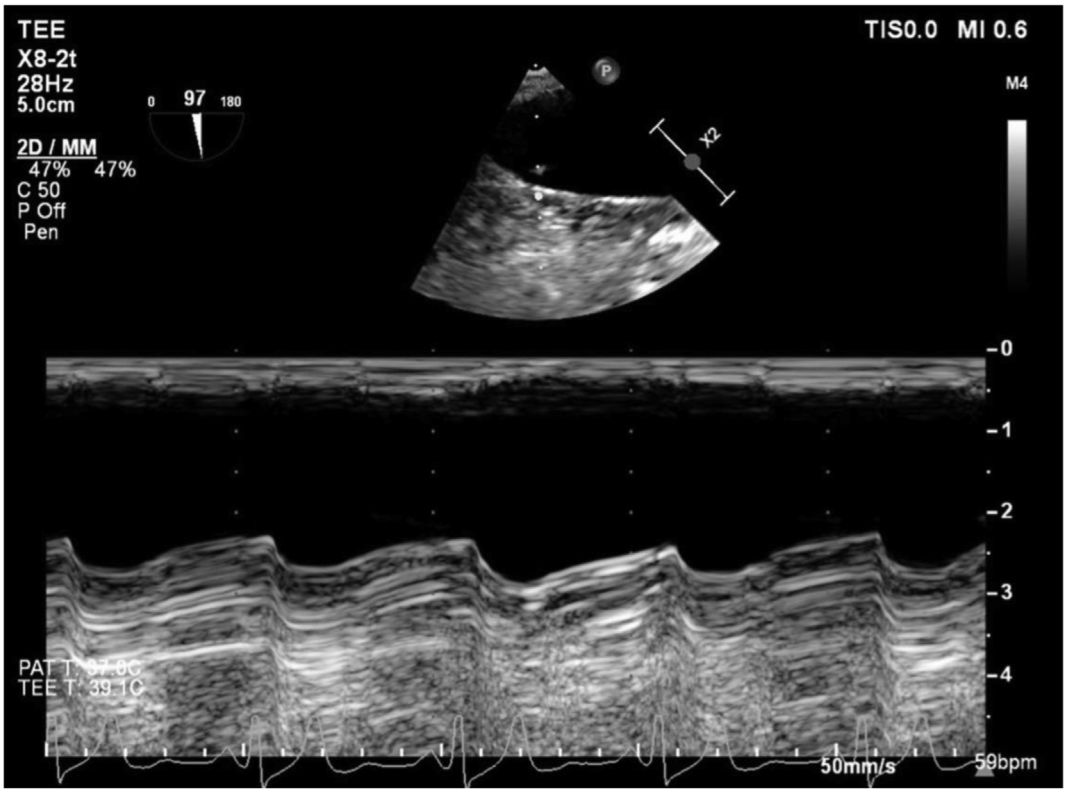

Figure 8 Two-dimensional TEE-guided M mode, long-axis (97°) view across the aorta, demonstrates increased aortic pulsatility.

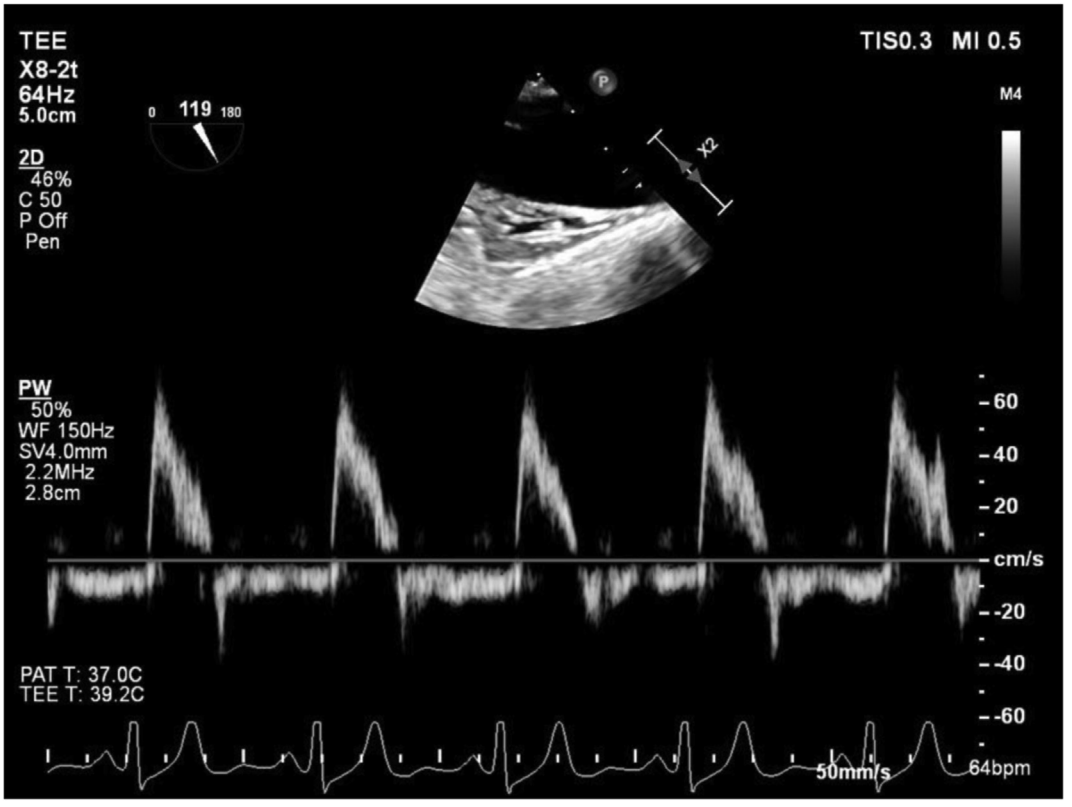

Figure 9 Two-dimensional TEE-guided pulsed-wave Doppler spectrum at the level of the descending aorta demonstrates low -velocity holodiastolic flow reversal, in aggregate, consistent with severe AR.

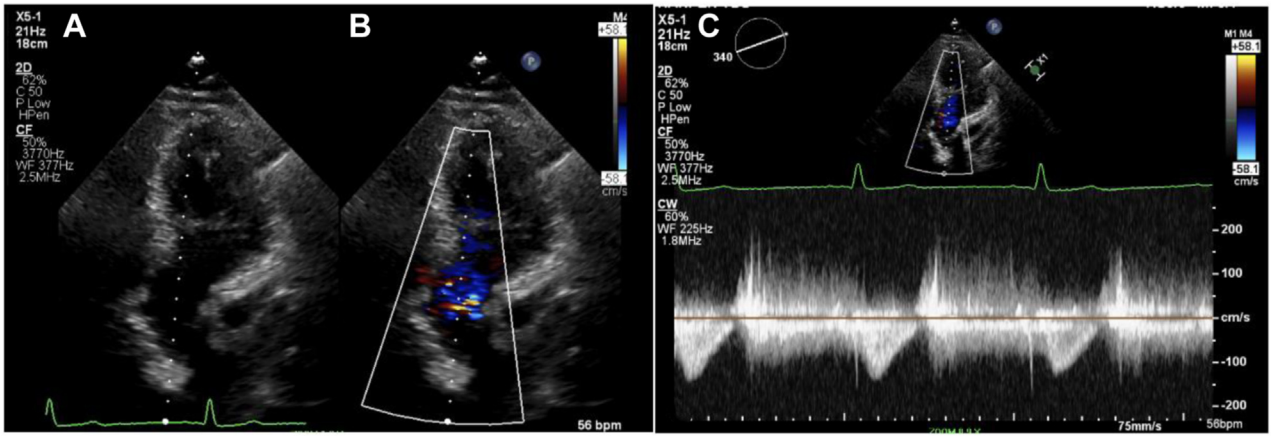

Figure 10 Two-dimensional TTE without **(A)** and with **(B)** color-flow Doppler-guided continuous-wave Doppler spectrum **(C)** demonstrates suboptimal signal quality precluding measurement of the pressure half-time.

226 (9.2%) patients underwent Ross-related reinterventions.[5] The median time to any reintervention was 6.5 years.[6] The most common causes of reintervention included valve deterioration and endocarditis.[6] Hauser *et al.*[7] followed 9 patients for about 4 years post–Ross procedure for any impact on myocardial blood flow and flow reserve in patients with coronary reimplantation following the Ross procedure. There were no exercise-induced perfusion defects detected in the Ross patients during the follow-up period.

In patients with suspected coronary ischemia caused by cyclic changes in blood vessel size and complex hemodynamics, it becomes crucial to assess their physiology during exercise rather than in the resting state.[8] In our patient's case, the initial test of choice for detecting ischemia was an exercise TTE. This test facilitated the detection of ischemia and an assessment of the pulmonary homograft and aortic autograft. Other imaging methods that could be considered include exercise stress myocardial perfusion imaging with positron emission tomography (PET).[9] A PET scan can provide quantitative assessment of myocardial blood flow. Low values of stress myocardial flow and/or myocardial perfusion reserve measured by PET can identify the hemodynamic significance of a stenosis.[10] Likewise, invasive hemodynamic measurement using fractional flow reserve with exercise (supine bike) when complex anatomy is detected on CCT could be considered depending on suitability and availability.[8] A pharmacologic stress cardiovascular magnetic resonance with coronary magnetic resonance angiography could be considered, albeit limited by its inability to be performed in real time with exercise.[11]

Dilation of the autograft (neoaorta) is one of the potential long-term complications following a Ross procedure and is reported with increasing frequency. In our case, the patient underwent the index procedure 25 years ago. Over the past 1, 3, and 7 years, serial TTE has shown progressive dilation of the aortic root and left ventricle (LV). The linear dimensions of the aortic root and LV systolic/diastolic diameters were measured at 44 mm/40 mm/60 mm, 45 mm/46 mm/65 mm, and 48 mm/46 mm/66 mm, respectively. The most recent TTE showed significant dilation, with measurements of 50 mm/52 mm/70 mm. Computed tomography angiography corroborated these findings, revealing a cross-sectional aortic diameter of 53 mm from cusp to cusp and a cusp to commissure diameter of 48 mm. Several factors may predispose to AR over time, including valve degeneration, endocarditis, structural changes in the neo-AV (like leaflet thickening and calcification), hemodynamic stress (especially in active individuals), and connective tissue disorders.[12] In our case, it is apparent that aortic root dilation led to the cusp malcoaptation with ensuing AR. When AR was initially visualized on the aortogram, it was debated whether this could be contributing to coronary ischemia, although the diastolic BP/pulse pressure profile did not quite support this hypothesis. Coronary perfusion pressure, which is determined by difference between the aortic diastolic pressure and the LV end-diastolic pressure, is very low in AR and could theoretically decrease myocardial perfusion, thereby lowering the myocardial ischemic threshold and resulting in exertional, anginal chest pain as well as nocturnal angina. The compensatory increase in LV mass and eccentric LV remodeling/dilation with ensuing elevation in wall stress all contribute to increased myocardial oxygen demand. Furthermore, a reduction in coronary flow reserve may be observed in patients with severe AR and angina, a consequence of epicardial coronary flow transitioning from predominantly diastolic flow to predominantly systolic flow. Our patient had regional wall motional abnormalities at peak stress that could not be exclusively attributed to AR alone, although AR could have lowered the myocardial ischemic threshold in the context of ostial left main distortion at peak exercise.

Pulmonary homograft stenosis is also another potential complication that should be identified early. In a 15-year study by González *et al.*[13] involving 107 patients, 29% developed homograft stenosis, with 10% requiring reintervention. In our patient, the pulmonary homograft was identified as stenotic on the CCT and subsequently replaced. Early identification of pulmonary homograft stenosis is crucial. If a patient develops clinical symptoms like chest pain and shortness of breath, a TTE should be considered initially, although it may have limitations for assessing the pulmonary homograft. A TEE or cardiovascular magnetic resonance imaging may be considered later for better visualization. Invasive assessments such as right heart catheterization and/or pulmonary angiography can also aid in the evaluation of pulmonary stenosis or regurgitation. Surveillance echocardiograms are key for timely diagnosis and management of homograft malfunction.

Three-dimensional TEE has been utilized in a similar way in other reported cases as well. Jung *et al.*[14] describe a case where a patient's allergy to iodinated contrast prevented coronary angiography. A TEE was used as a substitute and provided a substantial amount of information by utilizing three-dimensional volume images of coronary ostia. Doppler tracings of the coronary arterial flows confirmed the presence of high takeoff coronary arteries, and postprocedure TEE

confirmed correction of this disorder.[14] Yim *et al.*[15] elaborated on this further, describing techniques and proposing a guideline on how to visualize the coronary artery and flow in patients with congenital and acquired heart disease.

CONCLUSION

Our case highlights a unique pathophysiologic mechanism of coronary ischemia in a patient with a remote history of Ross procedure, comprehensively demonstrated by TEE. A stepwise approach with a multidisciplinary team approach resulted in timely diagnosis and intervention leading to complete symptom resolution for our patient.

ETHICS STATEMENT

The authors declare that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

CONSENT STATEMENT

Complete written informed consent was obtained from the patient (or appropriate parent, guardian, or power of attorney) for the publication of this study and accompanying images.

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DISCLOSURE STATEMENT

The authors report no conflicts of interest.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2023.12.021.

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