Transcatheter aortic valve implantation-related infective endocarditis: experience from an Irish tertiary referral centre

Anthony J. Buckley1 · Richard Tanner1 · Brian Armstrong1 · Saber Hassan2 · Barbara Moran2 · Jamie Byrne1 · Susan Groarke1 · Ronan Margey2 · Ivan P. Casserly1,2

Received: 20 December 2021 / Accepted: 28 March 2022 / Published online: 3 May 2022
© The Author(s), under exclusive licence to Royal Academy of Medicine in Ireland 2022

Abstract

Background Transcatheter aortic valve implantation-related infective endocarditis (TAVI-IE) is a well-recognised and serious complication following TAVI. The purpose of this study was to describe the clinical characteristics, microorganism spectrum, and outcomes of TAVI-IE in an Irish context.

Methods A prospective registry was used to assess the baseline demographics, procedural variables, and clinical outcomes of patients undergoing TAVI between 2009 and 2020 at two tertiary referral Irish Hospitals.

Results A total of 733 patients underwent TAVI during the study period. During a follow-up duration of 1,949 person-years (median 28 months), TAVI-IE occurred in 17 (2.3%) patients. The overall incidence was 0.87 per 100 person-years and the median time from TAVI to presentation with IE was 7 months [IQR: 5–13 months]. In those who developed TAVI-IE, the mean age was 78.7 years, 70.5% were male, and there was a trend towards more permanent pacemaker implantations post-TAVI (17.6% vs. 5.8%; p = 0.08). The dominant culprit microorganisms were streptococci (41.1%) and four (23.5%) cases were attributed to dental seeding. Major complications of TAVI-IE included one (5.8%) stroke, one (5.8%) in-hospital death, and two (11.7%) urgent surgical aortic valve replacements. The Kaplan–Meier estimate of survival at 1-year was 82% (95% CI = 55–95).

Conclusions This Irish cohort of TAVI-IE exhibited a similar incidence and time to presentation compared to prior international registries; however, the 1-year mortality rate was comparatively lower. The need for rigorous dental clearance pre-TAVI and maintenance of dental health post-TAVI is underscored by the high prevalence of oral streptococcus species in this cohort.

Keywords Dental · Infective endocarditis · Outcomes · TAVI

Background

To date, there have been no data published on TAVI-IE in the Republic of Ireland. Using a prospective TAVI database from two Irish tertiary TAVI sites, we sought to assess the incidence, clinical characteristics, microorganism spectrum, and outcomes of TAVI-IE in this patient cohort, with the goal of comparing our experience with other large national and international registries.

Methods

A prospective TAVI registry was used to follow all patients who underwent TAVI across two affiliated TAVI sites (i.e., Mater Misericordiae University Hospital and Mater Private Hospital) between February 2009 and August 2020. A computer-based database designed by Dendrite™ Clinical Systems (Reading, UK) was used to record all TAVI-
related data. A TAVI clinical nurse specialist (CNS) at each hospital (BM, SG, JB), with physician oversight (IC), held responsibility for maintaining the database. Clinical and procedural data was entered prospectively at the time of the TAVI procedure. Follow-up data was entered after each new follow-up interaction.

During follow-up, all patients diagnosed with TAVI-IE were identified prospectively in the database. For the current study, specific additional data were then acquired retrospectively from the patient’s clinical record to supplement the standard dataset.

The diagnosis of IE was made by consensus opinion of the Endocarditis team (which includes cardiologists, cardiothoracic surgeons, infectious disease consultant, microbiology consultant, and pharmacist) using clinical data, microbiological data, and multi-modality imaging. Baseline demographics, procedural characteristics, and clinical outcomes were compared between patients who developed IE (TAVI-IE) and those who did not (TAVI-NIE). Modified Duke criteria were retrospectively assessed for each TAVI-IE patient.

Ethical approval for this study was obtained from the Research Ethics Committee, Mater Misericordiae University Hospital, (Ref: 1/378/2247 TMR).

### Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD) or median [Q1; Q3]. Categorical data are presented as frequencies and percentages. Survival estimates were calculated using Kaplan–Meier curves and the difference in survival was assessed using a Cox model. Statistical significance was defined at a level of \( \alpha \leq 0.05 \). Unpaired Student’s \( t \) tests, chi-square tests, or Fisher exact test were used to detect clinical significance between independent variables in the TAVI-IE and TAVI-NIE cohorts. All analyses were performed with GraphPad Prism 8 (California, USA).

### Definitions

The risk of 30-day mortality was estimated using the Society of Thoracic Surgeons (STS) and updated EuroSCORE II risk assessment tools [8, 9]. Definitions for background medical conditions are in keeping with the Valve Academic Research Consortium-2 (VARC-2) criteria [10]. Early and late infective endocarditis were defined as any infective endocarditis occurring during or beyond the first 12 months after TAVI, respectively [3]. Early infective endocarditis was subdivided into peri-procedural (within 100 days) and early delayed (100 to 365 days after TAVI) [3].

### Results

A total of 733 patients underwent TAVI at the two clinical sites. During a follow-up of 1,949 person-years (median follow-up 28 months [IQR: 15–44 months]), infective endocarditis occurred in 17 patients (2.3%), with an overall incidence rate 0.87 per 100 person-years. The median time from TAVI to presentation with IE was 7 months [IQR: 5–13 months].

The incidence rate for early and late IE was 1.68 and 0.32 per 100 person-years, respectively. The peri-procedural period (195 person-years at risk) carried the highest incidence rate of 2.05 per 100 person-years, followed by the early delayed period (495 person-years at risk) with an incidence rate of 1.41 per 100 person-years.

### Baseline demographics (Table 1)

The mean age for patients who developed TAVI-IE was 78.7 ± 13.7 years and 70.5% were male. The baseline demographics were similar between the TAVI-IE and TAVI-NIE cohorts, except for a higher baseline creatinine clearance in the TAVI-IE group.

### Procedural characteristics (Table 2)

There was no significant difference in native valve morphology, TAVI access site, or procedural time between patients with and without TAVI-IE. There was a trend towards increased rates of TAVI-IE among those who underwent permanent pacemaker insertion following TAVI (17.6% vs. 5.86%; \( p = 0.08 \)).

### Clinical characteristics and echocardiographic features of TAVI-IE (Table 3)

According to modified Duke criteria, there were 6 (35.3%) definite and 11 (64.7%) possible cases of TAVI-IE, respectively. The most common symptom on presentation was fever (76.4%) and vascular phenomena were frequently recorded (29.4%). Dental extractions occurred in three (17.6%) cases during the month prior to presenting with IE. A single case (5.8%) required dental extraction for dental caries which was recognised following their presentation with TAVI-IE. Echocardiographic data revealed vegetations in 41.1% (\( n = 7 \)), aortic abscess in 17.6% (\( n = 3 \)) and aorto-atrial fistula in 5.8% (\( n = 1 \)) of cases. No echocardiographic valvular abnormality was seen in 29.4% (\( n = 5 \)) of cases.
Culprit microorganisms of TAVI-IE (Table 4)

Overall, 13 (76.4%) cases were blood culture positive. Streptococci were most frequently isolated (41.1%), followed by Enterococci and Staphylococci which were isolated with the same frequency (17.6%). Both cases of coagulase negative staphylococci occurred in the periprocedural period (<100 days) and all three enterococcus cases occurred in the early IE period (<365 days). Out of the four cases who underwent dental extractions, three isolated oral streptococcal spp. and one was culture negative. Additionally, the case of streptococcus infantarius (Streptococcus bovis) IE underwent subsequent colonoscopy which identified benign polyps and no colorectal malignancy.

Management and clinical outcomes of TAVI-IE (Table 3)

Overall, 88.2% of patients with TAVI-IE were successfully managed with medical therapy alone. There was one (5.8%) in-hospital death related to overwhelming sepsis despite urgent surgical intervention and one (5.8%) patient suffered a major stroke. There were no additional deaths in the first year following presentation. The Kaplan–Meier estimate for overall survival at 1 year was 82% (95% CI = 55–95%). The odds ratio (OR) of survival at 1 year for TAVI-IE versus TAVI-NIE showed no significant difference; OR 0.98 (95% CI 0.13–7.54).

During a mean follow-up of 2.9 ± 1.5 years, there were three additional deaths recorded in the TAVI-IE cohort;
causes of death included the following: end stage heart failure, advanced dementia, and Covid-19 pneumonitis, respectively. Of the TAVI-IE cohort alive at follow-up, ten (58.8%) were living at home, two (11.7%) living in long-term care facilities and one (5.8%) was lost to follow up.

Discussion

This study provides the first insight into the incidence, microbiological spectrum, and clinical outcomes among TAVI patients who developed IE at two tertiary referral centres in the Republic of Ireland. Compared to other large international registries, the incidence and time to presentation with TAVI-IE in this series was similar, with Streptococcus being the dominant culprit organism. In contrast to prior studies, the estimated mortality at 1 year was relatively low at 17.6%.

Incidence of TAVI-IE and consideration of Duke criteria

The overall incidence rate of 0.87 per 100 person-years in our patient cohort is in keeping with other large international registries which report rates of 0.3–2.1 per 100 person-years [1–7]. The considerable range in incidence rates is likely related to some studies including only “definite” IE according to the modified Duke criteria whereas, other studies, including ours, included cases of both “definite” and “possible” IE [5, 7, 11]. The inclusion of only “definite” IE may bias towards identifying fewer but potentially more severe cases. Moreover, the modified Duke criteria has not been validated for TAVI-IE and hence sensitivity may be limited [11, 12]. This was seen in the Swiss TAVI registry where only 63% of confirmed TAVI-IE cases met criteria for a “definite” diagnosis using the modified Duke criteria [3]. Finally, TAVI-IE may present with atypical IE manifestations and echocardiography can confer limited diagnostic yield due to prosthesis related artefacts and the frequent absence of overt vegetations [4, 11, 12].

Management and outcomes of TAVI-IE

The majority of the current TAVI-IE cohort were managed medically. This likely reflects the higher rate of less virulent Streptococcus species (as compared to Staphlococcus and enterococcus) as the culprit organism in the
cohort. In addition, the advanced age and comorbidity of a typical TAVI population likely result in a bias against surgical intervention for patients with TAVI-IE, leading to lower rates of surgical reintervention for TAVI-IE compared to the SAVR-IE population.

The 1-year estimate of one year survival of 82% in our TAVI-IE patient cohort is considerably higher than other large international registries (Table 5) [1–7]. The explanation for this difference is multifactorial but possible explanations include different spectrum of microbiological culprit species across series, the inclusion of a higher proportion of “possible” IE as per modified Duke criteria, and possibly earlier recognition and treatment of patients with TAVI-IE.

**Clinical implications**

Patients undergoing TAVI have proved just as vulnerable to IE as patients treated with SAVR [13, 14]. Hence, these patients warrant the same peri-operative assessment and post-operative advice on IE prophylaxis as those treated with SAVR [15–17].

In this cohort, seeding of oral microorganisms likely was responsible for four (23.5%) cases of IE in this cohort, based on the isolation of oral streptococcus species and/or the temporal relation of TAVI-IE to a dental extraction. Dental caries and procedures are recognised as a risk factor for TAVI-IE, similar to IE associated with SAVR [18–20]. When TAVI was initially applied in clinical practice, it was used typically in very elderly patients with very high surgical risk and limited prospects of long-term survival. Attention to dental care pre- and post-TAVI often did not meet the standards practiced by CT surgeons performing SAVR. Our data has reinforced the need to adopt surgical standards of dental clearance prior to all TAVI procedures and to reinforce the need maintaining daily dental hygiene practices and yearly dental review post-TAVI. Antibiotic prophylaxis is recommended for patients undergoing dental procedures that involve manipulation of gingival tissue or the peri-apical region of teeth, or perforation of oral mucosa including scaling and root canal procedures [15, 21]. These practices have even greater importance as TAVI is applied to younger and lower risk populations where patient survival is significantly prolonged compared the initial TAVI cohorts and the volumes of patients treated with TAVI are increasing dramatically. Yearly clinical follow-up post-TAVI should include a reiteration of these instructions for patients and their next of kin.

### Table 3: Clinical characteristics, echocardiographic features, and management of patients with TAVI-related infective endocarditis

| Clinical characteristics | N = 17 (%) |
|--------------------------|-----------|
| **Presenting symptoms**   |           |
| Fever                    | 13 (76.4) |
| Heart failure            | 7 (41.1)  |
| Delirium                 | 3 (17.6)  |
| Weight loss              | 3 (17.6)  |
| **Predisposition to IE** |           |
| New PPM                  | 3 (17.6)  |
| Dental extractions prior to presentation with IE | 3 (17.6) |
| Dental caries            | 1 (5.8)   |
| **Vascular phenomena**   |           |
| Intracerebral pseudoaneurysm/stroke | 1 (5.8) |
| Upper limb deep vein thrombosis | 1 (5.8) |
| Pulmonary embolism       | 1 (5.8)   |
| Discitis                 | 1 (5.8)   |
| Splenic infarcts         | 1 (5.8)   |
| **Echocardiographic findings** |       |
| Vegetation               | 7 (41.1)  |
| Aortic                   | 4 (23.5)  |
| Mitral                   | 3 (17.6)  |
| Tricuspid                | 1 (5.8)   |
| Pacemaker lead           | 1 (5.8)   |
| Normal                   | 5 (29.4)  |
| Aortic abscess           | 3 (17.6)  |
| New aortic regurgitation | 2 (11.7)  |
| New tricuspid regurgitation | 1 (5.8) |
| New mitral regurgitation | 1 (5.8)   |
| Aorto-atrial fistula     | 1 (5.8)   |
| **Management**           |           |
| Medical management       | 15 (88.2) |
| Urgent surgery           | 2 (11.7)  |
| SAVR + MV repair         | 1 (5.8)   |
| SAVR + TV repair + MV repair + fistula closure | 1 (5.8) |

IE infective endocarditis, PPM permanent pacemaker, Vascular phenomena, small or large vessel infective emboli, SAVR surgical aortic valve replacement, MV Mitral valve, TV tricuspid valve

### Table 4: Culprit microorganisms identified on blood cultures

| Culprit microorganism | N = 17 (%) |
|-----------------------|------------|
| Streptococci          | 7 (41.1)   |
| Strep mitis           | 2 (11.7)   |
| Strep salivarius      | 2 (11.7)   |
| Strep infantarius     | 1 (5.8)    |
| Strep gordonii        | 1 (5.8)    |
| Abiotrophia Defectiva | 1 (5.8)    |
| Enterococcus faecalis | 3 (17.6)   |
| Staphylococci         | 3 (17.6)   |
| Staph aureus          | 1 (5.8)    |
| Coagulase-negative staph | 2 (11.7) |
| Culture negative      | 4 (23.5)   |
Limitations

The data presented in this study should be interpreted within the inherent limitations of a registry-based study. Furthermore, our TAVI-IE cohort is small hence caution should be exercised when interpreting clinical outcomes. Adjudication of the diagnosis of infective endocarditis was based on the consensus decision of the Endocarditis team which may be imperfect.

Conclusions

In this prospective cohort of patients undergoing TAVI at a tertiary TAVI centre in Ireland, we found a similar incidence and time to presentation compared to prior international TAVI-IE registries. However, the 1-year mortality rate of 17.6% was lower than previously reported. The need for rigorous dental clearance pre-TAVI and maintenance of dental health after TAVI is underscored by the high prevalence of oral streptococcus species in this patient cohort.

Declarations

Conflict of interest The authors declare no competing interests.

References

1. Allen CJ, Patterson T, Chehab O et al (2020) Incidence and outcomes of infective endocarditis following transcatheter aortic valve implantation. Expert Rev Cardiovasc Ther 18(10):653–662. https://doi.org/10.1080/14779072.2020.1839419. Epub 2020 Dec 1 PMID: 33073603
2. Fauchier L, Bisson A, Herbert J et al (2020) Incidence and outcomes of infective endocarditis after transcatheter aortic valve implantation versus surgical aortic valve replacement. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis 26(10):1368–1374
3. Stortecky S, Heg D, Tueller D et al (2020) Infective endocarditis after transcatheter aortic valve replacement. J Am Coll Cardiol 75(24):3020–3030
4. Bjursten H, Rasmussen M, Nozohoor S et al (2019) Infective endocarditis after transcatheter aortic valve implantation: a nationwide study. Eur Heart J 40(39):3263–3269
5. Butt JH, Ihlemann N, De Backer O et al (2019) Long-term risk of infective endocarditis after transcatheter aortic valve replacement. J Am Coll Cardiol 73(13):1646–1655
6. Kolte D, Goldsweig A, Kennedy KF et al (2018) Comparison of incidence, predictors, and outcomes of early infective endocarditis after transcatheter aortic valve implantation versus surgical aortic valve replacement in the United States. Am J Cardiol 122(12):2112–2119
7. Regueiro A, Linke A, Latib A et al (2016) Association between transcatheter aortic valve replacement and subsequent infective endocarditis and in-hospital death. JAMA 316(10):1083–1092
8. Ad N, Holmes SD, Patel J et al (2016) Comparison of EuroSCORE II, original EuroSCORE, and the society of thoracic surgeons risk score in cardiac surgery patients. Ann Thorac Surg 102(2):573–579
9. Nashef SAM, Roques F, Sharples LD et al (2012) EuroSCORE II. Eur J Cardiothorac Surg 41(4):734–745
10. Kappetein AP, Head SJ, Genereux P et al (2013) Updated standardized endpoint definitions for transcatheter aortic valve implantation: the valve academic research consortium-2 consensus document. J Thorac Cardiovasc Surg 145(1):6–23
11. Olsen NT, De Backer O, Thyregod HG et al (2015) Prosthetic valve endocarditis after transcatheter aortic valve implantation. Circ Cardiovasc Interv 8(4):e001939. https://doi.org/10.1161/CIRCINTERVENTIONS.114.001939. PMID: 25873728
12. Li JS, Sexton DJ, Mick N et al (2000) Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis 30:633–638
13. Moriyama N, Laakso T, Biancari F et al (2019) Prosthetic valve endocarditis after transcatheter or surgical aortic valve replacement with a bioprosthesis: results from the FinnValve Registry. EuroIntervention 15(6):e500–e507
14. Summers MR, Leon MB, Smith CR et al (2019) Prosthetic valve endocarditis after TAVR and SAVR: insights from the PARTNER trials. Circulation 140(24):1984–1994
15. Habib G, Lancellotti P, Antunes MJ et al (2015) 2015 ESC guidelines for the management of infective endocarditis: the task force for the management of infective endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European. Eur Heart J 36(44):3075–3128
16. Nishimura RA, Otto CM, Bonow RO et al (2017) 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 135(25):e1159–e1195
17. Centre for Clinical Practice at NICE (UK) (2008) Prophylaxis against infective endocarditis in adults and children undergoing interventional procedures. London: National Institute for Health and Clinical Excellence (UK). (NICE Clinical Guidelines, No. 64.)
18. Carasso S, Amy DPB, Kusniec F et al (2019) Dental screening prior to valve interventions: should we prepare transcatheter aortic valve replacement candidates for “surgery”? Int J Cardiol 1(294):23–26. https://doi.org/10.1016/j.ijicard.2019.07.081. Epub 2019 Jul 26 PMID: 31378381
19. Silvestre FJ, Gil-Raga I, Martinez-Herrera M et al (2017) Prior oral conditions in patients undergoing heart valve surgery. J Clin Exp Dent 9(11):e1287–e1291. https://doi.org/10.4317/jced.53902. PMID:29302279;PMCID:PMC5741840
20. Lockhart P, DeLong H, Lipman R et al (2019) Effect of dental treatment before cardiac valve surgery. J Am Dent Assoc 150(9):739-747.e9
21. Horstkotte D, Follath F, Gutschik E et al (2004) Task Force Members on Infective Endocarditis of the European Society of Cardiology; ESC Committee for Practice Guidelines (CPG); Document Reviewers. Guidelines on prevention, diagnosis and treatments of infective endocarditis executive summary; the task force on infective endocarditis of the European society of cardiology. Eur Heart J 25:267–276

Publisher’s Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.