

Severe tricuspid bioprosthetic valve stenosis as an unusual cause of pulmonary embolism: a case report

Jwan A. Naser ¹, Arman Arghami ², Mackram F. Eleid³, and Sorin V. Pislaru ^{3*}

¹Department of Internal Medicine, Mayo Clinic College of Medicine, 200 First Street SW, Rochester, MN 55905, USA; ²Department of Cardiovascular Surgery, Mayo Clinic College of Medicine, 200 First Street SW, Rochester, MN 55905, USA; and ³Department of Cardiovascular Medicine, Mayo Clinic College of Medicine, 200 First Street SW, Rochester, MN 55905, USA

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Background

Bioprosthetic tricuspid valve stenosis (TS) is an uncommon and frequently under-diagnosed condition. Although the resulting right heart failure symptoms are well-known, the associated thrombogenic potential is under-recognized.

Case summary

A 44-year-old woman with bioprosthetic tricuspid valve (TV) replacement in 2001 was referred for urgent consultation due to acute worsening of dyspnoea and severe swelling and pain in her left arm and neck. She was diagnosed with atrial fibrillation 6 months before the presentation and was found to have right atrial (RA) thrombus with pulmonary embolism and extensive retrograde venous extension 1 month prior. Review of studies done at her local institution revealed 10 mmHg mean gradient (MG) across the bioprosthetic TV that was only reported as mild–moderate TS. Echocardiography done at our institution confirmed suspicion of severe TS with calcified immobile leaflets. Computed tomography showed persistent RA thrombus and therefore surgical replacement of the TV was undertaken. Subsequently, patient's dyspnoea rapidly improved.

Discussion

Progressive dyspnoea and symptoms of right heart failure in a patient with a history of bioprosthetic TV replacement should be investigated for prosthetic valve dysfunction. Due to its rarity, TS diagnosis can be overlooked on routine echocardiography. In our patient, despite a measured MG of 10 mmHg, the presence of critical TS was not initially recognized. As TS is associated with increased thrombogenic potential and given the rare occurrence of *in situ* RA thrombosis, physicians must have a high index of suspicion for TS in the appropriate clinical context.

Keywords

Tricuspid stenosis • Pulmonary embolism • Atrial thrombus • Bioprosthetic valves • Case report

Learning points

- Dyspnoea and signs of right heart failure in patients with bioprosthetic tricuspid valves should be considered secondary to prosthetic dysfunction until proven otherwise.
- Tricuspid stenosis can be associated with substantial thrombogenic potential similar to that described in mitral stenosis.
- Tricuspid stenosis can result in many complications including right atrial thrombi, pulmonary emboli, and venous thrombosis and prompt formal diagnosis and treatment is important.

* Corresponding author. Tel: +1 507 284 8612, Fax: +1 507 266 7929, Email: pislaru.sorin@mayo.edu

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Introduction

Thrombus formation in the right atrium (RA) was found to be less frequent than in the left atrium (LA) in atrial fibrillation (AF) due to the different anatomy of the atrial appendages.^{1,2} On the other hand, a large autopsy series found similar prevalence of thrombi in the RA and LA.³ Mitral stenosis (MS) is known to carry a high risk of LA thrombus formation.⁴ The presence of tricuspid valve (TV) prosthesis and tricuspid stenosis (TS) are also described as potential causes of RA thrombi.⁵ However, because TS is a less common disease in adults without congenital heart disease, diagnosis can be easily missed. Additionally, RA thrombus formation in the setting of bioprosthetic TS may be under-recognized compared to mechanical valves, which are traditionally linked to a higher thrombogenicity. We present a patient who developed a massive RA thrombus due to unrecognized critical bioprosthetic TS and in the setting of AF. This led to retrograde extension into the superior vena cava (SVC) and the left subclavian and axillary veins as well as pulmonary embolization (PE).

Timeline

2001	Bioprosthetic tricuspid valve (TV) replacement due to TV endocarditis
October 2019	Onset of dyspnoea Diagnosis of atrial fibrillation, cardioversion, and warfarin initiation Transthoracic echocardiography (TTE): mean gradient (MG) of 9 mmHg across the TV; stenosis reported as mild
March 2020	Intense neck and left arm pain as well as local swelling and acute worsening of dyspnoea Computed tomography angiography (CTA) at the local institution: pulmonary embolism and right atrial thrombus with massive retrograde venous extension up into the left axillary vein TTE: MG of 10 mmHg across TV; stenosis reported as moderate international normalized ratio (INR) of 2.4; switched to Rivaroxaban with improvement of arm and neck swelling, but not dyspnoea
April 2020	Referral to our institution Review of outside studies: concerns for severe tricuspid stenosis TTE: MG of 11 mmHg across TV with calcified immobile leaflets; massively enlarged right atrium CTA: persistent right atrial thrombus; improved pulmonary embolism burden Surgical replacement of the TV and right atrium reduction plasty

Case presentation

The patient is a 44-year-old woman who had bioprosthetic TV replacement for endocarditis in 2001. In October 2019, she developed dyspnoea and was diagnosed with AF and was cardioverted and started on warfarin. Transthoracic echocardiography (TTE) at that time at her local institution demonstrated a mean gradient (MG) of 9 mmHg, but TS was considered only 'mild'. In March 2020, the patient developed neck and left arm swelling and pain as well as acute worsening in her dyspnoea. Computed tomography angiography (CTA) at her local institution revealed PE, but also RA thrombus with massive retrograde extension into the SVC, left brachiocephalic, subclavian, and axillary veins (*Figure 1*). On TTE, MG was 10 mmHg and TS was labelled as 'moderate'. The patient was switched to Rivaroxaban. Left arm swelling improved, but dyspnoea worsened, in parallel with more oedema and abdominal distension. Plan for evaluation at specialized Valve Center was planned but not followed through due to the COVID-19 pandemic.

The patient was referred to our institution for urgent consultation in April 2020. In reviewing outside CTA and TTE, we were concerned for severe bioprosthetic TS. The patient was admitted to the hospital and was switched to intravenous unfractionated heparin. Transthoracic echocardiography showed a heavily calcified, immobile bioprosthesis with critical stenosis (MG: 11 mmHg) and a massively enlarged RA compressing the LA into a small conduit (*Figure 2* and *Video 1*). Colour Doppler on TTE suggested only mild tricuspid regurgitation (TR), but the presence of an enlarged right ventricle together with the triangular-shaped, low-velocity tricuspid regurgitant signal (*Figure 2*) raised the suspicion of significant TR.

Four-dimensional CTA showed persistent large RA thrombus, but significant improvement in the clot burden in the subclavian vein and pulmonary arteries. There was no significant coronary artery disease. The bioprosthesis was calcified and immobilized in a partially open / partially closed position (*Figures 3 and 4* and *Video 2*). The valve area at maximal diastolic opening was 1.2 cm², consistent with severe stenosis and 1.05 cm² at end-systole, consistent with severe regurgitation (*Figure 4*). Imaging revealed no thrombus in the inferior vena cava, hepatic, or iliofemoral veins. Thrombophilia testing was unremarkable.

Due to persistent RA thrombus and the need to reduce the volume of the giant RA, surgical intervention was recommended. Intraoperative transoesophageal echocardiography showed significant TR, presence of RA thrombus (*Figure 5* and *Video 3*), and immobile prosthetic cusps (*Supplementary material online, Video S1*). The RA pressure was massively elevated at 24 mmHg. The explanted valve appeared severely calcified (*Figure 5*). A 31 mm bioprosthesis was implanted, the RA thrombi were removed, and RA size was reduced.

Post-operative TTE showed excellent tricuspid bioprosthetic function (MG: 2 mmHg). The patient's overall status and dyspnoea rapidly improved after the surgery, and she was started on warfarin in the setting of the new bioprosthetic valve.

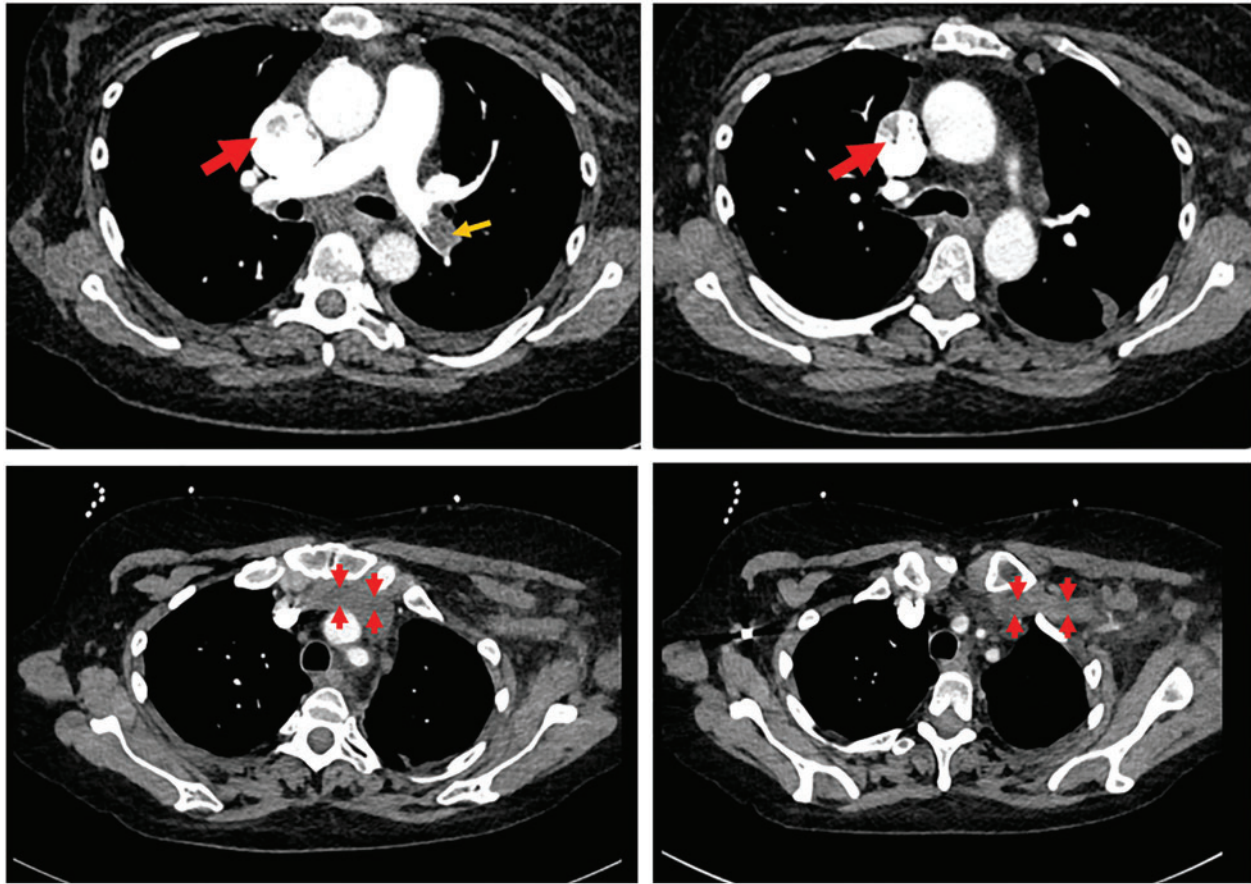


Figure 1 Initial computed tomography at the local institution demonstrated near occlusive thrombus in the left pulmonary artery (top panel, yellow arrow), but also massive thrombus extension (red arrows) from the right atrium into the superior vena cava (top panels), left brachiocephalic vein (bottom left panel), and left subclavian and axillary veins (bottom right panel).

Discussion

Tricuspid stenosis is a rare condition that can be caused by congenital heart disease, radiation, inflammatory diseases, carcinoid syndrome, infective endocarditis, and rheumatic heart disease.⁶ In patients with degenerated tricuspid bioprostheses, regurgitation is a more common manifestation than stenosis, but TS is a serious late sequela.⁷ Nakano *et al.*⁸ reported that 9/84 patients with bioprosthetic TV developed TS secondary to structural deterioration (calcification/degeneration) or non-structural dysfunction (pannus formation/native valve attachment) requiring redo replacement. Due to its rarity, TS diagnosis can be overlooked and its severity underestimated, as in our patient. Misdiagnosis can be due to lack of familiarity with normal two-dimensional echocardiographic appearance of tricuspid prostheses, acoustic shadowing from the sewing ring, and difficulty imaging patients with significant volume overload. Just like with native valves, the use of transvalvular gradients by continuous wave Doppler is the primary parameter to evaluate the degree of stenosis with TS being suggested if MG is >6 mmHg.⁹

Tricuspid stenosis can lead to increased thrombogenic potential due to a combination of stasis, low pressures, and low flow velocities

in RA. Secondary AF can develop and further increase the risk of thrombus formation. Given the rare occurrence of *in situ* RA thrombosis, physicians must have a high index of suspicion for TS in the appropriate clinical context. Failing to recognize severe TS with associated stasis as the main determinant of the RA thrombus,⁵ the local institution labelled the event as 'warfarin failure', and the patient was started on a direct oral anticoagulant; whether the thrombus was already present at the time of AF diagnosis is unknown. Direct oral anticoagulants have the advantage of easier dosing and more consistent achievement of therapeutic levels. However, their use for intracardiac thrombi is controversial, with both favourable (more effective resolution of intracardiac thrombi¹⁰) and unfavourable outcomes (increased peripheral embolism¹¹).

While it is hard to ascertain whether the thrombus started in the RA vs. the left upper extremity veins, the absence of both hypercoagulable status and history of local trauma along with the presence of severe bioprosthetic TS and AF make us believe that the thrombus most likely formed in the RA with retrograde extension into the venous system. Furthermore, the explanted prosthesis had thrombus attached to the commissure (Figure 5).

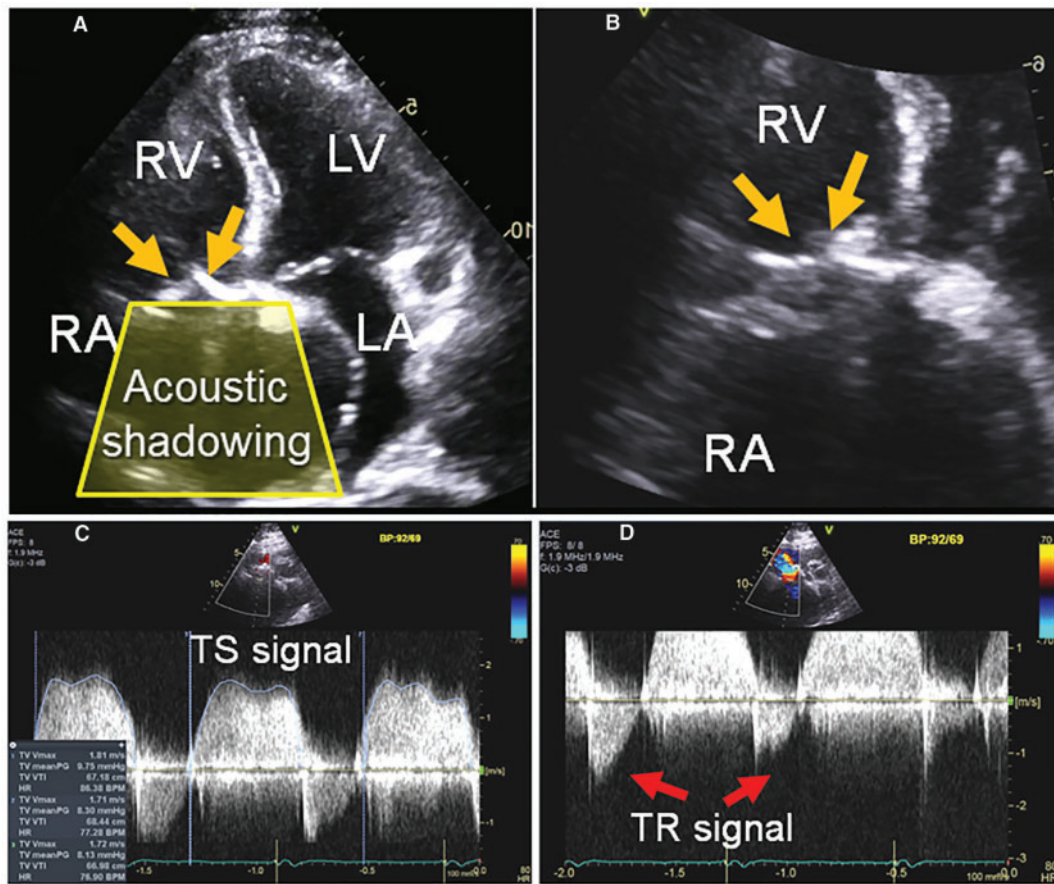
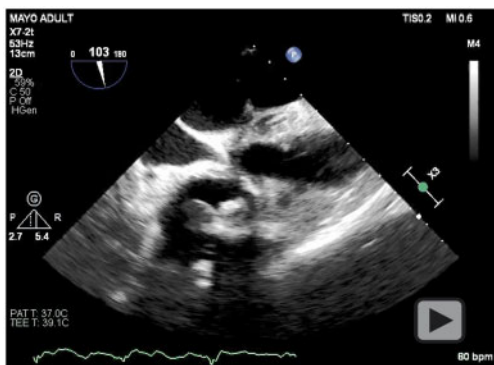


Figure 2 (A and B) Transthoracic echocardiography apical four-chamber view demonstrates massive enlargement of the right atrium with compression of the left atrium, but also the presence of a dilated right ventricle. Leaflets are completely immobile ([Supplementary material online, Video S1](#)). Note area of acoustic shadowing behind the calcified bioprosthesis, obscuring tricuspid regurgitation on colour Doppler. (C and D) Transthoracic echocardiography: continuous wave Doppler confirms suspicion of severe tricuspid stenosis (mean gradient was higher at 11 mmHg in a different window), but also of a very low velocity, triangular-shaped tricuspid regurgitation signal consistent of rapid pressure equalization between right atrium and right ventricle and highly suspicious for severe regurgitation. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; TR, tricuspid regurgitation; TS, tricuspid stenosis.



Video 1 Transthoracic echocardiography: massively enlarged right atrium compressing left atrium. Note immobile, severely calcified tricuspid bioprosthetic cusps.

Treatment options for RA thrombi include anticoagulation, surgical thrombectomy, or thrombolytic therapy. There are no randomized trials to guide treatment strategy. Our patient was started on Rivaroxaban with a subsequent decrease in the thrombus burden in the RA, venous system, and pulmonary arteries. Surgical thrombectomy was done given the need for surgical re-replacement of TV due to severe TS. Percutaneous intervention was not pursued given the presence of RA thrombus and risk of dislodgment and embolization.

An important clinical observation in our patient was that dyspnoea preceded her PE and worsened despite decreased thrombus burden. We hypothesize dyspnoea was a direct result of RA hypertension causing elevated LA pressure. Indeed, transmission of elevated pressures from right-sided chambers to left chambers is possible due to the restraining properties of the pericardial sac, with enhanced ventricular interdependence. This pathophysiological phenomenon has been well described as a cause of dyspnoea in patients with isolated TR¹² and could also occur in patients with TS.

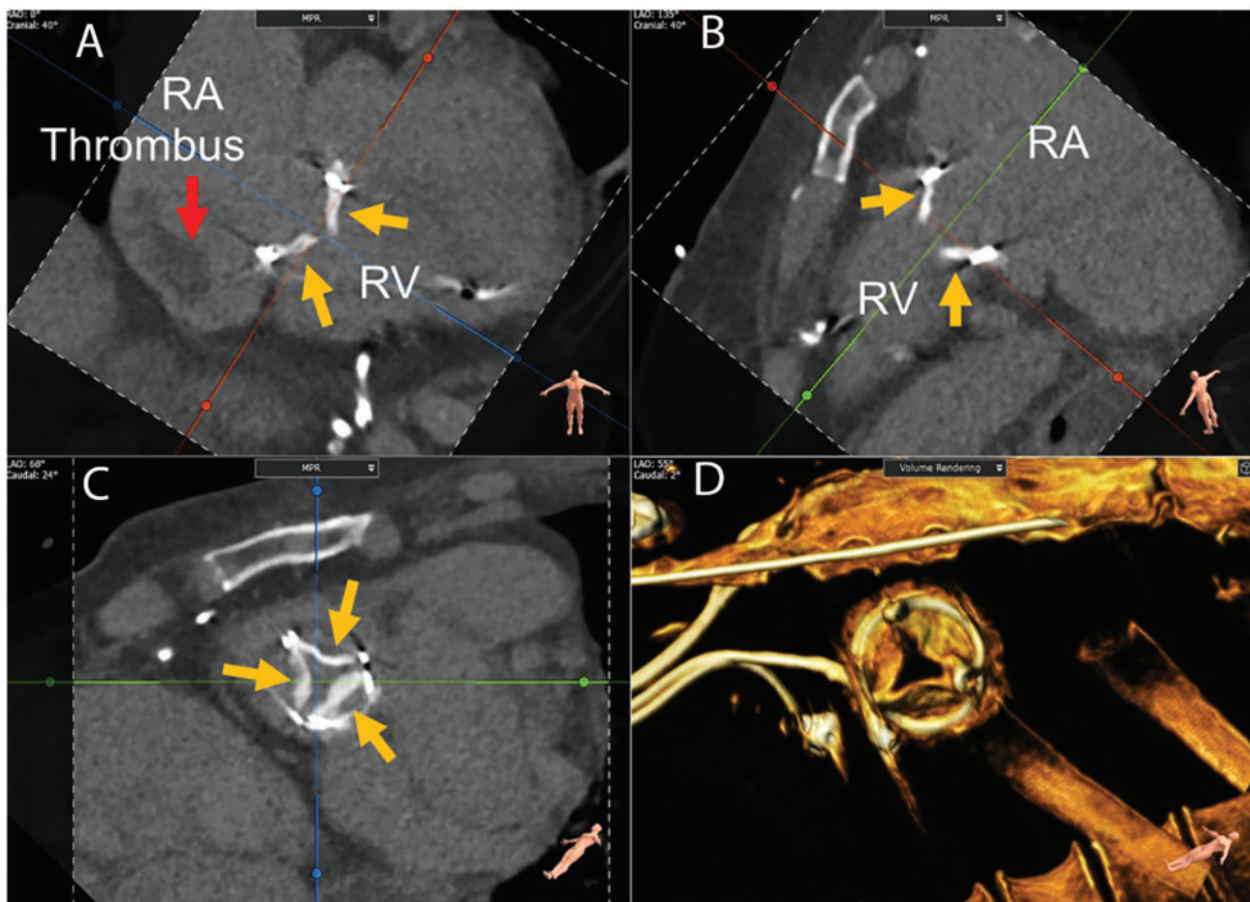


Figure 3 Computed tomography angiography at end-diastole showed severely restricted opening of all three prosthetic cusps (A, B, and C, yellow arrows) as well as the hyper-attenuating appearance of the cusps, with signal intensity similar to bone and metallic hardware of the prosthesis. A large right atrium thrombus is visible (red arrow). CT also confirmed the presence of calcified, essentially immobilized tricuspid bioprosthetic cusps in a partially closed / partially open position. RA, right atrium; RV, right ventricle.

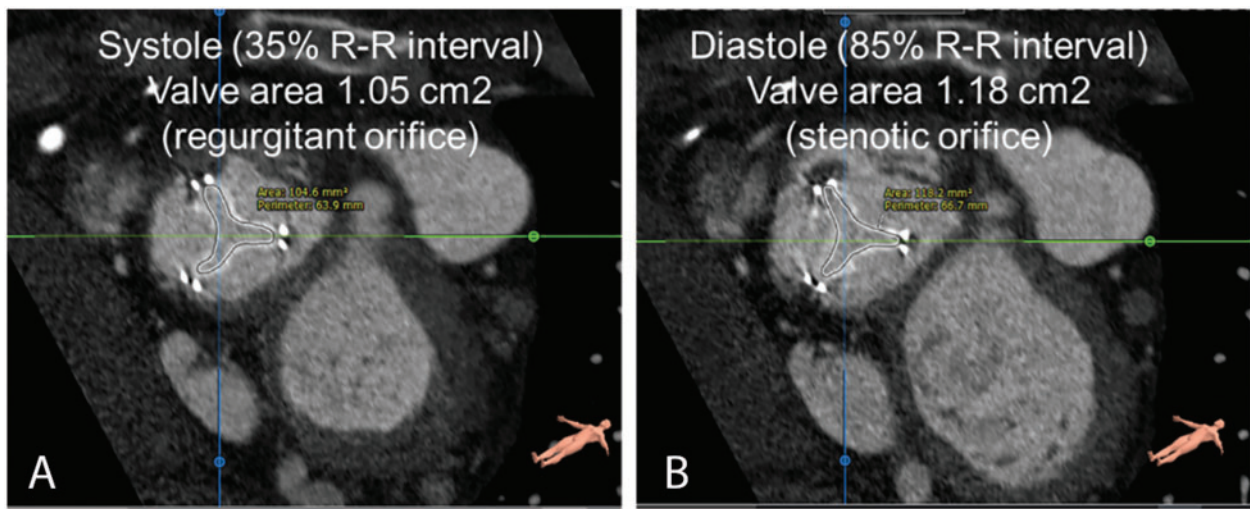


Figure 4 Four-dimensional computed tomography angiography showed an immobile valve, failing to close in systole (A, valve area 1.05 cm²) and failing to open in diastole (B, valve area 1.18 cm²).

Conclusion

Tricuspid stenosis may be easily under-recognized due to its rare occurrence but can be associated with severe adverse outcomes. The thrombogenic potential of severe TS may be as high as that in MS and can lead to PE and/or retrograde venous extension. The index of suspicion should be high whenever increased gradients are recorded in patients with bioprosthetic TV.

Lead author biography



Dr Jwan A. Naser completed medical school at Jordan University of Science and Technology in Irbid, Jordan. She is currently an internal medicine resident at Mayo Clinic, Rochester. She also worked as a research fellow at the Echocardiography Lab at Mayo Clinic, Rochester. She aspires to become a cardiologist upon completion of her training. Her research interests include echocardiography, valvular heart diseases, atrial fibrillation, and artificial intelligence.

Supplementary material

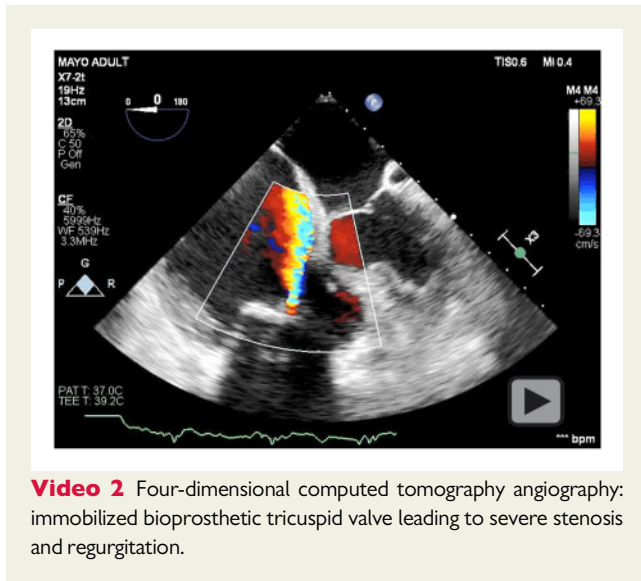
[Supplementary material](#) is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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Video 2 Four-dimensional computed tomography angiography: immobilized bioprosthetic tricuspid valve leading to severe stenosis and regurgitation.

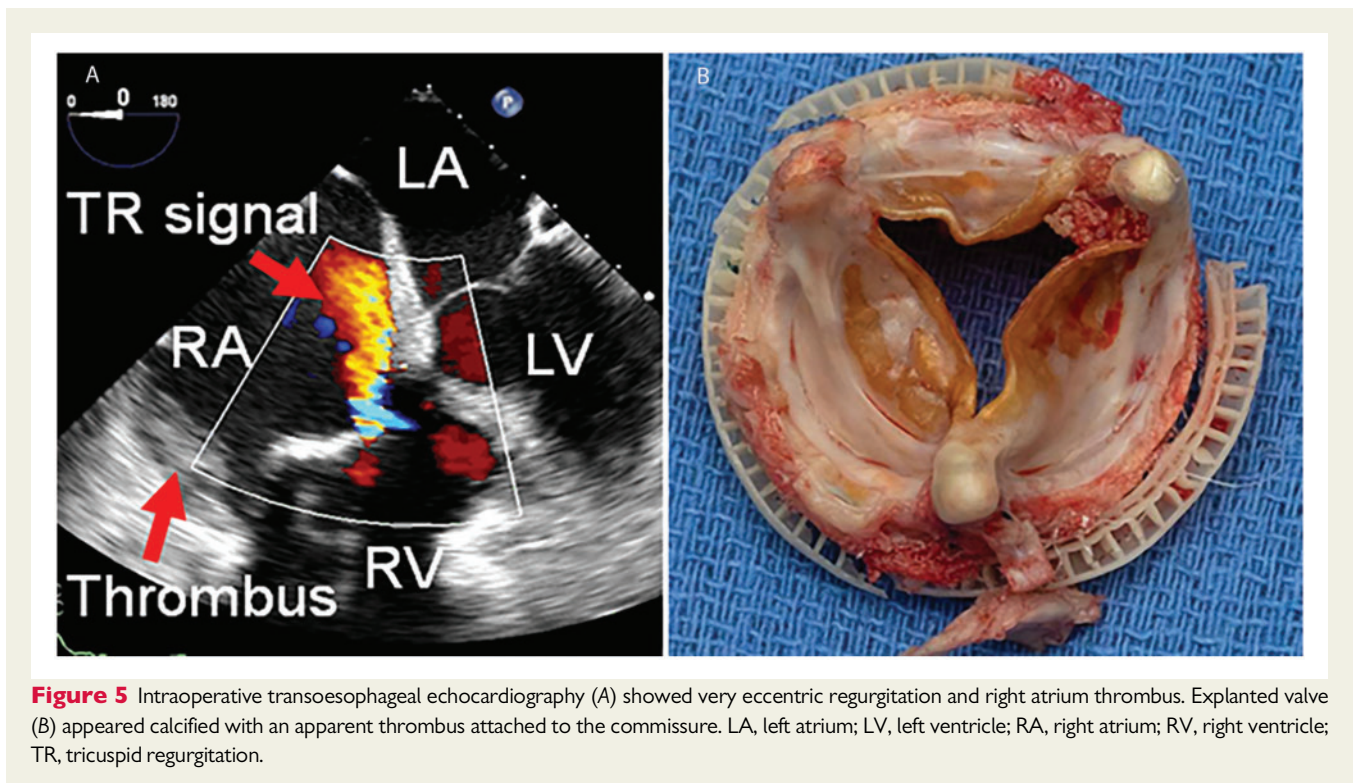
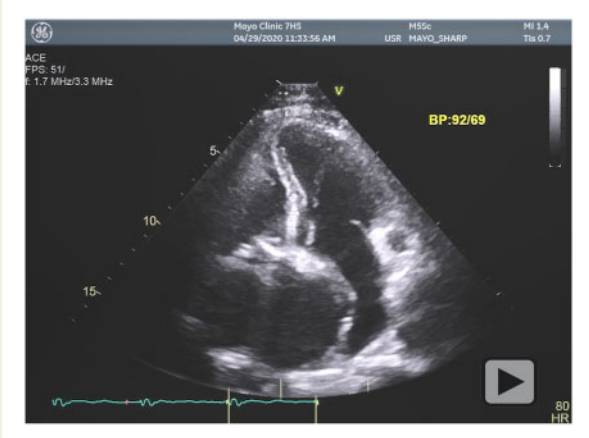


Figure 5 Intraoperative transoesophageal echocardiography (A) showed very eccentric regurgitation and right atrium thrombus. Explanted valve (B) appeared calcified with an apparent thrombus attached to the commissure. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; TR, tricuspid regurgitation.



Video 3 Intraoperative transoesophageal echocardiography confirms the presence of very eccentric jet tricuspid regurgitation that was not visible on transthoracic echocardiography. Note also marked acoustic shadowing from the sewing ring, completely obscuring the septal cusp.

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