TAVI Failure: A Systematic Review

Transcatheter heart valve failure: a systematic review

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ABSTRACT

Aims

A comprehensive description of transcatheter heart valve (THV) failure has not been performed. We undertook a systematic review to investigate the aetiology, diagnosis, management, and outcomes of THV failure.

Methods and results

The systematic review was performed in accordance with the PRISMA guidelines using EMBASE, MEDLINE, and Scopus. Between December 2002 and March 2014, 70 publications reported 87 individual cases of transcatheter aortic valve implantation (TAVI) failure. Similar to surgical bioprosthetic heart valve failure, we observed cases of prosthetic valve endocarditis (PVE) (n = 34), structural valve failure (n = 13), and THV thrombosis (n = 15). The microbiological profile of THV PVE was similar to surgical PVE, though one-quarter had satellite mitral valve endocarditis, and surgical intervention was required in 40% (75% survival). Structural valve failure occurred most frequently due to leaflet calcification and was predominantly treated by redo-THV (60%). Transcatheter heart valve thrombosis occurred at a mean 9 + 7 months post-implantation and was successfully treated by prolonged anticoagulation in three-quarters of cases. Two novel causes of THV failure were identified: late THV embolization (n = 18); and THV compression (n = 7) following cardiopulmonary resuscitation (CPR). These failure modes have not been reported in the surgical literature. Potential risk factors for late THV embolization include low prosthesis implantation, THV undersizing/underexpansion, bicuspid, and non-calcified anatomy. Transcatheter heart valve embolization mandated surgery in 80% of patients. Transcatheter heart valve compression was noted at post-mortem in most cases

Conclusion

Transcatheter heart valves are susceptible to failure modes typical to those of surgical bioprostheses and unique to their specific design. Transcatheter heart valve compression and late embolization represent complications previously unreported in the surgical literature.

Keywords: Aortic stenosis, Transcatheter aortic valve implantation, Transcatheter heart valve failure, Prosthetic valve endocarditis, Heart valve failure

INTRODUCTION

Transcatheter aortic valve implantation (TAVI) is a rapidly proliferating technology with the potential to become the dominant treatment strategy for aortic valve stenosis in patients at excessive- or high-operative risk.[1] Improving procedural safety and promising medium-term clinical efficacy have encouraged the application of transcatheter heart valve (THV) technology to lower risk cohorts.[2–5] In this context, understanding the modes of THV failure and demonstrating valve durability and long-term clinical efficacy are of vital importance.

It is estimated that ~200 000 patients worldwide undergo surgical aortic valve replacement (SAVR) annualy.[6] Bioprosthetic surgical heart valves are the most frequently implanted prostheses, especially in older patients, despite the potential for these valves to fail.[7] Avariety of failure modes have been described for surgical bioprostheses, including infective endocarditis (IE), thrombosis, and structural valve failure (SVF) (degeneration of bioprosthetic tissue or stent de-formation). Surgical bioprosthetic failure has been clearly described and quantified,[8,9] while in contrast, a systematic description of THV failure has not been performed.

We sought to describe the clinical characteristics, failure modes, and outcomes of THV failure by performing a systematic review of the published literature addressing this important subject.

METHODS

This systematic review was performed in accordance with the PRISMA guidelines.[10] We conducted an independent review of citations from EMBASE, Google Scholar, MEDLINE, and Scopus between December 2002 and March 2014. All published studies in English reporting patient-level data on THV failure were identified. Two authors (D.M. and A.A.) screened the title and/or abstract for suitability, and then examined, in detail, all potentially suitable manuscripts to finalise eligibility. Uncertainties were resolved by discussion with another reviewer (N.P.). Each publication was reviewed and in cases of duplication, only the most complete report was included. The citation lists of included articles were examined for further relevant publications. The following combined keywords were used: transcatheter aortic valve or THV or percutaneous valve and IE, abscess, complication, embolization, migration, malposition, valve failure, restenosis, cardiopulmonary resuscitation (CPR), chest compression, deformation, thrombosis, occlusion, and explant.

Published studies meeting the following criteria were included in the study: (i) case reports and series detailing individual causes of post-procedural TAVI failure; (ii) large registries and randomized controlled trials detailing specific incidences of TAVI failure, where sufficient patient-level detail is provided (failure mode, and/or presentation, and/or diagnosis, management, and outcome). Studies describing only an incidence of TAVI failure without specific case detail were excluded.

Definitions

Prosthetic valve endocarditis (PVE) was defined according to the updated Valve Academic Research Consortium (VARC) criteria,[11] and was classified as possible or definite according to the modified Duke criteria.[12] Transcatheter heart valve embolization represents an SVF occurring when the forces acting on the valve frame overcome the strength of the valve's attachment to the native aortic annulus.[13] Late THV embolization may be defined as valve migration after a successful TAVI procedure where further THV-related intervention is not envisaged. Transcatheter heart valve SVF was defined according to the updated VARC criteria:[11] valve-related dysfunction demonstrated by a mean aortic valve gradient ≥20 mmHg, an effective orifice area of ≤0.9 (BSA ≥ 1.6 cm^2) to 1.1 cm^2 (BSA ≤ 1.6 cm^2) and/or a Doppler velocity index ≤ 0.35, and/or moderate or severe prosthetic valve regurgitation (regurgitant volume . 30 mL, regurgitant fraction . 30%, effective regurgitant orifice area .0.10 cm^2), or the requirement for a repeat procedure (TAVI or SAVR). We defined THV compression as distortion of the valve on non-invasive imaging or at autopsy, potentially impairing valve function or necessitating further intervention. Compression had to be temporally related to chest wall trauma or CPR. Transcatheter heart valve thrombosis was defined according to the updated VARC criteria:[11] non-infective thrombus attached to the valve leaflets or frame that impedes blood flow, valve function, or is sufficiently large to require treatment.

Statistics

Categorical variables were reported as number (%), and continuous variables were reported as mean and SD or median and interquartile range, according to distribution. Analyses were performed with SPSS version 17.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

The initial literature search identified a total of 2400 publications (*Figure 1*). Removal of non-pertinent studies and duplicates by title screening yielded 82 potentially relevant articles that were examined in detail. Finally, 70 publications fulfilled our study inclusion and exclusion criteria, and reported 87 individual cases of THV failure (*Figure 2*). All studies discussed single case reports or small series and the baseline characteristics of these patients were typical of On average, late THV embolization occurred 43 + 41 days (range: 4 h to 370 days) after the index procedure. Valve embolization was retrograde into the left ventricular outflow tract (LVOT) in 16 (89%) cases and anterograde into the aorta in 2 (11%).

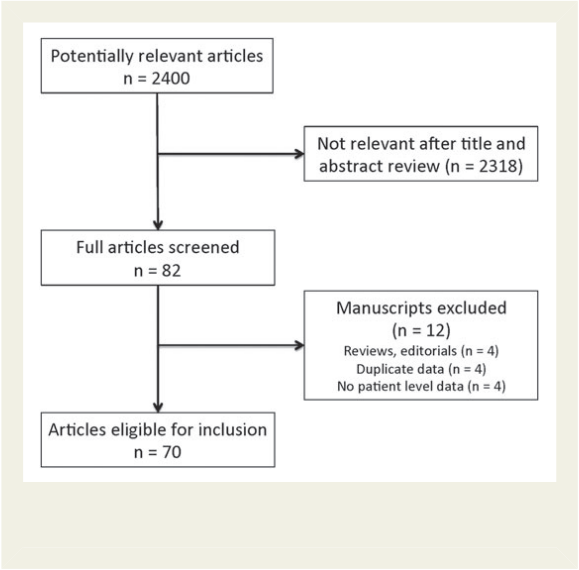

Figure 1 Electronic literature search. Summary of the literature search results.

Transcatheter heart valve-prosthetic valve endocarditis

A total of 26 publications, describing 34 cases of THV PVE were identified (*Table 1*).[17–42] Among these patients, the median age was 83 (77, 85) years and most (n = 20, 59%) presented risk factors predisposing to PVE: diabetes mellitus (n = 10), chronic kidney disease (n = 12), immunosuppression (n = 2), and recurrent infections (n = 4). Several factors may have con-

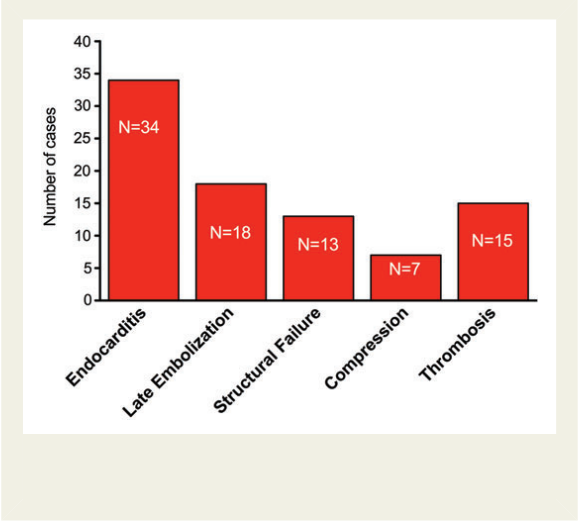

Figure 2 Transcatheter heart valve failure. Aetiology of transcatheter heart valve failure in this systematic review. the elderly high-risk cohorts undergoing TAVI in previously reported [14–16] large registries.

tributed to the development of PVE, including suboptimal THV positioning causing injury to the anterior mitral valve leaflet,[17,18,40] failure to administer antibiotic prophylaxis prior to TAVI (n = 1) or dental (n = 3) procedures.

There were 29 (85%) cases of definite and 5 (15%) cases of possible PVE according to the modified Duke criteria. The median time to IE diagnosis was 6 (3, 12) months, with early (<60 days), intermediate (60 days to 1 year), and late (>1 year) IE classified in 6 (18%), 21 (62%), and 7 (20%) patients, respectively. Cases of PVE were noted with both the Edwards SAPIEN (Edwards Lifesciences Inc., Irvine, CA, USA) (n = 20, 59%) and Medtronic CoreValve (Medtronic Inc., Minneapolis, MN, USA) (n = 14, 41%) prostheses. Similar numbers of PVE cases were observed with transfemoral and transapical vascular access (both n = 12). A total of 27 patients had positive blood cultures with a microbiological profile typical to that previously documented in surgical bioprosthetic PVE: *Enterococcus* species (n = 10), coagulase-negative *Staphylococci* (n = 5), *Staphylococcus aureus* (n = 3), *Streptococcus* species (n = 5), and *Histoplasma capsulatum* (n = 1). Three patients were culture negative and blood cultures were not performed in two cases. Echocardiography demonstrated mobile vegetations or abscess formation in 18 patients, progressive THV stenosis/regurgitation in 3 cases, and was reportedly normal in 3 patients. Abscess formation was described in 8 cases: aortic root (n = 3), aortic sinus (n = 2), annular (n = 1), and paravalvular (n = 2). Interestingly, 'bridging' endocarditis between the aortic THV and a satellite infection on the mitral valve was noted in 8 (24%) patients.

Treatment options for PVE include targeted antibiotic therapy or surgical intervention. In the current series, 20 (59%) patients were treated medically (7 died in-hospital, 13 discharged home [1 death at 3 months with sepsis, 6 alive at 1 year, 6 further outcome unknown), and 14 (41%) underwent surgical intervention (3 died, 9 discharged home, 2 outcome unknown). Surgical intervention consisted of THV retrieval and SAVR (n = 13), with concomitant aortic root replacement (n = 2), mitral or tricuspid repair/replacement (n = 5).

Discussion: prosthetic valve endocarditis

The incidence of surgical PVE is estimated at 0.3–1.2% per patient-year.[12] To date, the incidence of early THV PVE has been reported to be between 0.3 and 3.4%.[5,28,43] Amongst 180 consecutive TAVI recipients (median follow-up 319 days), Puls *et al.* observed five cases of PVE, thus yielding an incidence rate of 3.4% at 1-year.[28] Direct comparisons between these rates may be misleading given the complexity of patients undergoing TAVI and heterogeneity in reporting styles. In the PARTNER (Placement of Aortic Transcatheter Valves) trial (Cohort A), PVE occurred at a similar rate in the surgical and transcatheter groups (1.5 and 1.0%, respectively, P = 0.61).[5] The incidence of PVE mayalso be influenced by patient risk profile and behaviour: diabetes mellitus, oral hygiene, and adherence to antibiotic prophylaxis.[44] Physician behaviour, and in particular adherence to recommendations regarding antibiotic

Table 1 Infective Endocarditis

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing and IE classification	Case description
Wong *et al.*[17]	88-year-old male, STS 11.1%; IE risks: Dental procedure 6 weeks earlier: no endocarditis prophylaxis; CKD	26 mm Edwards SAPIEN	Low implant with the THV abutting the anterior mitral valve leaflet; repeated PID; final moderate PVL	11 months Definite IE	Presentation: Fever. Blood culture: *Streptococcus angiosus*. Imaging: Mild–moderate PVL; ruptured anterior mitral valve leaflet aneurysm (13 × 8 mm) contiguous with THV causing severe MR. Treatment: THV retrieval and SAVR; repair of mitral valve perforation with bovine pericardium. Note: Pathology confirmed THV endocarditis. Outcome: Discharged day 38
Comoglio *et al.*[18]	66-year-old male; EF 60%. IE risks: Myelodysplasia	Transfemoral; 29 mm CoreValve	PID for moderate PVL; final mild–moderate PVL; post-TAVI ventricular arrhythmias; ICD implant	3 months Definite IE	Presentation: Progressive malaise; fever and rigours. Blood culture: *Corynebacterium*. Imaging: Possible posterior aortic annulus. Pseudoaneurysm; moderate AR; anterior mitral valve leaflet perforation and severe MR. Treatment: THV retrieval and SAVR; repair of mitral valve perforation with bovine pericardial patch. Note: Small THV vegetations on cusps. THV 5 cm into LVOT abutting anterior mitral valve leaflet. Outcome: Discharged day 7
Carnero-Alcazar *et al.*[19]	83-year-old female; low EF. IE risks: Recurrent urinary tract infections; CKD	Transapical; 23 mm Edwards SAPIEN	Uneventful	3 months Definite IE	Presentation: Acute CHF; fever. Blood culture: *Enterococcus faecalis*. Imaging: 1.9 cm vegetation on aortic side of THV leaflet. Treatment: Antibiotic therapy; declined for surgery. Note: Autopsy confirmed vegetation occluding valve orifice and an LVOT to right atrium fistula. Outcome: Multiple peripheral emboli and refractory heart failure; died day 14

Table 1 Infective Endocarditis (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing and IE classification	Case description
Santos *et al.*[20]	91-year-old male. IE risks: CKD	Transapical; 23 mm Edwards SAPIEN	Uneventful; no PVL	Index hospitalization Definite IE	Presentation: Fever. Blood culture: *Candida albicans.* Imaging: Mild PVL; mild AS (PG/MG 20/10 mmHg). No vegetations seen. Treatment: Antifungal therapy. Note: Autopsy showed large polypous friable vegetations completely occupying a pericardial cusp and extending along aortomitral continuity. Outcome: Deceased day 54
Gotzmann *et al.*[21]	81-year-old male; LES 39.7%; low EF. IE risks: CKD	Transfemoral; 29 mm CoreValve	Uneventful; mild PVL	19 months Definite IE	Presentation: CHF; fever. Blood culture: *Staphylococcus lugdunesis.* Imaging: Imaging: PVL; large (8 × 16 mm) mobile vegetation on the THV frame with fistulae to right and left atria. Treatment: Antibiotic therapy; declined for surgery. Outcome: Deceased day 13
Head *et al.*[22]	78-year-old male; STS 10.3%. IE risks: N/A	Edwards SAPIEN	N/A	12 months Definite IE	Presentation: Fever (6 months post-TAVI). Blood culture: Negative. Imaging: Extensive large vegetations on THV. Treatment: THV retrieval and SAVR. Note: Large vegetations on left and right commissures extending into LVOT. THV culture positive for *Histoplasma capsulatum.* Outcome: Discharged day 10

Table 1 Infective Endocarditis (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing and IE classification	Case description
Chrissoheris *et al.*[23]	84-year-old male; LES 23.5%; AVA 0.7 cm^2; MG 64 mmHg. IE risks: Recrimping of THV; chronic pancreatitis	Transfemoral; 29 mm CoreValve	Difficult THV positioning requiring recrimping of THV twice; mild–moderate PVL	2.5 months Possible IE	Presentation: Sepsis syndrome. Blood culture: *Staphylococcus epidermidis*. Imaging: No clear evidence of IE. Treatment: Antibiotics for 4 weeks. Outcome: Well at 12-month follow-up
Rafiq *et al.*[24]	64-year-old female; IE risks: Myasthenia gravis on immunosuppression; no pre-TAVI antibiotic prophylaxis	CoreValve	Uneventful; IE prophylaxis	2 months Possible IE	Presentation: Fever, malaise. Blood culture: *Moraxella nonliquefaciens*. Imaging: Echo-free space within wall of ascending aorta at level of THV. No vegetations visualized. Treatment: Antibiotic therapy. Outcome: Well at 3-year follow-up
Castiglioni *et al.*[25]	73-year-old male; LES 6.6%; AVA 0.9 cm^2; MG 78 mmHg; EF 60%. IE risks: Dental procedure two months earlier without antibiotic prophylaxis	Transfemoral; 26 mm Edwards SAPIEN	Uneventful; mild PVL	12 months Definite IE	Presentation: Routine follow-up echocardiogram. Blood culture: Negative. Imaging: Severe PVL; THV dehiscence; abscess between right and non-coronary aortic cusps. Treatment: THV retrieval and SAVR. Note: No vegetations evident but abscess identified. Outcome: Well at 6-month follow-up
Garcia-Pardo *et al.*[26]	81-year-old male; LES 29%; low EF. IE risks: Colonoscopy without antibiotic prophylaxis 2 months earlier; DM; CKD	29 mm CoreValve	Uneventful; moderate AR	6 months Definite IE	Presentation: Malaise; fever; sepsis syndrome. Blood culture: *Staphylococcus aureus*. Imaging: 0.8 cm vegetation on THV. Treatment: Antibiotic therapy. Outcome: Discharged well

Table 1 Infective Endocarditis (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing and IE classification	Case description
Huan Loh *et al.*[27]	85-year-old male; LES 26%; STS 6.4%; AVA 0.8 cm^2 ; MG 40 mmHg; EF 40%. IE risks: Chronic urinary retention; DM	29 mm CoreValve	Uneventful	9 months Definite IE	Presentation: Weight loss; malaise; fever (4 months post-TAVI). Blood culture: *Enterococcus faecium.* Imaging: Vegetation on THV leaflets. Normal THV function. Treatment: Antibiotic therapy. Outcome: Discharged well.

Table 1 Infective Endocarditis (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing and IE classification	Case description
Puls *et al.*[28]	Case 1. 80-year-old male; LES 30%; MVR; low EF. IE risks: MRSA Colonisation; DM; CKD; MVR. Case 2. 81-year-old female; LES 48%; severely reduced EF. IE risks: Reactivation of pulmonary tuberculosis; DM. Case 3. 80-year-old female; LES 41%. Case 4. 85-year-old male; LES 23%. IE risks: Recurrent UTI; post-TAVI AKI with haemodialysis. Case 5. 91-year-old female; LES 25%. IE risks: N/A	Transfemoral; 29 mm CoreValve. Transapical; 23 mm Edwards SAPIEN. Transapical; 23 mm Edwards SAPIEN. Transfemoral; 23 mm Edwards SAPIEN. Transapical; 23 mm Edwards SAPIEN	Uneventful. Uneventful; moderate PVL. Uneventful; trace PVL after PID. Uneventful; moderate PVL; post-TAVI AKI with haemodialysis. Uneventful	7 months Definite IE 10 months Definite IE 10 months Definite IE 5 months Definite IE 23 months Possible IE	Presentation: Acute congestive heart failure; fever. Blood culture: Methicillin-resistant *Staphylococcus aureus.* Imaging: Dynamic PVL; diffuse aortic root thickening; suggestive of aortic root abscess. Treatment: Antibiotic therapy. Outcome: Deceased day 18. Presentation: Fever. Blood culture: *Enterococcus faecalis.* Imaging: Mobile vegetation attached to THV stent; moderate PVL. Treatment: Antibiotic therapy. Outcome: Discharged day 42. Presentation: Rigours. Blood culture: *Enterococcus faecalis.* Imaging: Large vegetation on THV cusp; moderate transvalvular AR. Treatment: Antibiotic therapy. Outcome: Cardioembolic stroke; discharge well. Presentation: Fever. Blood culture: *Escherichia coli and Proteus mirabilis.* Imaging: No vegetation; moderate PVL. Treatment: Antibiotic therapy. Outcome: Deceased at 3 months from septicaemia. Presentation: Fever. Blood culture: *Streptococcus gordonii.* Imaging: No vegetation; mild PVL. Treatment: Antibiotic therapy. Outcome: Discharged well

Table 1 Infective Endocarditis (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing and IE classification	Case description
Seeburger *et al.*[29]	82-year-old male. IE risks: N/A	Transfemoral; 26 mm CoreValve within a 23 mm St. Jude Epic	N/A	9 months Definite IE	Presentation: Recurrence of AS symptoms. Blood cultures: Not performed. Imaging: Severe AS (PG 95 mmHg; EOA 0.6 cm^2). Treatment: THV and SAVR retrieval, redo SAVR, and root replacement. Note: Histopathology detected IE. Outcome: N/A
Citro *et al.*[30]	72-year-old female; LES 39.7%. IE risks: Liver cirrhosis	Transfemoral; 23 mm Edwards SAPIEN within a St. Jude n. 21 Biocore	Uneventful; no PVL	5 months Definite IE	Presentation: Fever. Blood culture: *Staphylococcus epidermidis*. Imaging: Anterior PVL; right coronary sinus abscess; mitroaortic intervalvular fibrosa fistula into LV Treatment: Antibiotic therapy. Outcome: Deceased day 14
Orban *et al.*[31]	70-year-old male; LES 33.1%; low EF. IE risks: Haemodialysis with failed renal transplant; DM	CoreValve	N/A	12 months Definite IE	Presentation: Right forearm ischaemia due to infected embolic occlusion of brachial artery; Spondylodiscitis. Blood culture: *Staphylococcus epidermis*. Imaging: 3-cm mass within the THV lumen; non-coronary cusp paravalvular abscess. Treatment: TV retrieval and SAVR. Note: Large leaflet vegetations colonized by multiresistant coagulase-negative *Staphylococcus* spp. Outcome: Discharged day 14
Zytowski *et al.*[32]	84-year-old male. IE risks: N/A	Transapical; Edwards SAPIEN XT	N/A	4 months Definite IE	Presentation: N/A Blood culture: *Enterococcus durans*. Treatment: THV retrieval and SAVR. Note: Annulus destruction with abscess. Outcome: N/A

Table 1 Infective Endocarditis (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing and IE classification	Case description
Loeser *et al.*[33]	Case 1. 84-year-old female. IE risks: N/A Case 2. 84-year-old female. IE risks: N/A	Transapical; Edwards SAPIEN. Transapical; Edwards SAPIEN.	N/A N/A	14 days Definite IE 3 days Definite IE	Presentation: N/A Blood culture: Methicillin-resistant *Staphylococcus aureus.* Treatment: N/A Note: Neutrophilic infiltration of THV and MRSA colonization. Outcome: Deceased. Presentation: N/A Blood culture: N/A Treatment: N/A Note: Acute endocarditis and pericarditis with THV Neutrophilic infiltration. Outcome: Deceased
Wilbring *et al.*[34]	76-year-old male; LES 61.1%. IE risks: N/A	Transapical; 23 mm Edwards SAPIEN within a 23 mm Medtronic Hancock II Ultra	Uneventful	4 years Definite IE	Presentation: Fever. Blood culture: Negative. Imaging: Large aortic root abscess with covered rupture of aortic base; perforation to tricuspid annulus and large tricuspid valve vegetation. Treatment: THV and SAVR retrieval; aortic root reconstruction; tricuspid valve repair. Note: Explanted valves were culture negative. Outcome: Deceased day 7.

Table 1 Infective Endocarditis (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing and IE classification	Case description
Aung *et al.*[35]	Case 1. 72-year-old male; LES 28.1%. IE risks: DM; CKD. Case 2. 91-year-old female; LES 15.2%. IE risks: DM; CKD; breast cancer; cellulitis. Case 3. 88-year-old female; LES 55.3%; prior MVR. IE risks: Steroid therapy; DM; CKD; prior MVR IE. Case 4. 90-year-old female; LES 26.5%. IE risks: Recurrent cellulitis; DM; CKD	Transapical; 23 mm Edwards SAPIEN. Transfemoral; 29 mm CoreValve. Transfemoral; 29 mm CoreValve. Transfemoral; 29 mm CoreValve within a bioprosthetic aortic valve	Uneventful. Uneventful. Uneventful procedure; post-TAVI respiratory tract infection. Uneventful procedure; post-TAVI AKI with haemodialysis, and cellulitis	3.5 months Definite IE 18 days Definite IE 1 month Definite IE 3 months Possible IE	Presentation: Fever. Blood culture: *Enterococcus faecalis.* Imaging: Multiple mitral valve vegetations; echo-lucent space anterior to THV; mild PVL. Treatment: Antibiotic therapy. Outcome: Well at 1-year follow-up. Presentation: Fever. Blood culture: *Streptococcus mitis*. Imaging: Mitral valve vegetation; normal THV function. Treatment: Antibiotic therapy. Outcome: Well at 1-year follow-up. Presentation: Fever. Blood culture: *Enterococcus faecium.* Imaging: No vegetation; cavity suggestive of abscess anterior to THV. Treatment: Antibiotic therapy. Outcome: Well at 1-year follow-up. Presentation: Lower limb cellulitis. Blood culture: *Enterococcus faecalis.* Imaging: No vegetation; mild PVL. Treatment: Antibiotic therapy. Outcome: Well at 1-year follow-up
Hirnle *et al.*[36]	80-year-old female; LES 14.2%. IE risks: N/A	Transapical; 23 mm Edwards SAPIEN XT	Uneventful procedure; post-TAVI TIA	1 month Definite IE	Presentation: Fever. Blood culture: *Enterococcus faecalis.* Imaging: Mitral valve vegetation. Treatment: MVR. Outcome: Discharged to another hospital with tracheostomy day 14

Table 1 Infective Endocarditis (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing and IE classification	Case description
Seok Koh *et al.*[37]	85-year-old male; LES 25%. IE risks: N/A	Transfemoral; 26 mm Edwards SAPIEN	N/A	12 months Definite IE	Presentation: Fever; stroke. Blood culture: *Streptococcus angiosus.* Imaging: Multiple vegetations attached to THV. Treatment: Initial antibiotic therapy followed by THV retrieval and SAVR after stroke. Outcome: Discharged well
Drews *et al.*[38]	82-year-old female; LES 45%; STS 23%; prior MVR. IE risks: DM; CKD; MVR	Transapical; 23 mm Edwards SAPIEN	Uneventful procedure	8 months Definite IE	Presentation: N/A. Blood culture: *N/A.* Imaging: N/A. Treatment: Reoperation. Outcome: Deceased at 4 weeks from multiorgan failure
Pasic *et al.*[39]	N/A	Transapical; Edwards SAPIEN	N/A	3 months Definite IE	Presentation: N/A. Blood culture: N/A. Imaging: N/A. Treatment: Reoperation. Outcome: Discharged well
Nietlispach *et al.*[40]	N/A IE risks: Dental procedure without IE prophylaxis 6 weeks earlier.	Edwards SAPIEN	N/A	11 months Definite IE	Presentation: N/A Blood culture: Streptococcus angiosus. Imaging: N/A Treatment: THV retrieval, SAVR, and MVR Note: IE spread to the mitral valve at the contact point of the THV leading to mitral leaflet perforation and regurgitation. Outcome: Deceased

Table 1 Infective Endocarditis (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing and IE classification	Case description
Bozdag-Turan *et al.*[41]	80-year-old male; LES 10%. IE risks: CKD	Transfemoral; CoreValve	Uneventful procedure	4 months Possible IE	Presentation: Fever; dyspnoea. Blood culture: Enterococcus faecalis. Imaging: Mobile (18 × 7 mm) mass on THV. Treatment: Antibiotic therapy. Outcome: Discharged well
Raschpichler *et al.*[42]	84-year-old male. IE risks: N/A	31 mm CoreValve	N/A	6 months Definite IE	Presentation: Fever; dyspnoea. Blood culture: Staphylococcus epidermis. Imaging: Moderate AR; perforation of the anterior mitral leaflet and severe MR. Treatment: THV retrieval, SAVR and MVR. Outcome: Discharged well

IE, infective endocarditis; STS, Society of Thoracic Surgeons mortality risk score; CKD, chronic kidney disease; THV, transcatheter heart valve; PID, post-implant dilation; PVL , paravalvular leak; MR, mitral regurgitation; SAVR, surgical aortic valve replacement; EF, ejection fraction; TAVI, transcatheter aortic valve implantation; ICD, implantable cardiac defibrillator; AR, aortic regurgitation; LVOT, left ventricular outflow tract; CHF, congestive heart failure; AS, aortic stenosis; MG, mean gradient; PG, peak gradient; LES, logistic EuroSCORE; AVA, aortic valve area; DM, diabetes mellitus; MRSA, methicillin-resistant staphylococcus aureus; MVR, mitral valve replacement; AKI, acute kidney injury; EOA, effective orifice area; N/A, not available; TIA, transient ischaemic attack.

prophylaxis, can also impact on the development of PVE.[45] Accurate quantification of the risk of THV PVE will require further study of large patient populations with extended follow-up.

While one can speculate that the less invasive nature of TAVI could be reflected in lower rates of early PVE, the converse is also plausible. The non-sterile environment of many cardiac catheterization laboratories, high-risk profile of TAVI patients, and specific technical issues, including the infrequent requirement to remove, resheath, and reim-plant a malpositioned THV could potentially increase the risk of PVE (*Figure 3*). It is therefore of critical importance that every effort is made to minimize the risk of PVE: patient education, especially regarding the importance of post-implantation antibiotic prophylaxis; early treatment of coincident infections; and maintenance of a sterile environment during the index procedure. Interestingly, 24% of PVE cases involved 'satellite' endocarditis of the mitral valve,[17,18,20,35,36] suggesting that 'bridging-PVE' may occur when a low-lying aortic THV that is in direct contact with the mitral apparatus.[46] Secondary mitral valve involvement has been reported in ~10% of native aortic valve endocarditis cases and is associated with a poor prognosis.[47]

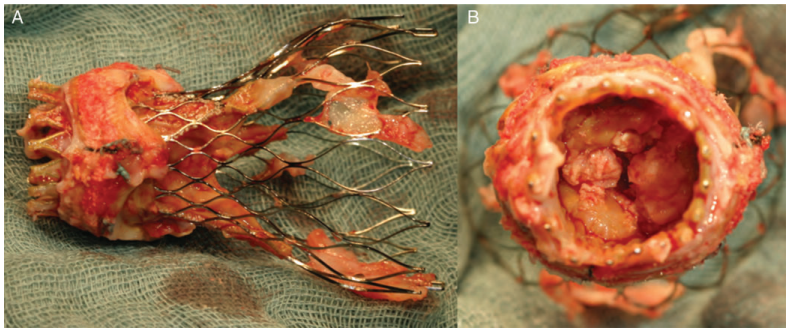

Figure 3 Transcatheter heart valve-prosthetic valve endocarditis. (*A* and *B*) An explanted CoreValve implanted within a 23-mm St. Jude Epic bioprosthesis with evidence of infective endocarditis. Reprinted with permission from Seeburger *et al.*[29]

Confirming the diagnosis of THV PVE can be challenging as elderly TAVI patients may present insidious and atypical symptomatology, and have a co-existing predisposition to infectious pathogens.[12] High rates of empiric antibiotic therapy in the elderly and difficulty in assessing the typical echocardiographic features of PVE can also hinder diagnostic certainty.[48,49] New valvular regurgitation is also difficult to differentiate from post-procedural paravalvular leaks and prosthetic dehiscence does not occur as radial force rather than sutures anchor the THV *in situ*. Consequently, the modified Duke criteria may be more difficult to apply in TAVI cohorts.[12] This diagnostic uncertainty is demonstrated by delayed diagnosis observed among several THV PVE cases.[18,22,25,27,28]

Targeted antibiotic therapy remains the first line of treatment for THV PVE. While conventional indications for operative intervention in the setting of PVE may be less applicable to high-risk TAVI cohorts, in this series surgical management of PVE (THV retrieval and SAVR

and concomitant aortic root replacement, mitral or tricuspid repair) was associated with encouraging outcomes (75% survived to hospital discharge). Thus, surgery for PVE should not be discounted among TAVI recipients, and Heart Team discussion is encouraged for all such cases.

Late transcatheter heart valve embolization

Late THV embolization represents a new complication previously unreported in the surgical bioprosthetic valve literature. We identified 18 cases of late THV embolization associated with the Edwards SAPIEN (n = 15) and Medtronic CoreValve (n = 3) (*Table 2*).[40,50–66] The mean age of these patients was 77 + 6 years.

The initial THV position was described as correct in 4 patients and low in 6 (THV position not described in 8 cases: 6 uneventful procedures, 2 no procedural outcome reported). Suboptimal procedural outcomes resulted in implantation of a 2nd THV (n = 2), elevated transvalvular gradients (n = 4), and/or moderate aortic regurgitation (n = 1: severe transvalvular regurgitation; n = 3: moderate paravalvular regurgitation). The clinical presentation of THV embolization was usually with rapid haemodynamic collapse (n = 2) or acute pulmonary oedema (n = 10). Two patients had late embolization diagnosed as an incidental finding on echocardiography and one developed progressive heart failure. Echocardiographic studies demonstrated severe aortic incompetence in 10 (56%) of cases, LVOT obstruction in 5 (28%), and interaction with the anterior mitral valve leaflet and mitral regurgitation in 4 (22%).

Management of THV embolization included acute haemodynamic stabilization or heart failure management, as required. Subsequent surgical intervention (THV retrieval and SAVR) was performed in 14 of 18 patients (78%), with survival to hospital discharge noted in 62% of cases. One patient deteriorated rapidly following THV embolization, and the Heart Team considered further surgical intervention to be futile. Three patients were treated by implantation of a second THV within the embolized prostheses in the LVOT (TAV-in-TAV): successful implantation of a 29 mm Edwards SAPIEN within a 26 mm Edwards SAPIEN (patient discharged home); implantation of a 29 mm CoreValve within a 31 mm CoreValve (patient died from cerebral anoxia); and successful implantation of a 26 mm Edwards SAPIEN in a 29 mm CoreValve (patient discharged home).

Discussion: late transcatheter heart valve embolization

Several patient and procedural factors may pre-dispose to late THV embolization (*Figure 4*): (i) undersizing of the THV,[54,63] (ii) underexpansion of an appropriately sized THV due to aortic root calcification,[51,60] (iii) low implantation of the THV,[56,57,60,64,65] (iv) bicuspid aortic valve,[53,63] (v) sparsely calcified native anatomy providing insufficient THV anchoring,[50,55,59] (vi) asymmetric aortic root calcification,[55,60] (vii) presence of a surgical mitral bioprosthetic valve that may displace the THV superiorly,[51,52] (viii) initial unstable THV position, and (ix) basal septal bulging.

Table 2 Late transcatheter heart valve embolization

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing	Case description
Clavel *et al.*[50]	79-year-old male; STS 11.5%; AVA 0.76 cm^2; MG 20 mmHg; annulus diameter 24 mm; EF 28%	Transapical; 26 mm Edwards SAPIEN	Severe central AR after implant; 2nd 26 mm SAPIEN implanted. Final mild AR	2 days	Presentation: Refractory cardiogenic shock. Embolization: LV with LVOT obstruction. Treatment: THV retrieval and SAVR. Outcome: Progressive shock, multiorgan failure, and death
Maroto *et al.*[51]	75-year-old female; LES 29.5%; AVA 0.4 cm^2 ; PG 67 mmHg; annulus diameter 20 mm, EF 40%, mechanical MVR	Transapical; 23 mm Edwards SAPIEN	Acceptable acute THV position, mild PVL	21 days	Presentation: Acute CHF. Embolization: Aortic (tilted) with severe AR. Treatment: THV retrieval and SAVR. Outcome: Stroke and Deceased on Day 7
Baumbach *et al.*[52]	82-year-old female; ES 37%; STS 5.3%; AVA 0.7 cm^2; PG 73 mmHg; annulus diameter 20–21 mm; bioprosthetic MVR	Transapical; 23 mm Edwards SAPIEN	Uneventful; MG 8 mmHg	14 days	Presentation: Recurrent CHF. Embolization: Aortic (tilted) with severe AR. Treatment: THV retrieval, SAVR and aortic root replacement. Outcome: Discharged well on Day 14
Schroeter *et al.*[53]	85-year-old male; LES 20.1%; AVA 0.5 cm^2 ; PG/MG 75/44 mmHg; aortic annulus 27 mm	Transapical; 29 mm Edwards SAPIEN XT	Uneventful; trace PVL	42 days	Presentation: Acute CHF. Embolization: LVOT (tilted) with severe AR. Treatment: THV retrieval, SAVR, and aortic root replacement. Note: Bicuspid aortic valve noted. Outcome: Discharged well on Day 7

Table 2 Late transcatheter heart valve embolization (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing	Case description
Radu *et al.*[54]	85-year-old male; LES 26%; STS 9.0%; AVA 0.6 cm^2; MG 39 mmHg; EF 45%; aortic annulus 21.4 × 26.1 mm	Transfemoral; 23 mm Edwards SAPIEN XT	Uneventful; trace PVL, MG 19 mmHg	5 days	Presentation: Incidental finding on discharge echocardiography. Embolization: LVOT, impairing anterior mitral leaflet function. Treatment: THV retrieval and SAVR. Note: Aortic annulus was 24 mm diameter at SAVR. Outcome: Uneventful post-operative course
Pang *et al.*[55]	75-year-old male; LES 23%; STS 12.8%; AVA 0.4 cm^2; MG 63 mmHg; aortic annulus 18 mm; EF 51%	Transfemoral; 23 mm Edwards SAPIEN XT	Uneventful; mild PVL, MG 24 mmHg	43 days	Presentation: Acute CHF. Embolization: LVOT and obstructing mitral inflow. Treatment: THV retrieval and SAVR. Note: THV was inverted at SAVR. Outcome: Discharged well on Day 7
Gul *et al.*[56]	75-year-old male; LES 18.4%; 2.8%; AVA 0.5 cm^2 ; MG 55 mmHg; aortic annulus 22 mm; EF 30%	Transfemoral; 26 mm Edwards SAPIEN	Uneventful; mild PVL, MG 8 mmHg	4 h	Presentation: Acute haemodynamic instability. Embolization: LVOT, with LVOT obstruction, and severe MR. Treatment: Inotropic support, and CPR during which the TVH embolized into LV; THV retrieval and SAVR. Outcome: Discharged well; asymptomatic at 3 month follow-up
Nietlispach *et al.*[40]	N/A	Edwards SAPIEN	N/A	109 days	Presentation: N/A Embolization: LVOT with severe AR. Treatment: THV retrieval and SAVR. Outcome: Death

Table 2 Late transcatheter heart valve embolization (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing	Case description
Toggweiler *et al.*[57]	N/A	Transapical; Edwards SAPIEN	Initial THV implant was too low so a 2nd THV implanted	2 days	Presentation: N/A Embolization: Both THVs embolized to LVOT with severe AR. Treatment: THV retrieval and SAVR. Outcome: Death
Stangl *et al.*[58]	N/A	Transfemoral; 26 mm Edwards SAPIEN		2 months	Presentation: N/A Embolization: LVOT. Treatment: THV retrieval and SAVR. Outcome: N/A
Iida *et al.*[59]	77-year-old male; ES 20%; STS 17%; AVA 0.9 cm^2; MG 27 mmHg; aortic annulus 23 mm; EF 30%	Transfemoral; 26 mm Edwards SAPIEN	Uneventful; moderate PVL; MG 9 mmHg	24 h	Presentation: Routine echocardiographic surveillance. Embolization: LVOT; moderate AS and severe AR. Treatment: THV retrieval and SAVR. Note: Moderate annular calcification. Outcome: Discharged well
Naganuma *et al.*[60]	67-year-old male; LES 32.5%; STS 13.6%; AVA 0.8 cm^2; MG 60 mmHg; aortic annulus 24 mm; EF 50%; previous CABG with LIMA and RIMA	Transfemoral; 26 mm Edwards SAPIEN XT	Initial THV implant was slightly low; mild–moderate PVL	27 days	Presentation: Acute CHF. Embolization: LVOT with severe AR. Treatment: THV retrieval and SAVR complicated by LIMA occlusion and requirement for redo CABG. Outcome: Discharged to rehabilitation on day 8
Lauten *et al.*[61]	72-year-old female	Transfemoral; 26 mm Edwards SAPIEN XT	MG 23 mmHg at 6 months	4 months	Presentation: Acute CHF. Embolization: LVOT with severe AR. Note: Native leaflets protruding over THV. Treatment: Transapical TAV-in-TAV. Outcome: Discharged well

Table 2 Late transcatheter heart valve embolization (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing	Case description
Wendeborn *et al.*[62]	84-year-old male; LES 19%	Subclavian; 31 mm CoreValve	Uneventful	N/A	Presentation: CHF and AKI. Embolization: LVOT with moderate paravalvular AR and severe MR. Note: MitraClip and transcatheter atrial septal defect closure 2 weeks earlier. Treatment: THV retrieval, SAVR, MVR, and CABG. Outcome: Discharged after 1 month; asymptomatic at 3 months
Wijesinghe *et al.*[63]	N/A	Transapical; 26 mm Edwards SAPIEN	Initial THV implant was low and undersized	63 days	Presentation: N/A. Embolization: LVOT with severe AS and worsening AR. Note: Native leaflets protruding over THV. Treatment: THV retrieval and SAVR. Outcome: Death
Nijhoff *et al.*[64]	83-year-old female	Transfemoral; 23 mmEdwards SAPIEN XT	Initial THV implant was low; trace AR	4 days	Presentation: Acute CHF. Embolization: LVOT obstruction and severe AR. Treatment: Patient deemed inoperable. Outcome: Death
Nijhoff *et al.*[65]	N/A	Transfemoral; 31 mm CoreValve	Initial THV implant was low	6 days	Presentation: Acute CHF. Embolization: LVOT with severe AR. Treatment: TAV-in-TAV with 29 mm CoreValve. Outcome: Death due to multiorgan failure
Schleger *et al.*[66]	59-year-old male; LES 24%; STS 13%	Transfemoral; 29 mm CoreValve	Residual grade II AR	1 year	Presentation: Progressive CHF. Embolization: LVOT with severe AR. Treatment: TAV-in-TAV with 26 mm Edwards SAPIEN. Outcome: Discharged well on day 10

CABG, coronary artery bypass grafting; CPR, cardiopulmonary resuscitation; ES, EuroSCORE; LIMA, left internal mammary artery; LV, left ventricle; RIMA, right internal mammary artery; TAV, transcatheter aortic valve. Other abbreviations as in *Table 1*.

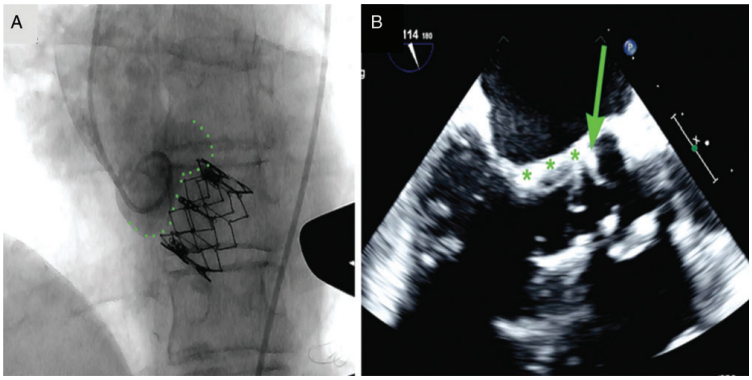

Figure 4 Late transcatheter heart valve embolization. (*A* and *B*) Fluoroscopic and echocardiographic images of late embolization of an Edwards SAPIEN valve into the left ventricular outflow tract. Green arrow showing the hinge point of the native valve leaflets. Reprinted with permission from Lauten *et al.*[61]

Suboptimal acute procedural results were noted in several cases of late THV embolization: moderate paravalvular aortic regurgitation,[57,59] and high transvalvular gradients.[54,55,61] In this setting, elevated gradients could potentially be explained by undersizing or incomplete expansion of the THV,[54] low implantation with consequent 'overhang' of the native stenotic leaflets,[61,63] or by inversion of the THV following rotation within the LVOT.[55] Initial excessively deep implantation of the THV is obviously a risk factor for delayed embolization into the LVOT, and was described in 6 cases in the current series.[56,57,60,63–65] Indeed, low implantation may have been more prevalent in this series, but the depth of prosthesis implantation was not described in all reports.

Left ventricular (89%) rather than aortic (11%) embolization was predictably more common given the fact that the retrograde forces acting on the THV in diastole amount to 10 times the anterograde forces in systole,[13] and that deep THV implantation may have been a precipitating factor. The clinical presentation of late THV embolization was variable, but most patients (80%) developed abrupt left ventricular failure and cardiogenic shock. Urgent operative intervention, to remove the embolized THV and replace the aortic valve, was performed in most cases (78%). Two-thirds of patients that underwent urgent surgery survived to hospital discharge. This observation underscores the importance of the Heart Team and supports operative intervention among selected TAVI recipients. Among the three patients treated with TAV-in-TAV, two survived to hospital discharge. The haemodynamic results of the TAV-in-TAV procedures were not reported.

Structural valve failure

To date, 13 individual reports of THV SVF have been reported: 9 Edwards SAPIEN and 4 CoreValve (*Table 3*).[67–77] The mean age of these patients was 80 + 7 years and the mean time to SVF was 24 + 26 months (range: several days to 5.5 years). Among the 7 cases detailing

acute procedural results, 3 had no aortic regurgitation, 3 mild paravalvular leaks, and 1 mild transvalvular leak. The latter case initially required post-implantation balloon dilatation for moderate paravalvular leak and over subsequent days developed progressive transvalvular aortic regurgitation requiring implantation of a 2nd THV. Excluding this patient, 3 asymptomatic patients were diagnosed with moderate valve dysfunction on echocardiography, and the remaining 7 cases represented with recurrent dyspnoea or congestive heart failure. Echocardiography demonstrated moderate prosthesis stenosis or regurgitation in 5 cases, severe stenosis in 5, and severe regurgitation in 3 cases.

Structural valve failure was attributed to severe leaflet calcification (n = 3), cusp rupture (n = 1), THV underexpansion (n = 2), and tissue ingrowth (n = 2) causing restrictive leaflet function. The failure mode was unclear or not described in 6 cases. Three asymptomatic patients with moderate valve dysfunction were managed conservatively, and the remaining patients underwent THV retrieval and SAVR (n = 4) or implantation of a second THV within the previously sited valve (n = 6) (TAV-in-TAV). Among the 4 patients who underwent THV retrieval and SAVR, intraoperative findings were: (Case 1) normal functioning CoreValve with no pannus or paravalvular leak, (Case 2) ingrowth of inflammatory tissue restricting the non-coronary leaflet of an Edwards SAPIEN XT, (Case 3) incomplete expansion of an Edwards SAPIEN valve within a 21 mm Hancock bioprosthesis, and (Case 4) severe calcification of both surfaces of the CoreValve leaflets. Favourable clinical outcomes were reported in all cases, except in one patient that underwent TAV-in-TAV and suffered a peri-procedural stroke.

Discussion: structural valve failure

Bioprosthetic SVF is a chronic degenerative process characterized by calcium phosphate deposition and extracellular matrix deterioration. The aetiology primarily relates to the chronic mechanical stresses on the valve leaflet's regions of maximal flexion, thus compromising structural integrity of leaflet tissue and initiating calcium deposition.[78] Glutaraldehyde fixation, residual leaflet antigenicity, and systemic [79–81] atherosclerosis may also contribute to the pathogenesis of SVF.

With surgical bioprosthetic valves, freedom from re-operation or death at 10 and 15 years are between 70–90 and 50–80%, respectively.[82] Freedom from re-operation or death, however, is not synonymous with SVF, which is defined according to echocardiographic or haemodynamic criteria. Thus, surgical SVF may be under-reported in the literature.

With respect to TAVI, the relative infancy of this technique prohibits meaningful discussion of the rates of long-term SVF. Nevertheless, the short- to medium-term incidences of THV SVF are low.[14,75,83] In a pan-Canadian study of 339 TAVI recipients, Rodes-Cabau *et al.*[14] reported no cases of SVF at a mean follow-up of 42 + 15 months. Among 88 consecutive patients with 5-year follow- up, Toggweiler *et al.*[75] reported structural valve deterioration in 3.4% of cases: moderate stenosis (n = 1), moderate regurgitation (n = 1), and moderate mixed

Table 3 Structural valve failure

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing	Case description
Pagnotta *et al.*[67]	73-year-old male; LES 36%; bicuspid aortic valve; EF ,30%	Transfemoral; 29 mm CoreValve	PID required for PVL; final mild transvalvular AR	Several days	Presentation: Hypotension, renal failure, pulmonary oedema. Aetiology: Severe transvalvular AR. Failure Mode: Rupture of CoreValve cusp. Treatment: Transfemoral TAV-in-TAV with a 29 mm CoreValve. Outcome: Discharged well on day 7
Van der Lienden *et al.*[68]	87-year-old male	Transapical; 26 mm Edwards SAPIEN	Uneventful; no AR	10 months	Presentation: Persistent CHF. Aetiology: Moderate-severe transvalvular AR and decreased LVEF. Failure Mode: Unclear. Treatment: Transaortic TAV-in-TAV with a CoreValve. Outcome: Uneventful recovery
Blumenstein *et al.*[69]	83-year-old female; ES 26%; STS 7%	Transapical; Edwards SAPIEN XT	Uneventful; mild AR	12 months	Presentation: Recurrent CHF. Aetiology: Severe transvalvular AR with immobile non-coronary leaflet. Failure Mode: Histology: tissue ingrowth causing leaflet retraction. No THV IE or thrombosis. Treatment: THV retrieval and SAVR. Outcome: Discharged well
Klotz *et al.*[70]	74-year-old male	23 mm Edwards SAPIEN XT within a 23 mm Hancock bioprosthesis	Uneventful; no AR; MG 20 mmHg	3 months	Presentation: Recurrent CHF. Aetiology: Severe AS (MG 43 mmHg; EOA 0.6 cm^2). Failure Mode: Incomplete THV expansion within the Hancock with abnormal leaflet function. Treatment: THV/Hancock retrieval and redo SAVR. Outcome: Uneventful recovery

Table 3 Structural valve failure (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing	Case description
Ong *et al.*[71]	74-year-old male	CoreValve	N/A	5 years	Presentation: N/A Aetiology: Severe AS (MG 53–79 mmHg). Failure Mode: Severe calcification of THV leaflets. Treatment: THV retrieval and SAVR Outcome: N/A
Hammerstingl *et al.*[72]	92-year-old female; LES 38.2%; STS 27%	Transfemoral; 26 mm CoreValve (2nd generation), with CPB	Successful	5.5 years	Presentation: Acute CHF. Aetiology: Severe AS (MG 54 mmHg; EOA 0.4 cm^2). Failure Mode: Severe calcification of THV leaflets. Treatment: Transfemoral TAV-in-TAV with a 26 mm CoreValve (3rd generation). Outcome: Discharged on day 8
Hoffmann *et al.*[73]	75-year-old male; LES 32%; EF 20%; haemodialysis	Transapical; 26 mm Edwards SAPIEN	Uneventful; MG 5 mmHg	3.5 years	Presentation: Recurrent dyspnoea. Aetiology: Severe AS (MG 45 mmHg). Failure Mode: Severe calcification of the THV leaflets. Treatment: Transfemoral TAV-in-TAV with a 26 mm CoreValve. Outcome: Successful procedure (MG 5 mmHg)
Kiefer *et al.*[74]	86-year-old male; LES 31%; STS 12%; EF 60%	Transapical; 26 mm Edwards SAPIEN XT	Uneventful; No AR; PG/MG 15/10 mmHg	3 years	Presentation: Recurrent dyspnoea. Aetiology: Severe AS (PG/MG 83/49 mmHg; EOA 0.4 cm^2) Failure Mode: Unclear. Treatment: Transapical TAV-in-TAV with 26 mm Edwards SAPIEN XT. Outcome: Successful procedure (PG/MG 14/10 mmHg). Post-operative stroke. Discharged to rehabilitation on day 7

Table 3 Structural valve failure (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing	Case description
Toggweiler *et al.*[75]	Case 1. N/A Case 2. N/A Case 3. N/A	Cribier-Edwards Cribier-Edwards Edwards SAPIEN	N/A N/A N/A	5 years 5 years 5 years	Failure Mode: Moderate AS (MG 26 mmHg; EOA 1.2 cm^2) and moderate transvalvular regurgitation. Treatment: None Failure Mode: Moderate transvalvular regurgitation. Treatment: None Failure Mode: Moderate AS (MG 23 mmHg; EOA 1.1 cm^2) Treatment: None
Thyregod *et al.*[76]	76-year-old male; LES 16%; STS 18%; Previous CABG	Transfemoral; 26 mm CoreValve	Uneventful	4 months	Presentation: Progressive dyspnoea. Aetiology: Moderate paravalvular and transvalvular AR. No AS. Failure Mode: Unclear. No obvious paravalvular leak or pannus evident at surgery. Treatment: THV retrieval, SAVR and CABG. Outcome: Discharged to rehabilitation on day 8
Kiefer *et al.*[77]	53-year-old female; mechanical MVR; previous CABG; porcelain aorta	Transapical; 26 mm Edwards SAPIEN	N/A	3 years	Presentation: Recurrent dyspnoea. Aetiology: Moderate AS (PG/MG 56/31 mmHg) and moderate transvalvular AR. Failure Mode: Incomplete THV expansion. Treatment: Transapical TAV-in-TAV with Symetis Acurate. Outcome: Successful procedure (No AR; PG 9 mmHg). Discharged to rehabilitation on day 7

Other abbreviations as in *Table 1*. CPB, cardiopulmonary bypass.

disease (n = 1). There were no cases of reoperation. Similarly, in the PARTNER trial (Cohort A), no patients in either the surgical or transcatheter groups had SVF at 2 years of follow-up.[4] Although much longer-term follow-up (.10 years) will be required to demonstrate the true incidence of SVF associated with TAVI, this may be difficult to accrue due to the elderly and high-risk nature of TAVI recipients.

Among the reported cases of THV SVF, leaflet calcification, tissue ingrowth (pannus), and incomplete THV expansion were the most commonly described failure mechanisms.[69,71–73,77] There may be, however, specific failure mechanisms unique to THV (*Figure 5*). In particular, the haemodynamic sheer stress on the THV leaflets may be significantly increased in cases of incomplete THV expansion or in very elliptical annuli.[68,70,77,84,85] THV thrombosis can also mimic SVF, by presenting with elevated transvalvular gradients, and should be excluded using multimodal imaging. In one case, the authors speculated that post-implantation balloon dilatation may have resulted in tearing of a CoreValve leaflet, inducing severe transvalvular aortic regurgitation.[67] Balloon expansion has been demonstrated to cause microscopic leaflet

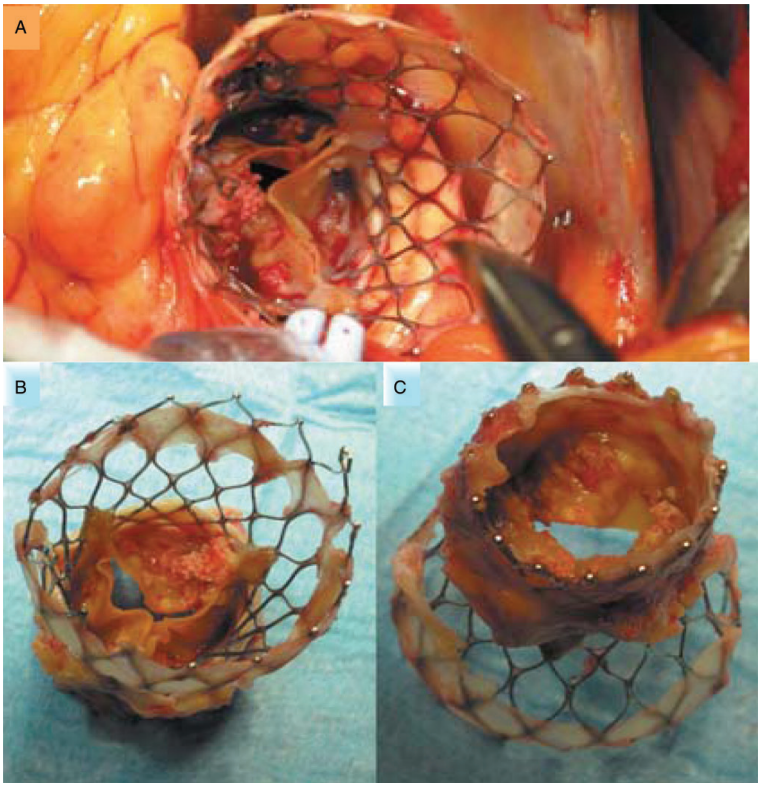

Figure 5 Transcatheter heart valve structural failure. (*A*–*C*) Extensive leaflet calcification on the outflow and inflow aspects of an explanted CoreValve. Reprinted with permission from Ong *et al.*[71]

injury;[86] however, the frequency with which post-implantation is performed suggests that balloon-related trauma is unlikely to represent an important cause of SVF. In surgically implanted bioprosthetic valves, tearing of valve leaflets has been observed in up to 70–80% of cases implanted for over 10 years, and is often accompanied by calcification.[87] Tearing of the valve leaflet in a horizontal plane running parallel to the sewing ring is unique and is reported in 10–15% of cases.[87] This type of leaflet tearing, to our knowledge, has not yet been observed in TAVI.

The majority of patients with SVF requiring intervention were treated with TAV-in-TAV (60%), rather than SAVR (40%). Outcomes of both procedures were excellent, with no deaths and only one peri-procedural stroke in a patient that underwent transapical TAV-in-TAV.[74]

Transcatheter heart valve compression

Compression of a bioprosthetic heart valve is a recently described phenomenon that may be to be unique to balloon-expandable THVs. We identified seven cases of Edwards SAPIEN valve compression that occurred following CPR in the setting of cardiac arrest (*Table 4*).[33,40,88–92] The median time to cardiac arrest was 3 days (range: 12 min to 42 days). Transcatheter heart valve compression was identified on fluoroscopy in one case and at autopsy in all others. Although the resuscitation efforts were ultimately unsuccessful in all patients, it was not possible to implicate THV compression in the demise of these patients that had suffered serious life-threatening complications. No patient received any specific intervention for THV compression.

Discussion: Transcatheter heart valve compression

Prior studies have reported compression of both coronarystents and of the Melody transcatheter pulmonary valve (Medtronic) following CPR.[93,94] Despite the relative frequency of peri-procedural CPR in the setting of TAVI, THV compression remains a rarely reported event.[95] Underreporting is likely as almost all cases were diagnosed post-mortem. To date, all cases of THV compression involve balloon-expandable TAVI systems, specifically the Edwards SAPIEN prostheses. Although speculative, balloon-expandable THV may be more susceptible to deformation compared with self-expanding THV, as the stainless steel (SAPIEN) or cobalt-chromium (SAPIEN XT) composition does not have the shape memory properties of Nitinol (CoreValve) (*Figure 6*). Although normal CoreValve integrity has been reported following prolonged CPR (Personal communication; Nawwar Al-Attar, PCR London Valves 2011), self-expanding THV compression is conceivable in the presence of significant frame fracture, and thus, a thorough evaluation of THV function is recommended following CPR irrespective of the prosthesis design. Outside of the setting of CPR, THV frame fracture has not been reported.

It has been suggested that relocating the site of chest compressions toward the left hemithorax could provide adequate haemodynamic support and avoid potential THV

Table 4 Transcatheter heart valve compression

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing	Case description
Scherner *et al.*[88]	87-year-old female; LES 39%; STS 25%	Transapical; 23 mm Edwards SAPIEN	Uneventful	6 h	Event: Cardiac arrest with CPR. Compression: Autopsy revealed compressed and deformed THV. Outcome: Deceased
Kim *et al.*[89]	75-year-old male; LES 16.6%	Transapical; 26 mm Edwards SAPIEN	Uneventful; trace AR; MG 8 mmHg; post-TAVI shock	42 days	Event: Inhospital cardiac arrest with CPR. Compression: Fluoroscopy revealed severe THV deformation. Outcome: Deceased day 16
Kirov *et al.*[90]	N/A	Transapical; Edwards SAPIEN XT	Uneventful	5 days	Event: Cardiac arrest with CPR. Compression: Autopsy revealed severe THV deformation. Outcome: Deceased
Damen *et al.*[91]	73-year-old female; ES 22.5%	Transfemoral; 23 mm Edwards SAPIEN	Uneventful	12 min	Event: Cardiac arrest post-TAVI with CPR. Compression: Autopsy revealed an inverted THV. Intraprocedural imaging suggested normal THV orientation, so inversion during CPR suspected. Outcome: Deceased day 1
Nietlispach *et al.*[40]	Post-mortem series describing four cases of THV deformation	Edwards SAPIEN	N/A	N/A	Events: 8 cases of cardiac arrest with CPR. Compression: 4 of 8 cases had THV deformation at autopsy. Outcome: Deceased
Spangenberg *et al.*[92]	88-year-old female; ES II 12.3%	Transapical; 26 mm Edwards SAPIEN XT	Uneventful	5 days	Event: PEA cardiac arrest with CPR due to ruptured aortic aneurysm. Compression: Autopsy revealed severe THV deformation. Outcome: Deceased
Loeser *et al.*[33]	82-year-old female	Transfemoral; Edwards SAPIEN	N/A	1 day	Event: Cardiac arrest with CPR. Compression: Autopsy revealed subtotal THV compression. Outcome: Deceased

Other abbreviations as in *Table 1*.

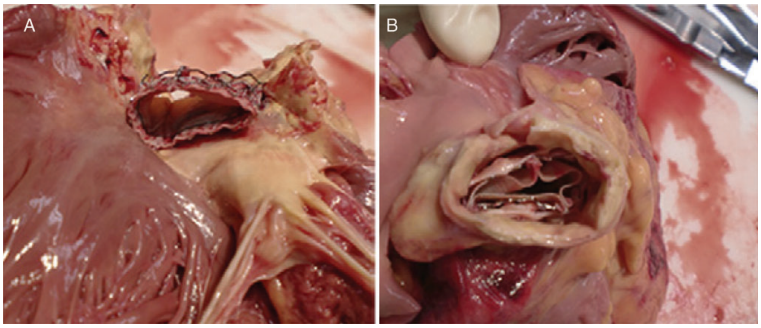

Figure 6 Transcatheter heart valve compression. (*A* and *B*) Autopsy finding of a deformed Edwards SAPIEN valve following cardiopulmonary resuscitation. Reprinted with permission from Kirov *et al.* [90]

compression.[88] Treatment options for patients with THV deformation depend on the clinical scenario, and haemodynamic consequences of THV compression, but could include balloon post-dilatation, valve-in-valve implantation, or THV retrieval and SAVR.

Transcatheter heart valve thrombosis

Ten publications, comprising 15 individual cases of THV thrombosis, were identified (*Table 5*).[96–105] The majority of cases (14 of 15) involved the Edwards SAPIEN THV. Excluding two cases of peri-procedural thrombosis, the mean time to diagnosis was 9 + 7 months (range: 1–24 months). The post-implantation antiplatelet regimen was described in 13 cases: 12 patients were prescribed dual antiplatelet therapy (DAPT) consisting of aspirin and clopidogrel; one case was treated with aspirin monotherapy. One patient on aspirin alone and one non-compliant patient had THV thrombosis at 2 weeks and 8 months, respectively. The remaining patients had THV thrombosis after completing the recommended course of DAPT (on-going aspirin) (n = 5) or despite on-going DAPT (n = 6). Most patients with THV thrombosis presented with progressive dyspnoea (n = 12). One patient was asymptomatic and the thrombosis was evident on post-implantation CT, one had a non-ST-segment myocardial infarction, and one patient with peri-procedural THV thrombosis suffered cardiac arrest. The most commonly observed echocardiographic features were increasing transvalvular gradients (n = 12), thickened THV leaflets with impaired mobility (n = 8), and visualization of thrombus formation on the valve (n = 5).

Transcatheter heart valve thrombosis was treated with either systemic anticoagulation (n = 11) or surgical intervention (n = 3). Thrombolytic therapy was not performed in any case. In all patients treated with anticoagulation, the transvalvular gradients diminished towards the post-procedural gradient and leaflet mobility normalized. Favourable clinical outcomes were noted for all patients, except the case of peri-procedural THV thrombosis complicated by cardiac arrest, progressive cardiogenic shock and death. Protracted hospital stay was described for two of the three patients who underwent surgical thrombectomy and SAVR.

Table 5 Transcatheter heart valve thrombosis

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing	Case description
Trepels *et al.*[96]	84 year-old female; LES 22%	Transapical; 23 mm Edwards SAPIEN	Uneventful. Antiplatelet therapy: Non-compliance with DAPT from 6 weeks	8 months	Presentation: Progressive dyspnoea. Imaging: Increasing MG: 11, 19, 40, and 53 mmHg at 2, 7, 24, and 32 months, respectively. Echo-density on THV leaflet. Treatment: THV retrieval and SAVR. Note: Histology: non-infective thrombi on THV leaflets. Thrombophilia screen: mild protein S reduction, + cold agglutinin. Outcome: Discharged home
Kefer *et al.*[97]	78-year-old male; LES 44%. EF 30%	Transapical; 26 mm Edwards SAPIEN	Uneventful; trace AR; PG 15 mm Hg; AVA 1.6 cm^2 Antiplatelet therapy: Initial DAPT, clopidogrel stopped at 1 month	4 months	Presentation: NSTEMI; CHF. Imaging: ICE and TTE showed thrombus on THV leaflets; severe AS with PG 72 mmHg; EOA 0.4 cm^2. Treatment: Anticoagulation. Note: Negative thrombophilia screen. Outcome: PG reduced to 22 mmHg at 1 month
Tay *et al.*[98]	Case 1. 66 year-old male; EF 30%. Case 2. 77-year-old female; prior MVR for rheumatic mitral stenosis	23 mm Edwards SAPIEN. Transapical; 26 mm Edwards SAPIEN within failing MVR	Uneventful procedure; post-TAVI TTE showed thrombi on THV. Antiplatelet therapy: On-going DAPT. Uneventful; no MR; MG reduced from 10 to 7 mmHg. Antiplatelet therapy: On-going DAPT	3 days 1 month	Presentation: Cardiac arrest. Treatment: Intravenous heparin continued post-TAVI. Note: Autopsy showed normal THV position and leaflet mobility with thrombi on the stent frame. Outcome: Deceased. Presentation: Dyspnoea. Imaging: TOE showed thrombus on edge of THV. Treatment: Anticoagulation. Outcome: Discharged home

Table 5 Transcatheter heart valve thrombosis (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing	Case description
Latib *et al.*[99]	Case 1. 83-year-old male; ES 30%; STS 5%. EF normal. Case 2. 81-year-old male; ES 11%; STS 3.9%. Case 3. 83-year-old male; LES 20%; STS 17%	Transfemoral; 26 mm Edwards SAPIEN XT. Edwards SAPIEN XT. 83-year-old male; Edwards SAPIEN XT; LES 20%; STS 17%	Uneventful; no AR; MG 11 mmHg. Antiplatelet therapy: On-going DAPT. Uneventful; trivial AR; MG 8 mmHg. Antiplatelet therapy: Initial DAPT, clopidogrel stopped at 3 months. Uneventful; mild AR; MG 8 mmHg. Antiplatelet therapy: N/A	6 months 15 months 24 months	Presentation: Dyspnoea. Imaging: Increasing MG: 47 and 68 mmHg 6 and 6.5 months, respectively; no THV thrombus. Treatment: Anticoagulation. Outcome: Asymptomatic at 8 months; THV MG 11 mmHg. Presentation: Dyspnoea. Imaging: Normal THV function at 3 and 9 months; MG increased to 45 mmHg at 15 months; no thrombus seen. Treatment: Anticoagulation. Outcome: Asymptomatic; MG gradient 19 mmHg. Presentation: Dyspnoea. Imaging: Normal THV function at 12 months; MG increased to 37 mmHg; no thrombus seen. Treatment: Anticoagulation. Outcome: Symptom improved; MG 13 mmHg

Table 5 Transcatheter heart valve thrombosis (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing	Case description
Cota *et al.*[100]	Case 1. 80-year-old male. Case 2. 81-year-old male; prior bioprosthetic SAVR Case 3. 74-year-old female	23 mm Edwards SAPIEN XT. 23 mm Edwards SAPIEN XT within 25 mm Carpentier Edwards. 26 mm Edwards SAPIEN XT	Uneventful; MG 10 mmHg. Antiplatelet therapy: On-going DAPT. Uneventful; MG 15 mmHg. Antiplatelet therapy: N/A Uneventful; MG 7 mmHg. Antiplatelet therapy: On-going DAPT	10 months 4 months 2 months	Presentation: Dyspnoea. Imaging: MG increased to 54 mmHg; suspected thrombotic fusion of two THV leaflets. Treatment: Anticoagulation. Note: Thrombophilia screen: negative. Outcome: Asymptomatic; MG 13 mmHg. Presentation: Dyspnoea. Imaging: MG increased to MG 51 mmHg; suspected thrombotic fusion of two THV leaflets. Treatment: Anticoagulation. Outcome: Asymptomatic; MG 9 mmHg. Presentation: Dyspnoea. Imaging: MG increased to 34 mmHg; suspected thrombotic apposition of THV leaflets. Treatment: Anticoagulation. Outcome: Asymptomatic; MG 9 mmHg
Greason *et al.*[101]	74-year-old female; STS 18.7%	Transiliac; 23 mm Edwards SAPIEN	Uneventful; MG 5 mmHg. Antiplatelet therapy: On-going aspirin monotherapy	2 weeks	Presentation: Dyspnoea. Imaging: MG increased to of 43 mmHg with restricted leaflet mobility. Treatment: THV retrieval and SAVR. Note: Explanted THV thrombosis. Outcome: Discharged after long hospitalization

Table 5 Transcatheter heart valve thrombosis (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing	Case description
Lancellotti *et al.*[102]	86-year-old male; ES 7%	26 mm CoreValve	Uneventful; Antiplatelet therapy: Initial DAPT, clopidogrel stopped at 3 months	12 months	Presentation: Dyspnoea. Imaging: MG increased to 41 mmHg; EOA 0.7 cm^2 ; thickened restricted THV leaflets; no thrombus seen. Treatment: THV retrieval and SAVR. Note: Explanted THV showed thrombosis of THV with pannus restricting leaflet mobility. Outcome: Discharged after long hospitalization
Pache *et al.*[103]	86-year-old male	29 mm Edwards SAPIEN XT	Uneventful; Mild paravalvular AR. Antiplatelet therapy: Initial DAPT, post-TAVI heparin (for prior pulmonary embolism) stopped due to perianal bleeding	7 days	Presentation: Incidental finding on post-implant CT. Imaging: CT revealed a crescent shaped thrombus in THV left-coronary cusp. TOE showed restricted cusp movement but normal haemodynamic function (MG 9 mmHg). Treatment: Anticoagulation. Outcome: Discharged home. Repeat CT at 10 weeks showed no evidence of thrombus
Orbach *et al.*[104]	81-year-old female	26 mm Edwards SAPIEN	N/A Antiplatelet therapy: Initial DAPT, then aspirin monotherapy	21 months	Presentation: CHF. Imaging: MG increased to 53 mmHg; $EOAi_i$ 0.4 cm^2/m^2; thickened restricted THV leaflets; distinct thrombus on TOE. Treatment: Anticoagulation. Outcome: Asymptomatic and normal THV function at 10 months

Table 5 Transcatheter heart valve thrombosis (continued)

Study	Patient characteristics	Access and THV characteristics	Procedural details	Timing	Case description
Pergolini *et al.*[105]	87-year-old male; ES 29%; STS 15.6%	29 mm Edwards SAPIEN XT	Uneventful; MG 8 mmHg. Antiplatelet therapy: Initial DAPT, clopidogrel stopped at 3 months. Aspirin interrupted 4 months later due to epistaxis and clopidogrel reinstituted	8 months	Presentation: Progressive dyspnoea. Imaging: MG increased to 50 mmHg; thickened restricted THV leaflets; TOE showed echodense homogenous layer on aortic side of the three THV cusps. Treatment: Anticoagulation. Note: Negative thrombophilia workup. Outcome: Discharge on day 11 with gradual decrease in MG and resolution of symptoms

ICE, intracardiac echocardiogram; NSTEMI, non-ST elevation myocardial infarction; TOE, transoesophageal echocardiogram; THV, transcatheter heart valve; other abbreviations as in *Table 1*.

Discussion: Transcatheter heart valve thrombosis

Thrombosis of surgical aortic bioprostheses is rare, with incidence estimates of 0.03–0.7% per patient-year.[106,107] Transcatheter heart valve thrombosis appears to be an equally rare event: there were no reported cases of prosthesis thrombosis in the PARTNER randomized trials or in large consecutive TAVI registries.[4,5,16] One case of THV thrombosis (0.8%) wasreported among the 130 TAVI recipients enrolled in the PARTNER EU trial.[96]

There exist, however, several theoretical mechanisms that could potentially increase the risk of THV thrombosis relative to SAVR (*Figure 7*):[108] (i) the elderly TAVI population is more likely to have coexisting prothrombotic conditions (e.g. Cancer), (ii) the metallic THV frame could potentially provide a nidüs for thrombosis, (iii) incomplete THV expansion can create leaflet folds and potential recesses for thrombus formation, (iv) incomplete THV apposition to the aortic wall may delay endothelialization, and (v) the native leaflets may overhang balloon-expandable systems creating areas of diminished blood flow and stagnation.

It appears that the highest risk of valve thrombosis following bioprosthetic SAVR occurs in the first 3–6 months post-operatively.[109] Consequently, aspirin therapy (75–100 mg) is recommended by societal guidelines.[110,111] More recently, short-term use of oral anticoagulation has been associated with a reduction in thromboembolic events and cardiovascular mortality.[109] There are currently few data evaluating the efficacy of either antiplatelet or anticoagulant therapy following TAVI.[112] Dual antiplatelet therapy (aspirin and clo-pidogrel) is presently recommended for 3–6 months post-TAVI, though there is scant evidence to support the selection or duration of this regimen. This rather arbitrary duration of therapy aims to provide antiplatelet cover in the immediate post-operative period, allowing THV frame endothelialization, without exposing the patient to excessive bleeding risk. It is unclear if a short period of oral anticoagulation could reduce the risk of both stroke and potential for THV thrombosis without prohibitively increasing the bleeding risk. On-going research will help define the optimal duration of antiplatelet therapy post-TAVI (Aspirin Versus Aspirin and ClopidogRel

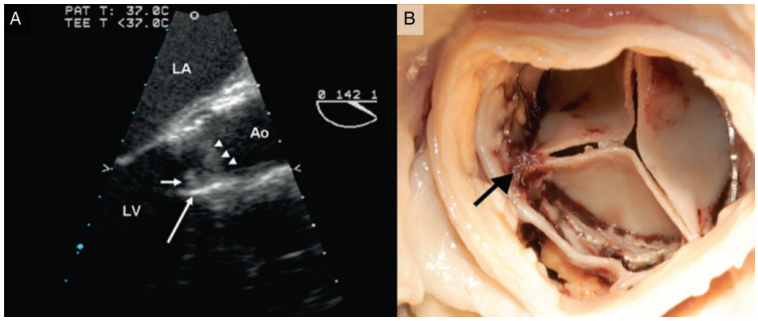

Figure 7 Transcatheter heart valve thrombosis. (*A*) Transesophageal echocardiogram of a case of transcatheter heart valve thrombosis demonstrating the valve stent (long white arrow), thrombus on the stent (short white arrow), and thickened valve leaflets. (*B*) Post-mortem image of thrombi on the outflow of the stent frame (black arrow). Reprinted with permission from Tay.[98]

Following Transcatheter Aortic Valve Implantation: the ARTE Trial: NCT01559298) and/or need for anticoagulation.

It should be noted that the diagnosis of THV thrombosis requires a high index of suspicion: thrombus was not seen on either the THV leaflets or frame in two-thirds of cases. Diagnostic clues include a history of non-compliance with DAPT,[96] echocardiographic evidence of progressive valve dysfunction (usually stenosis),[96,99,102,101–103] leaflet thickening, and immobility.

The optimal management of THV thrombosis is currently unclear. It is noteworthy that three-quarters of cases were successfully treated with prolonged systemic anticoagulation and that thromboly-sis was not performed in any case, probably due to the high risk of bleeding in TAVI patients. Surgical thrombectomy and SAVR was successful performed in three cases, without procedural mortality.

DISCUSSION

The main findings of this systematic review of published data on TAVI failure are that THVs appear to be susceptible to failure modes both similar to those of surgical bioprosthetic valves and unique to the specific design features of THVs. Late embolization and THV compression represent complications previously unreported in the surgical literature.

Surgical aortic valve replacement failure

Surgical bioprosthetic failure may be attributed to SVF, IE, thrombosis, or paravalvular leak. First generation bioprosthetic valves were particularly prone to SVF, with up to one-third of younger patients requiring reoperation within 10 years of implantation.[113] Advances in prosthesis design, leaflet fixation, and anti-calcification treatment have rendered these early prostheses obsolete, and have improved valve durability: freedom from SVF at 15 years was reported in 43% of those treated with the first generation Hancock (Medtronic, Minneapolis, MN, USA) and in 19% treated with the second-generation Hancock.[114,115] Current, third-generation bioprostheses are expected to further reduce the incidence of SVF and long-term follow-up data on these prostheses are eagerly awaited.

Transcatheter heart valve failure

We observed three THV failure modes (PVE, SVF, and thrombosis) that are synonymous with surgical bioprosthesis failure. We observed some variance, however, in the presentation and management of these complications between TAVI and SAVR. For example, confirming the diagnosis of PVE appeared to be more difficult among TAVI recipients than expected; echocardiographic diagnosis appeared to be hindered by limited visualization of the THV and by the frequent presence of post-implantation paravalvular leaks. Structural valve failure was also more frequently treated with redo TAVI rather than SAVR.

Two failure modes, unique to THVs were also identified. Late THV embolization is a rare, but potentially catastrophic complication of TAVI. The limited number of events precludes an analysis of potential risk factors for late embolization, though insufficient THV anchoring, low implantation, and the presence of a mitral prosthesis were prevalent amongst cases. Compression of balloon-expandable THV was reported among patients that had undergone CPR in the setting of fatal peri-procedural complications. Thus, THV function should be evaluated following CPR in all THV recipients.

Implications

Understanding the modes of TAVI failure, their presentation, treatment, and outcomes is of particular relevance as TAVI technology is applied to greater patient numbers worldwide and increasingly to intermediate-risk cohorts.[1,2] The current study highlights several modes of TAVI failure that will be seen with greater frequency as experience with the technique increases. It is likely that the current case report and small series literature on TAVI failure reflects a significant underreporting of events. Therefore, determining the true incidence of adverse events will require high-quality dedicated post-marketing surveillance registries, such as the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy registry.[116] The objective performance criteria developed by the U.S. Food and Drug Administration will provide benchmark performance for evaluating the long-term performance of TAVI technology.[117] Systematic autopsy of TAVI recipients could also facilitate our understanding of the modes of TAVI failure as distinct from bioprosthetic SAVR failure.

Limitations

This study has the limitations inherent to all systematic reviews. We present only the information described in each individual publication and therefore potentially omit relevant data. All the articles in the literature were either case reports or small series, precluding comparison with the entire TAVI population at risk. Furthermore, accurate estimation of the true incident rates of each THV failure mode was not possible, and the likely underreporting of adverse events would be expected to result in a significant underestimation of event rates. In addition, the management of patients in published case reports and small series may not represent common clinical practice but nonetheless provide some clinical guidance in circumstances where an evidence base is not available. The results of this review are also subject to publication bias as the reported incidences and individual patient outcomes may have been superior to those that were not published. Furthermore, imaging data and other relevant background information were not available in all the reported cases.

CONCLUSIONS

Transcatheter heart valves appear to be susceptible to failure modes both similar to those of surgical bioprosthetic valves and unique to the specific design features of THVs. Late embolization and THV compression represent complications previously unreported in the surgical literature. Large patient series with extended follow-up are required to better characterize and quantify THV failure.

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