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CASE REPORT
Cardiac imaging

The role of four-dimensional computed tomography in transcatheter aortic valve replacement prosthesis endocarditis with concurrent leaflet thrombosis: a case report

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Background Transcatheter aortic valve replacement (TAVR) is becoming increasingly utilized for the treatment of severe aortic valvular heart disease. Infective endocarditis of TAVR is rare but associated with higher mortality and morbidity. The potential for leaflet thrombosis following TAVR is also becoming increasingly recognized. Diagnosis of these conditions on echocardiography can be challenging due to prosthesis artefact.

Case summary An 84-year-old man with a previous transcatheter aortic valve replacement presented with a febrile illness and bacteraemia. Transthoracic and transoesophageal echocardiography demonstrated high transvalvular gradients with features of prosthesis endocarditis, though leaflet morphology could not be fully assessed due to prosthesis artefact. Four-dimensional computed tomography revealed hypo-attenuated leaflet thickening with reduced leaflet motion, consistent with prosthesis leaflet thrombosis. The patient was successfully treated with antibiotics and anticoagulation, with resolution of the infection and normalization of the transvalvular gradient after 6 weeks.

Discussion Echocardiography should be the first-line investigation for assessing leaflet morphology in suspected prosthetic valve endocarditis or leaflet thrombosis but its accuracy may be limited by artefact. Our case highlights that four-dimensional computed tomography provides further evaluation of prosthesis leaflet morphology/motion, providing valuable diagnostic information.

Keywords Aortic stenosis • Case report • Computed tomography • Endocarditis • Leaflet thrombosis • Transcatheter aortic valve replacement/implantation

Learning points

- Transcatheter aortic valve replacement (TAVR) infective endocarditis is rare and most commonly involves the Enterococcus species.
- Leaflet thrombosis (LT) imaging with echocardiography may be less accurate due to prostheses artefacts.
- Four-dimensional computed tomography provides an accurate assessment of LT with TAVR prostheses.
- Anticoagulation with warfarin may successfully reverse LT with TAVR.

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Introduction

Transcatheter aortic valve replacement (TAVR) is an increasingly utilized treatment for severe symptomatic aortic stenosis in intermediate-to-high risk surgical patients.[1] Infective endocarditis (IE) and leaflet thrombosis (LT) are rare complications which may occur following TAVR and may result in significant morbidity and mortality.[2–4] We report a unique case of a patient with TAVR bacterial endocarditis and concurrent LT, where the diagnosis was confirmed on four-dimensional computed tomography (CT).

Timeline

January 2017	• Elective transfemoral transcatheter aortic valve replacement (TAVR)
July 2017	• Routine follow-up transthoracic echocardiogram (TTE) showing satisfactory TAVR prosthesis function (mean gradient 9 mmHg)
5 December 2017	• Emergency Department presentation with fevers, malaise, and shock. • Raised neutrophil count (11.99 × 10^9/L) and C-reactive protein (149 mg/L) • Blood cultures positive for Enterococcus faecium • Commenced on intravenous antibiotics
8 December 2017	• Transthoracic echocardiogram demonstrating increased mean TAVR prosthesis gradient (40 mmHg) with thickened leaflets
12 December 2017	• Transoesophageal echocardiogram demonstrating marked leaflet thickening suggestive of leaflet thrombosis, and a mobile linear echo density suggestive of infective endocarditis • Four-dimensional computed tomography revealed hypo-attenuated leaflet thickening and reduced leaflet motion
13 December 2017	• Rivaroxaban ceased and commenced on warfarin therapy with bridging therapeutic enoxaparin.
28 December 2017	• Transoesophageal echocardiogram showing reduction in aortic bioprosthetic leaflet thickening with improved leaflet motion (mean gradient 20 mmHg)
2 January 2018	• Heart team discussion and decision to treat conservatively
8 January 2018	• Discharged home lifelong warfarin and oral antibiotics
15 January 2018	• Follow-up TTE demonstrating normalization of mean TAVR gradient (5 mmHg)

Case presentation

An 84-year-old man presented with a 3-day history of fevers (38.4°C) and general malaise. He had a transfemoral TAVR (Lotus valve system, Boston Scientific, Boston, MA, USA) for symptomatic severe aortic stenosis with preserved left ventricular function, 11 months prior. His comorbidities included previous coronary stenting, atrial fibrillation, stroke, and hypertension. There were no discernible risk factors for infective endocarditis. His medications included rivaroxaban, bisoprolol, and irbesartan. He presented in shock (blood pressure 70/33 mmHg and heart rate 102 b.p.m.) and was successfully resuscitated with crystalloids. Cardiac examination revealed an ejection systolic murmur without peripheral stigmata of endocarditis.

His initial blood tests revealed neutrophilia 11.99 × 10^9/L (reference range 4.0–11.0 × 10^9/L) and a C-reactive protein of 149 mg/L (reference range 0–5 mg/L). A chest X-ray and urine specimen did not demonstrate any abnormalities. Multiple blood cultures from separate sites were positive for Gram-positive cocci, with intravenous ampicillin and gentamicin being commenced. This later cultured positive for *Enterococcus faecium*, and his antibiotic regimen was changed to intravenous vancomycin and gentamicin once sensitivities returned.

A transthoracic echocardiogram revealed a significant increase in mean TAVR prosthesis gradient from 9 mmHg (at 6 months following TAVR) to 40 mmHg with thickened prosthesis leaflets. A transoesophageal echocardiogram demonstrated a mobile linear echo density on the anterior cusp, strongly suggestive of infective endocarditis. The leaflets appeared abnormally thickened and variegated, though prosthesis shadowing artefact limited accurate assessment (*Figure 1*). Computed tomography imaging (320 slice Aquilion One Vision, Toshiba, Tokyo) was performed to provide further assessment of the leaflet morphology and motion. This revealed features consistent with leaflet thrombosis, exhibiting both hypo-attenuated leaflet thickening (HALT) and reduced leaflet motion (RELM) on four-dimensional images (*Figures 1* and *2*, *Video 1*).

He was commenced on warfarin (target International Normalized Ratio 2.5–3.0), and rivaroxaban was ceased. The heart team deemed he was high risk for aortic valve surgery and a decision was made to manage conservatively as inflammatory markers and repeat cultures confirmed ongoing response to antibiotics. His hospital stay was protracted from complications including decompensated heart failure, renal impairment from sepsis and general deconditioning. Repeat echocardiography revealed a reduction in valve gradient to 20 mmHg after 2 weeks, and normalization of the gradient (5 mmHg) and leaflet morphology after 6 weeks of antibiotics and warfarin therapy (Supplementary material online, *Figure S1*, *Videos 2* and *3*). The patient recovered well and was asymptomatic at 6 weeks of follow-up.

Discussion

Infective endocarditis following TAVR is a rare but life-threatening complication. Younger age with multiple comorbidities, history of diabetes mellitus, and paravalvular regurgitation may account for the higher risk of IE.[4,6,7] Infective endocarditis has an overall incidence of 2.0% in TAVR, which is comparable to surgical AVR (1.3%).[6] Despite the similar incidence, Enterococcus species has been identified as the

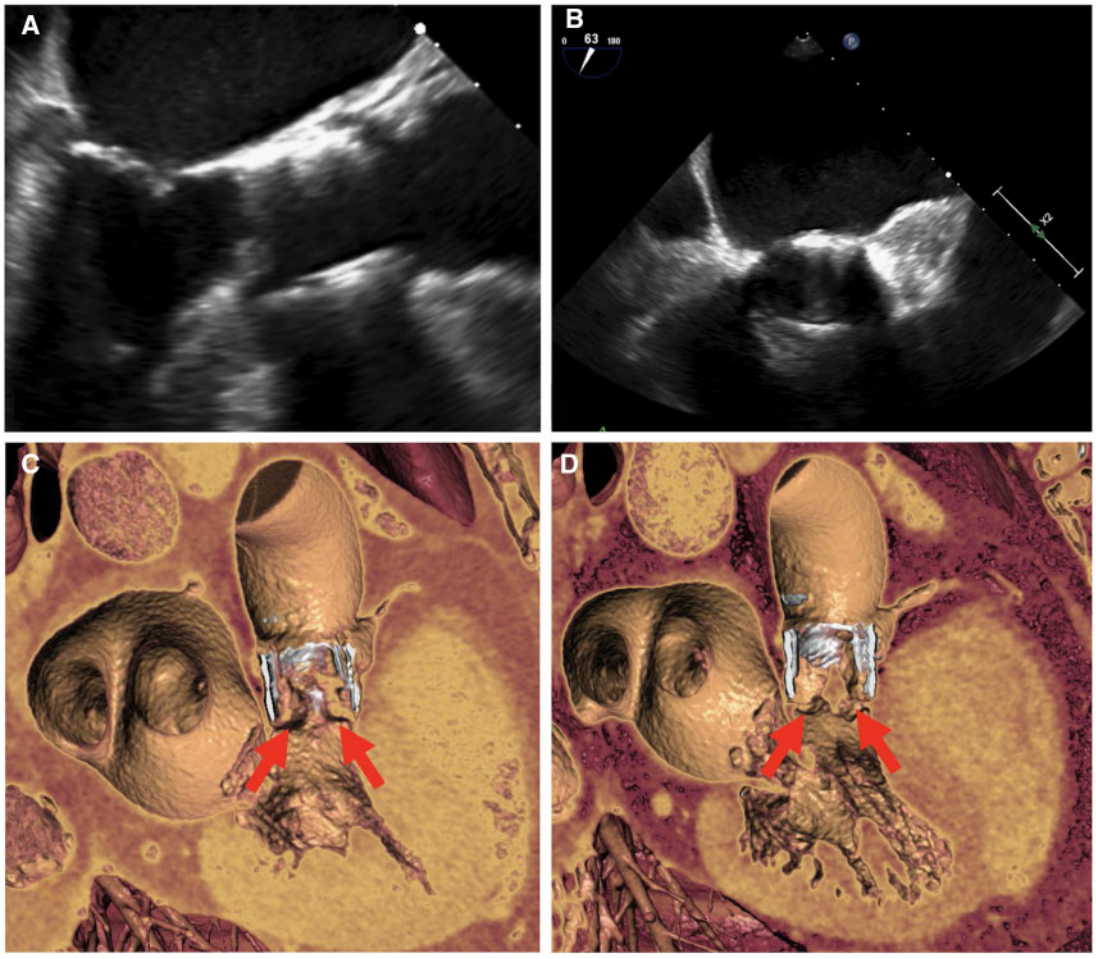
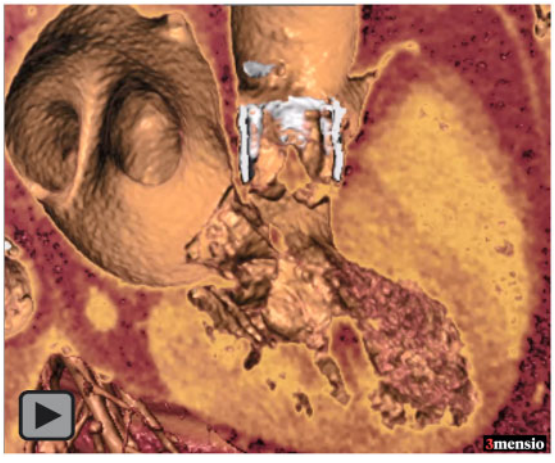
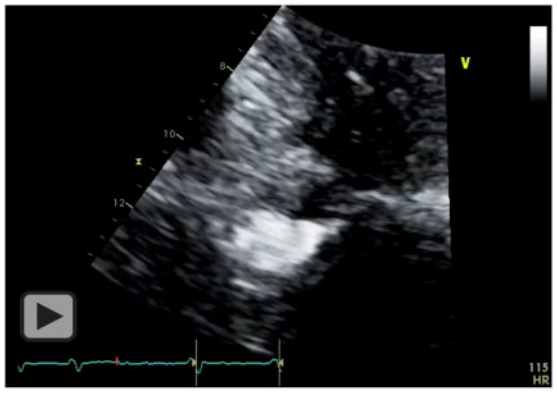


Figure 1 Transoesophageal echocardiography long-axis (*A*) and short-axis (*B*) images of Lotus Valve prosthesis, showing significant prosthesis artefact, limiting visualization of the leaflets, and assessment of leaflet thrombosis. Four-dimensional computed tomography images during systole (*C*) and diastole (*D*) demonstrating hypo-attenuated leaflet thickening (arrows).

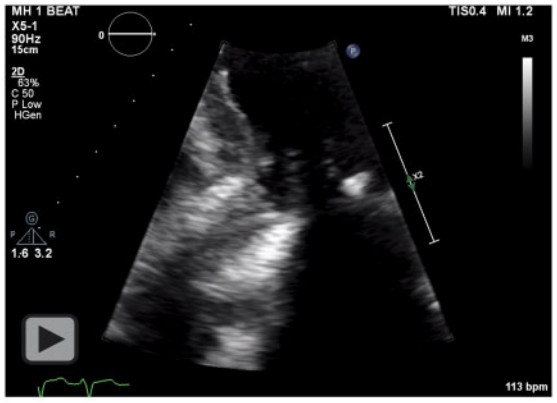
Figure 2 Computed tomography images of Lotus Valve prosthesis demonstrating hypo-attenuated leaflet thickening (arrows) affecting the top left (NR leaflet) and bottom left (LN leaflet) in transverse view and severe reduced leaflet motion (affecting greater than 75% of the leaflet) with sagittal view from leaflet thrombosis. Nomenclature for prosthesis leaflets based on recent classification on prosthesis and native leaflet orientation.[5] LN, left and non-coronary; NR, non-coronary and right.



Video 1 Four-dimensional computed tomography demonstrating leaflet thickening and reduced leaflet motion.



Video 2 Five-chamber transthoracic echocardiography view of prosthetic valve pre-treatment with anticoagulation and antibiotics, showing significant prosthesis artefact, limiting view of leaflet motion and thickness.



Video 3 Five-chamber transthoracic echocardiography view of prosthetic valve after 6 weeks of anticoagulation and antibiotic therapy, demonstrating improved leaflet motion, although prosthesis artefact limits visualization.

major causative microorganism of IE in TAVR as opposed to Staphylococcus species in surgical valves.[6] This may be due to the preference for transfemoral access with TAVR, where Enterococcus species frequently colonize. Transcatheter aortic valve replacement endocarditis is associated with significantly higher rates of mortality and morbidity, including heart failure, acute kidney injury, bleeding, and myocardial infarction.[4]

In addition to appropriate anti-microbial therapy, early surgery should be strongly considered in patients with prosthetic valve endocarditis with high-risk features including severe valve dysfunction, heart failure, abscess, or persistent fever.[8] However, surgical valve explantation is rare, reflecting TAVR patients who are generally of high surgical risk and associated technical challenges with valve retrieval.[7]

Leaflet thrombosis is becoming increasingly recognized following bioprosthetic AVR. It includes a spectrum of conditions ranging from subclinical LT (asymptomatic with normal transvalvular gradients) through to overt clinical LT that is associated with adverse outcomes.[9] Factors increasing the risk of LT include patient factors (hypercoagulability, chronic renal failure), reduced transvalvular flow (impaired left ventricular function), prosthesis factors (large prostheses, intra-annular devices), and lone antiplatelet regimen.[3,10] Although echocardiography has traditionally been the main imaging modality for LT, its ability to define leaflet morphology is limited by prosthesis artefact. Computed tomography has been shown to be an accurate, non-invasive method to assess LT.[11] The hallmark feature of LT on CT is HALT at the prosthesis leaflet cusps, and as the thrombotic burden increases, this may lead to RELM.[5]

The prevalence of CT-defined LT ranges from 7% to 40% depending on the valve system,[11,12] with an overall prevalence reported at 13%.[13] Though the majority of patients with CT-defined LT are asymptomatic, pooled analyses have demonstrated an association between LT and an increased risk of cerebrovascular events, particularly in valves with RELM or a higher degree of thrombotic burden.[9] Subclinical LT may also have the potential to progress and lead to valve dysfunction over time.[2] Though antiplatelet therapy is recommended post-TAVR,[14,15] low bleeding risk patients may be considered for anticoagulation with a vitamin K antagonist (VKA) for at least 3 months following TAVR[15] to reduce the risk of HALT.

A sub-study of the Global Study Comparing a Rivaroxaban-Based Antithrombotic Strategy to an Antiplatelet-Based Strategy after Transcatheter Aortic Valve Replacement to Optimize Clinical Outcomes (GALILEO-4D) demonstrated reduced rates of CT-defined subclinical leaflet motion abnormalities in patients receiving antithrombotic therapy (rivaroxaban 10 mg plus aspirin) compared with antiplatelet-based therapy (clopidogrel 75 mg plus aspirin), with Grade 3 or higher leaflet motion reduction demonstrated (2.1% vs. 10.9%, $P = 0.01$), and thickening of at least one leaflet in 12.4% compared with 32.4% of patients, respectively.[16] However, in the main GALILEO trial, rivaroxaban therapy was associated with a higher risk of death, thrombotic complications, and risk of life-threatening, disabling, or major bleeding, compared with antiplatelet therapy,[17] highlighting the difficulty in identifying the appropriate patient-group for anticoagulation therapy at the present time. In this study, echocardiography was not useful in identifying these valvular abnormalities, further demonstrating the limitations of echocardiography in the assessment of prosthetic leaflet thrombosis.

Conclusion

We present a rare case of concurrent IE and LT following TAVR. With appropriate antimicrobials and commencement of anticoagulation with a VKA, the patient improved with complete normalization of transvalvular gradients. Diagnosis of dual pathologies in this case was critical, as elevated transvalvular gradients on echocardiography could have been attributed to either pathology alone, and without an accurate assessment of the leaflets, one pathology may have remained untreated. Regression of LT is possible with oral anticoagulation; however, appropriate diagnostic imaging is required when there is a strong index of suspicion. This case highlights the crucial role of four-dimensional CT in the diagnosis of LT, which may

provide further evaluation of leaflet morphology in cases where echocardiography is inconclusive.

Lead author biography

Dr Nancy Khav obtained her Bachelor of Medicine/Surgery degree at The University of Melbourne in 2013. She is a cardiology registrar at MonashHeart, Monash Health, Australia, with an interest in cardiac imaging, specifically cardiac computed tomography.

Dr Hashrul Rashid is the interventional fellow at MonashHeart, after completing cardiology training in 2019. He is passionate about cardiovascular research, with almost 25 publications and numerous research awards including TCT Asia Pacific Best Abstract Presenter 2016 and 2018, and Monash Health Best Clinical Research Award 2017. His PhD is titled 'CT-defined leaflet thrombosis following transcatheter aortic valve implantation'.

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 author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidelines.

Conflict of interest: none declared.

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