Midterm Degeneration of Transcatheter Heart Valve Device following Valve-in-Valve Transcatheter Aortic Valve Replacement Requiring Repeat Transcatheter Aortic Valve Replacement

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INTRODUCTION

Transcatheter aortic valve replacement (TAVR) is an alternative therapeutic intervention to surgical aortic valve replacement (SAVR) for patients with severe aortic stenosis (AS).[1] With the broadening of indications for TAVR to include younger and lower-risk patients, the long-term durability of transcatheter heart valves (THVs) has become relevant. For TAVR in native AS, the incidence of THV deterioration requiring SAVR or TAVR-in-TAVR is low[2,3]; however, the long-term durability and outcomes of THV after valve-in-valve (ViV) TAVR for degenerated SAVR is less well defined.[4,5] In this case study, we present an elderly patient with early THV failure 18 months after ViV-TAVR who went on to have a successful TAVR-in-TAVR procedure.

CASE PRESENTATION

An 87-year-old man with a 27 mm bioprosthetic Perimount (Edwards Lifesciences, Irvine, CA) aortic valve replacement (AVR) implanted in 2005 presented acutely to our institute in January 2018 with decompensated heart failure. His past medical history included permanent pacemaker implantation for complete heart block following SAVR, and he had only one functional kidney following a road traffic accident as a child. On examination, chest auscultation was consistent with severe aortic incompetence (AI) and pulmonary edema, with no clinical evidence of right heart overload. At presentation, he had acute kidney injury (urea [Ur] 36.6 mmol/L, creatinine [Cr] 209 umol/L, estimated glomerular filtration rate [eGFR] 29 mL/minute), and his brain natriuretic peptide (BNP) was elevated at 1,485 ng/L (normal $<$ 20 ng/L). Transthoracic echo (TTE; Figure 1) reported a dilated and impaired left ventricle (end-diastolic volume 100 mL/m^2, left ventricular ejection fraction [LVEF] 38%) in the presence of severe transprosthetic AI; the right ventricle was normal in size and function, but there was moderate tricuspid regurgitation and he had significant pulmonary hypertension (pulmonary arterial systolic pressure [PASP] 85 mm Hg).

Transesophageal echo (TEE) confirmed complete degeneration of the noncoronary leaflet of the AVR, severe transvalvular AI, and no evidence of an aortic root fistula or abscess.

The patient was discussed at a Structural Heart Disease Multi-Disciplinary meeting where he was felt to be too high risk for redo-SAVR (European System for Cardiac Operative Risk EuroSCORE II 64%, Society of Thoracic Surgeon Prediction of Mortality score 12.9%) and should be offered ViV-TAVR. The patient therefore underwent a multidetector computerized tomography (MDCT) scan (Figure 2A and 2B) to determine aortic root and coronary anatomy and define TAVR access routes.

The coronaries were reported to contain eccentric plaque (at ostia of left main stem, left anterior descending, circumflex but none thought to be flow limiting) and a large, diffusely diseased, ectatic unobstructed right coronary artery. The patient therefore underwent conventional coronary angiography, which reported diffuse ectasia and moderate coronary disease (Figure 2C and 2D, Videos 1 and 2). However, the contrast load resulted in further deterioration of the patient's clinical condition and renal function (Ur 40.7 mmol/L, Cr 319 umol/L, eGFR 16 mL/minute), and the patient was commenced on hemofiltration to aid management of his fluid balance and pulmonary edema. Given the patient's unstable clinical condition, the heart team felt that coronary intervention was not required at that stage and that he should proceed directly to semiemergent ViV-TAVR. The patient gave his informed consent for the procedure. A 26 mm CoreValve Evolut R device (Medtronic, Minneapolis, MN) was deployed via a left femoral arterial approach (Video 3) using only 25 mL of dilute contrast. Despite several attempts to achieve a supra-annular position, optimal positioning of the THV proved difficult and the THV device was finally deployed suboptimally low in the left ventricular outflow tract (LVOT; Figure 3A and 3B). Nevertheless, the THV was fully expanded (Figure 3C), peak/mean gradients across the THV device were 18/12 mm Hg, respectively (Figure 3D), and periprocedural paravalvular leak (PVL) was judged mild-moderate (Figure 3E and 3F, Video 4). Given the patient's clinical state preprocedure, the deployment result was accepted.

Despite a suboptimal procedure, the patient made a rapid clinical response, hemofiltration was discontinued, and he was discharged back to his home 4 days after his ViV-TAVR procedure, in New York Heart Association class II and independent of activities of daily living. On discharge, his renal function had improved (Ur 12.6 mmol/L, CR 162 umol/L, eGFR 35 mL/minute) and his BNP had decreased to 478 ng/L. On discharge TTE, LVEF was 36%, peak/mean gradients across the THV device were 18/10 mm Hg, respectively, mild PVL was reported (Video 5), mitral and tricuspid regurgitation both reduced in severity to mild, and PASP had

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VIDEO HIGHLIGHTS

Video 1: Right coronary angiogram.
Video 2: Left coronary angiogram.
Video 3: Initial ViV-TAVR.
Video 4: Mild-moderate PVL.
Video 5: Mild paravalvular leak on discharge echo.
Video 6: Severe transvalvular AI 18-months after ViV TAVR.
Video 7: TAVR-in-TAVR.

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decreased to 49 mm Hg. His discharge medications included aspirin, bumetanide, and bisoprolol. At 6-week follow-up, candesartan was re-introduced, and although consideration was given to upgrade the patient's permanent pacemaker to a cardiac resynchronization device, this was not performed as 6-month follow-up TTE documented LVEF of 49%.

Eighteen months after ViV-TAVR, the patient presented acutely again in decompensated heart failure and on examination, chest auscultation was consistent with severe AI and pulmonary edema. Biochemical testing reported acute on chronic kidney derangement (Ur 29.6 mmol/L, Cr 147 umol/L, eGFR 39 mL/minute), and BNP had increased to 2,003 ng/L. An urgent TEE was performed, which demonstrated a low-lying THV device: on detailed assessment it

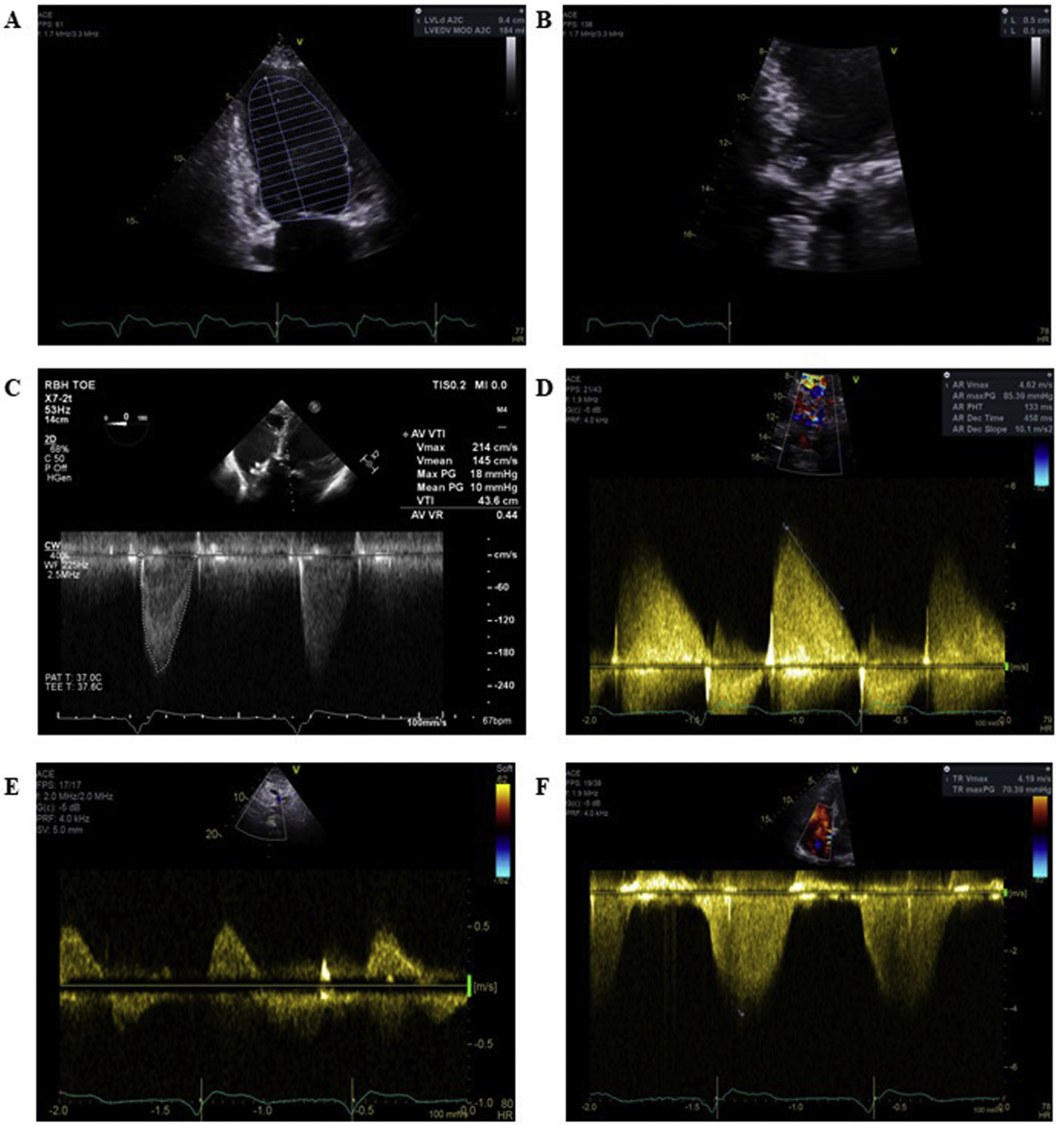

Figure 1 TTE 13 years after AVR showing a dilated left ventricle **(A)**, degenerate aortic valve **(B)**, mean forward pressure gradient of 10 mm Hg **(C)**, severe AI with pressure half-time 133 msec **(D)**, flow reversal in abdominal aorta **(E)**, and significant pulmonary hypertension **(F)**.

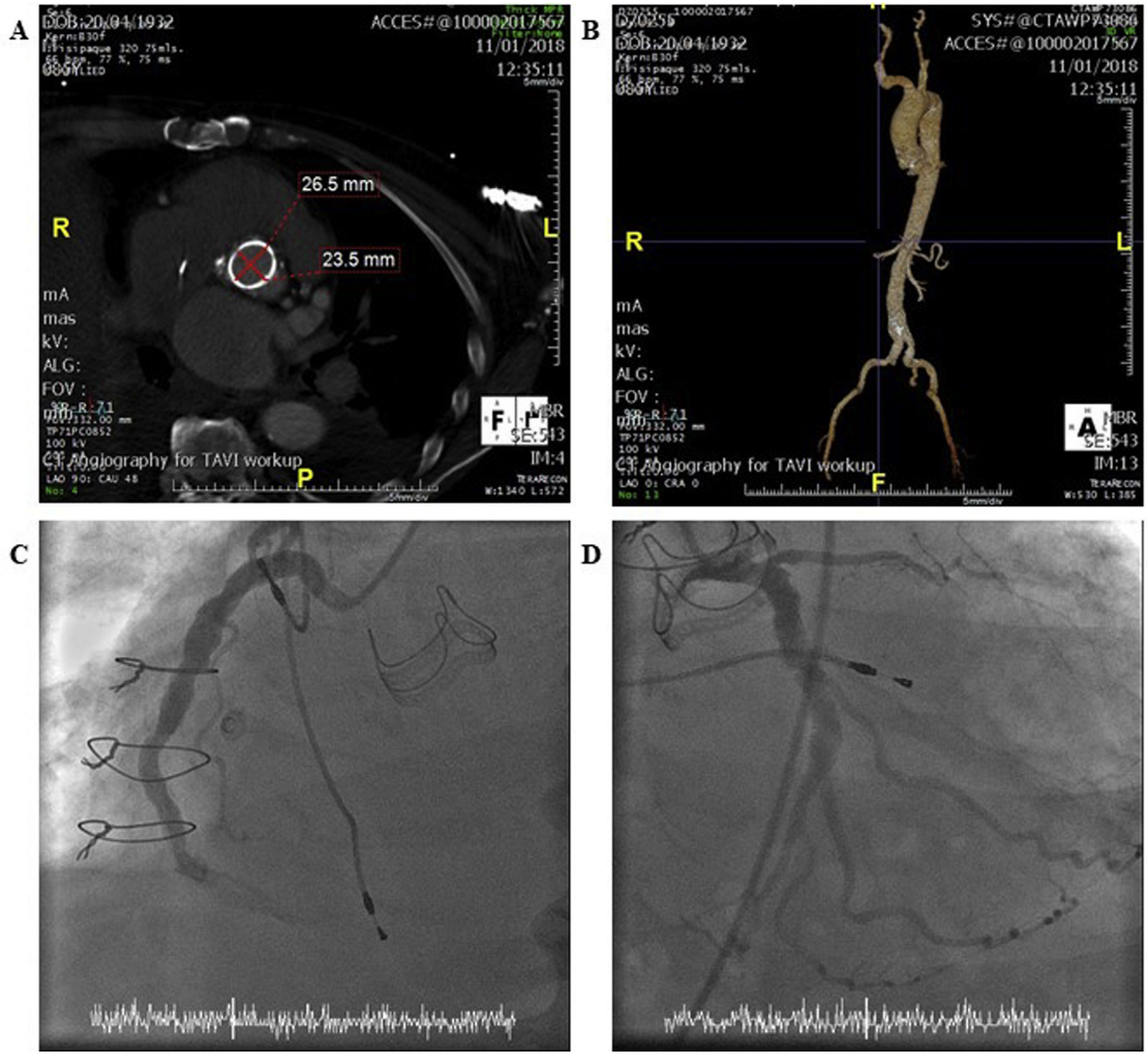

Figure 2 MDCT scan showing the noncircular shape of the surgical aortic valve bioprosthesis **(A)** and tortuous but adequate caliber iliac and femoral arterial access routes for TAVR **(B)**. On coronary angiography, the patient had a diffusely diseased right coronary artery **(C)** and eccentric plaque of the left anterior descending and circumflex ostia **(D)**, but neither were felt to be flow limiting.

was confirmed that the THV device had migrated down the LVOT by 5 mm since the initial ViV-TAVR (Figure 4A and 4B). The THV device was trileaflet with no evidence of neoleaflet fracture (Figure 4C). There was new severe transvalvular AI (Figure 4D, Video 6) and moderate posterior PVL (Figure 4D); concurrent TTE reported LVEF 30%, moderate secondary mitral regurgitation (Figure 4E), right ventricle impairment, moderate tricuspid regurgitation, and significant pulmonary hypertension (PASP 70 mm Hg, Figure 4F).

A repeat coronary angiogram reported no significant changes from 2018: there were diffusely ectatic vessels but no flow-limiting coronary disease. Once again following coronary angiography, the patient's renal function deteriorated (Ur and Cr 31.8 mmol/L and 215 umol/L and eGFR 25 mL/minute).

The patient was rediscussed at a Structural Heart Disease Multi-Disciplinary meeting where again he was felt too high risk for redo-SAVR and should undergo urgent TAVR-in-TAVR. The patient already had a significant acute kidney injury, and to avoid further deterioration in renal function and repeat requirement for hemofiltration, the group felt that the heart team had enough information on TAVR access routes and position of the coronary ostia in the aortic root from the previous MDCT. However, without a repeat MDCT, there was no preprocedural information on the position of the coronary ostia relative to the THV leaflets. Since the patient had significant biventricular impairment, severe AI and significant mitral regurgitation, and pulmonary hypertension, and to provide support in the event of coronary arterial obstruction, the heart team recommended that the TAVR-in-TAVR procedure should be performed during a brief period of cardiopulmonary bypass. The patient again gave his informed consent for the procedure.

Under general anesthesia, access to the left coronary artery was achieved (Figure 5A), and a Sion blue protective coronary wire with a 2.5 mm * 1.5 mm Emerge balloon were placed in the left anterior

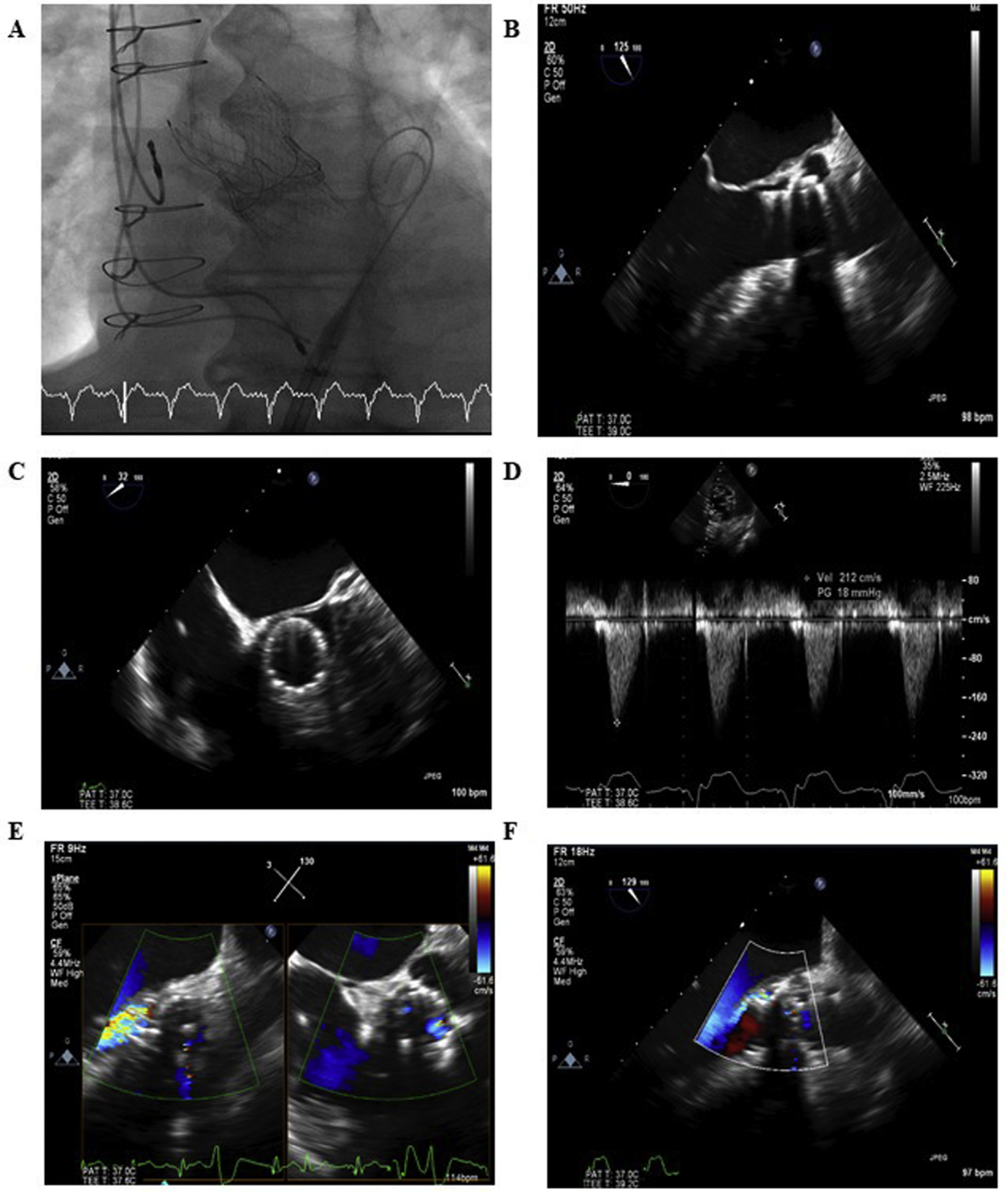

Figure 3 A 26 mm CoreValve Evolut R device deployed low within the failing Perimount aortic valve bioprosthesis on fluoroscopy **(A)** and TOE **(B)**. The THV device was fully expanded **(C)**, and peak THV gradient was 18 mm Hg **(D)**. Two jets of PVL (judged overall to be mild-moderate) were noted **(E** and **F**; the pixel of color within the THV device was associated with a wire across the THV device).

descending coronary artery (Figure 5B) and left in situ for the duration of the procedure. Under femoral-femoral bypass, a 26 mm Edwards Sapien 3 (Edwards Lifesciences, Irvine, CA) was implanted under rapid ventricular pacing via a right transfemoral approach (Figure 5C). Although well positioned, the second TAVR device was constrained within the leaflets of the initial THV device, so was post-dilated with a 25 mm True balloon under rapid ventricular pacing (Figure 5D), following which there was a pleasing angiographic result, with no evidence of coronary obstruction or paravalvular leak on check aortography (Video 7).

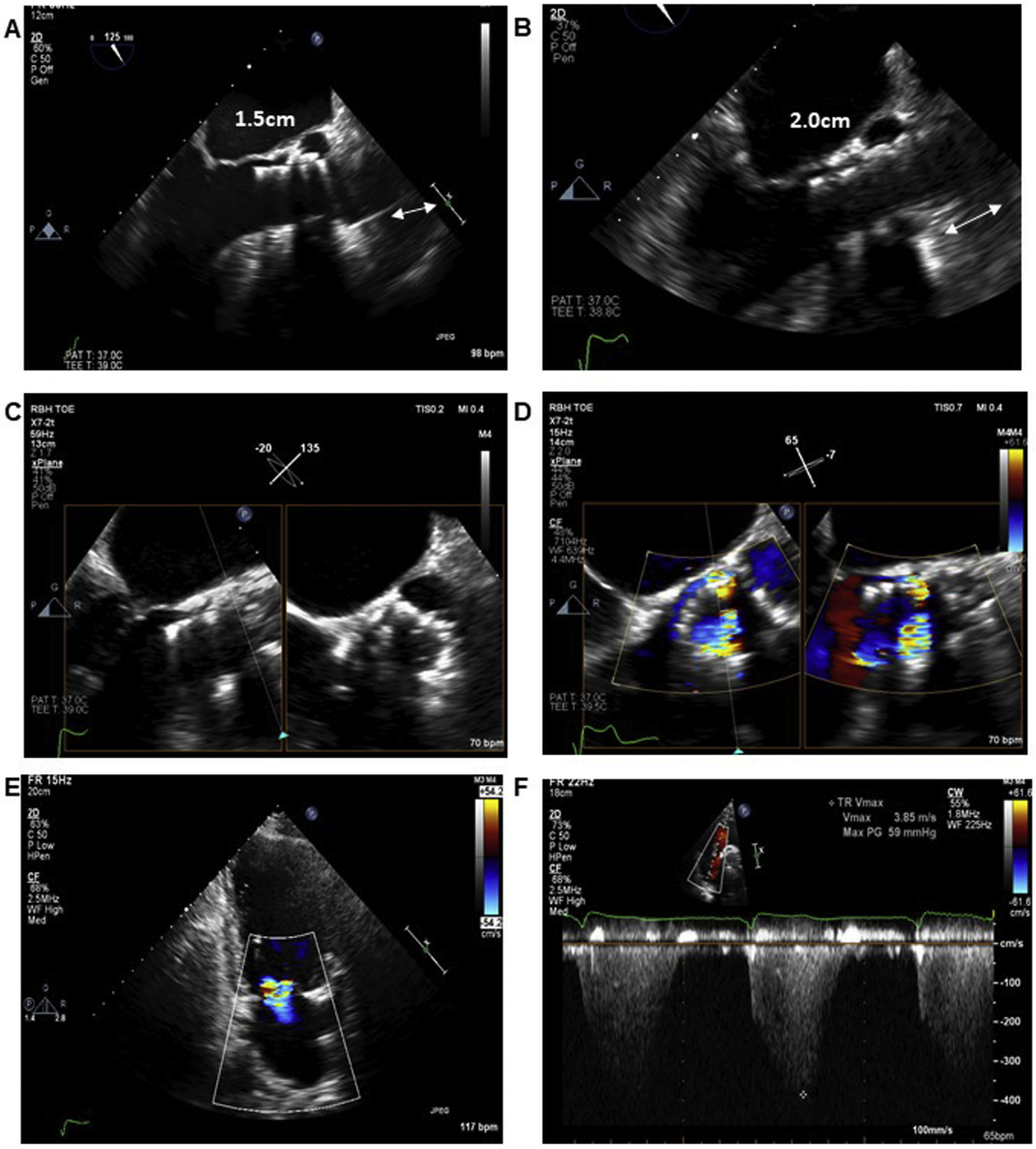

Figure 4 Eighteen months after ViV-TAVR, TOE demonstrated a low-lying CoreValve with migration further into the LVOT by 5 mm **(A** and **B**; *double-sided arrows* depicting length from aortic annulus to ventricular end of TAVR device**)**, three THV leaflets with no evidence of leaflet fracture **(C)**, new severe transvalvular AI, and moderate posterior PVL **(D)**. Concurrent TTE demonstrated a dilated and impaired LV with moderate mitral regurgitation **(E)** and significant pulmonary hypertension **(F)**.

The patient again made a rapid clinical response after TAVR-in-TAVR, and he was discharged back to his home 8 days after the TAVR-in-TAVR procedure, in New York Heart Association class II. On discharge, renal function had improved (Ur 12.1 mmol/L, Cr 125 umol/L, eGFR 47 mL/minute) and BNP had decreased to 1,582 ng/L. His discharge TTE reported LVEF 37%, peak/mean gradients across the THV device of 16/8 mm Hg, respectively; there was no PVL, mitral and tricuspid regurgitation both reduced in severity to mild, and PASP had decreased to 50 mm Hg (Figure 6). He was initiated on warfarin (with a target international normalized ratio of 2.5-3.0), and his other discharge medications included aspirin, bumetanide, and bisoprolol. At 2-month follow-up, renal function was stable, BNP had decreased further to 896 ng/L, LVEF was 42%, peak/mean gradients across the THV device were 26/13 mm Hg respectively, there was no PVL, mitral and tricuspid regurgitation were both mild, and PASP had decreased to 45 mm Hg.

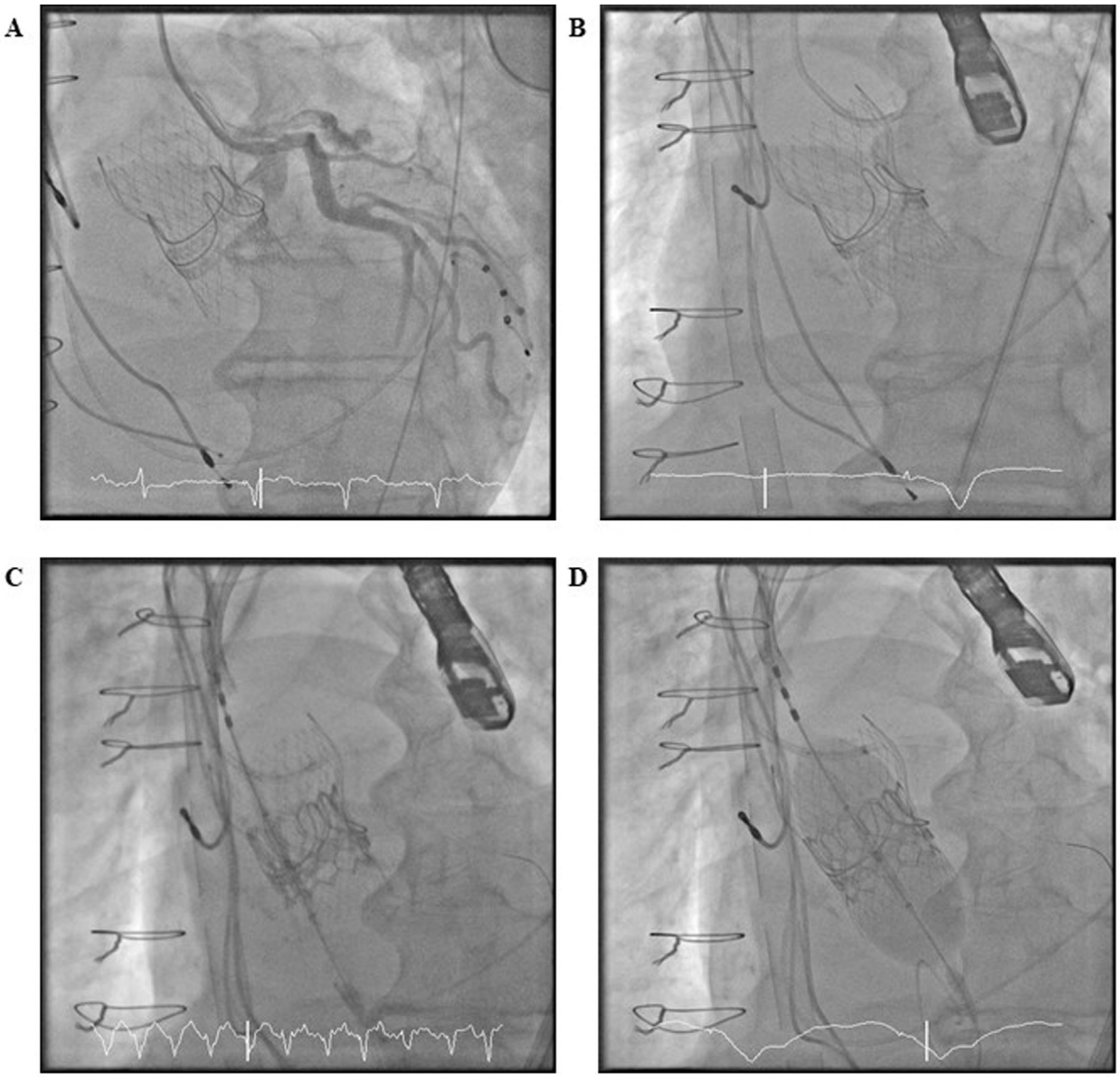

Figure 5 Immediately prior to TAVR-in-TAVR, access to the left coronary artery was achieved **(A)**, and a protective coronary wire and balloon was placed in the left anterior descending coronary artery **(B)**. Under femoral bypass, a 26 mm Edwards Sapien 3 was implanted **(C),** which required postdilatation femoral **(D)** to achieve a good result.

DISCUSSION

With increasing numbers of patients undergoing ViV-TAVR for degenerate SAVR, the long-term durability of THV has become an important clinical issue. Standardization of the definition of structural valve deterioration has permitted evaluation of THV durability with validated comparable endpoints.[6] Using such criteria, studies reporting on structural valve dysfunction after TAVR have described low rates of THV deterioration requiring a TAVR-in-TAVR procedure during follow-up of between 0.4% and 3.3%.[3,7-9] However, the most common indication for TAVR-in-TAVR is to correct significant PVL rather than THV degeneration per se. In the case presented, we safely and successfully performed a TAVR-in-TAVR 18 months after a ViV-TAVR for a degenerate stented AVR.

Potential causes for early THV deterioration include infective endocarditis (but there was no clinical or biochemical evidence of infection in our patient), fractured leaflet, thrombus or pannus formation (but we elected not to perform a repeat MDCT scan that might have elucidated THV leaflet pathology due to the patient's extremely brittle renal function), suboptimal position of the initial ViV-TAVR THV device, underexpansion of the initial ViV-TAVR THV device, or device migration. In our patient, the initial ViV-TAVR THV appeared well expanded but was suboptimally deployed somewhat low in the LVOT. Intra-annular rather than supra-annular CoreValve leaflets within the SAVR annulus may have resulted in constraining forces on the THV leaflets, leading to earlier degeneration than might otherwise have otherwise been expected.[10] Furthermore, the position of the waist of the THV device at the level of the sewing ring of the failing SAVR meant that there would have been less radial expansive force

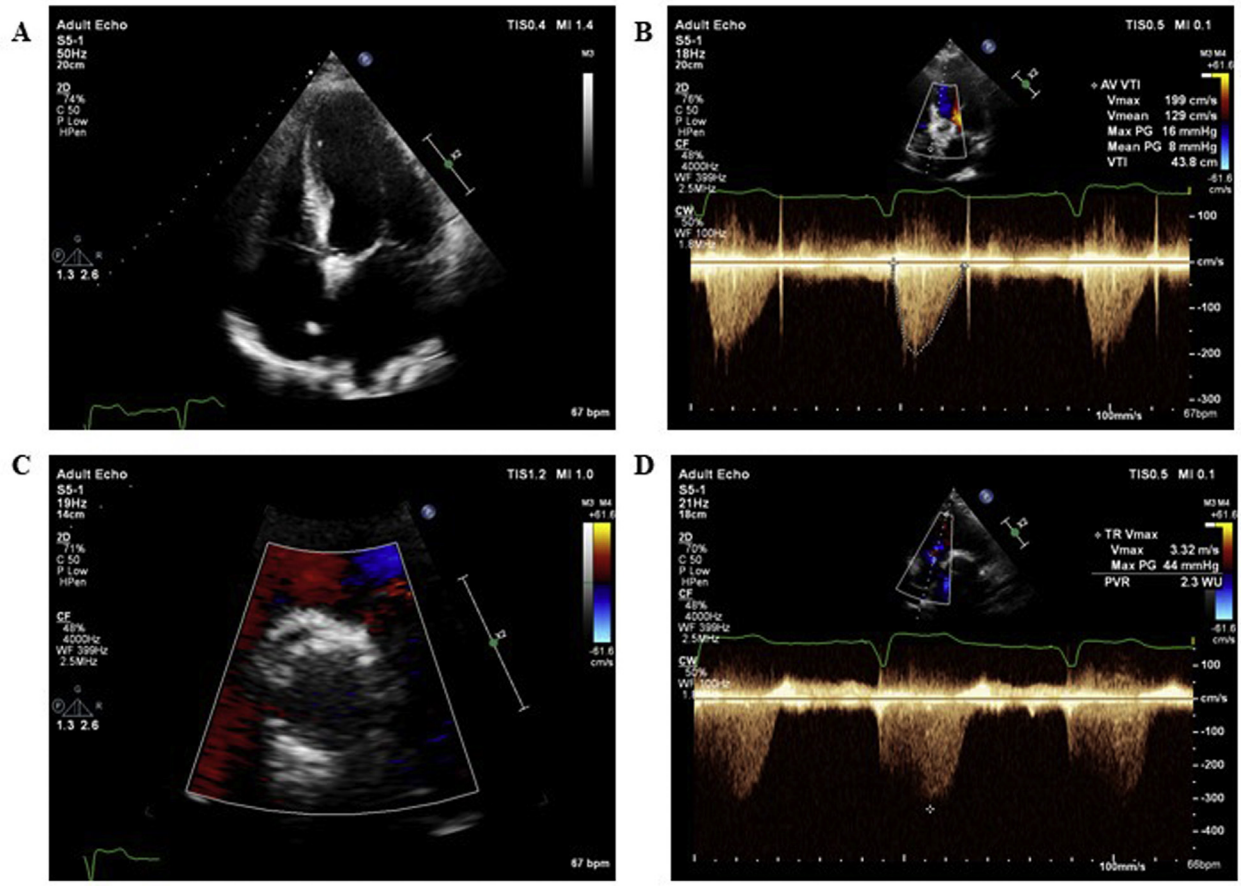

Figure 6 On discharge, LVEF was 37% **(A)**, peak THV gradient was 16 mm Hg **(B)**, there was no PVL or transprosthetic AR **(C)**, and PASP had decreased to 50 mm Hg **(D)**.

against the SAVR than would have been provided by the inflow of the device had the THV device been implanted higher in the LVOT. The subsequent device migration may have been a secondary contributing factor to early device failure.

A major concern for patients undergoing TAVR-in-TAVR is the potential for causing coronary ostial obstruction, since both the native aortic valve leaflets *and* the THV leaflets might act as potential causes of coronary obstruction if they face the coronary ostial orifices. Our patient did not have a MDCT prior to TAVR-in-TAVR due to very brittle renal function, and therefore we could not confirm the anatomy of the coronary ostia in relation to the THV leaflets. However, there is currently no predictable mechanism to align TAVR-in-TAVR neocommissures with either the native or the ViV-TAVR commissures even if this anatomy were known. In ViV-TAVR procedures, coronary protection or techniques such as BASILICA leaflet splitting have been advocated to reduce the risk of coronary obstruction.[11] After extensive discussion with our Structural Heart Team, we chose a low-profile Edwards Sapien TAVR-in-TAVR device that might potentially facilitate easier access to the coronary arteries following the procedure, and during the procedure we protected access to the native left coronary by placing a coronary balloon and wire system into the left anterior descending artery while deploying the TAVR-in-TAVR device during a short period of cardiopulmonary bypass to support the circulation should coronary obstruction have occurred.

Our patient was taking a single antiplatelet agent and no anticoagulant agent in the 18 months following his ViV-TAVR. Given recent thrombosis reports after ViV-TAVR,[12] we have adopted a pragmatic approach of initiating warfarin in patients undergoing ViV-TAVR in the absence of contraindications to anticoagulation. Following TAVR-in-TAVR after ViV-TAVR, there is perhaps even more reason to do so, especially in patients with a low cardiac output state, due to increased risk of stasis between the AVR and two implanted THV devices. However, an "anticoagulation for all" approach should be approached with caution in patients without an established indication for oral anticoagulation, as administration of antithrombotic strategy may reduce the risk of thromboembolic complications after TAVR but is associated with a higher risk of death and thromboembolic complications.[13]

CONCLUSION

Valve-in-valve transcatheter aortic valve implantation is an excellent therapeutic intervention for patients with a degenerated SAVR, but long-term durability depends on optimal transcatheter device placement. Complications of performing a TAVR-in-TAVR procedure in a patient who has already undergonr SAVR include limitation to the coronary ostia, patient-prosthesis mismatch, and the potential increased risk of device thrombosis.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2020.04.008.

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