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## Surgical treatment of transcatheter aortic valve infective endocarditis

P. G. Malvindi · S. Luthra · S. Sarvananthan · A. Zingale · C. Olevano · S. Ohri

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**Abstract** There is growing interest in infections occurring after transcatheter aortic valve implantation (TAVI). The incidence, and clinical and anatomical features suggest many similarities with prosthetic valve endocarditis. The survival of patients with an infected TAVI prosthesis is generally poor; however, only a minority of them (10%) have undergone treatment with surgical explantation of the infected prosthesis. A literature search was performed using online databases. Papers reporting surgical treatment of TAVI prosthesis infections were retrieved, focusing on pre- and intraoperative characteristics and early outcome. Thirty-seven papers ultimately provided information on 107 patients. Their mean  $\pm$  standard deviation (SD) age was  $76 \pm 8$  years and 72% were male. The mean  $\pm$  SD time interval between the TAVI procedure and reoperation was  $10 \pm 10$  months. Annular abscess formation was described in 34% of cases and mitral valve involvement in 31%. All patients underwent TAVI prosthesis explantation and surgical aortic valve replacement; concomitant mitral valve replacement was necessary in 22% of cases. Postoperative in-hospital mortality was 28%. Surgical explantation of infected TAVI prostheses was associated with a high postoperative mortality, although these initial experiences included elderly and high-risk patients. Considering the expansion of TAVI procedures towards younger and lower-risk patients,

surgical treatment of TAVI endocarditis may represent the best option for a life-saving procedure.

**Keywords** TAVI · endocarditis · aortic valve · reoperation · aortic valve replacement

### Introduction

Infective endocarditis is still associated with high mortality and morbidity rates [1, 2]. Contemporary population surveys reported an annual incidence of 3–7 per 100,000 person-years [3–5]. Prosthetic valve endocarditis is associated with a much higher risk of 0.3–1.2% per patient-year [6–10]. Substantial heterogeneity exists between studies due to differences in population characteristics, risk profile, predisposing factors, microbiological diagnosis and different definitions of infective endocarditis [11–15]. Studies with a longer follow-up time in which large cohorts of patients were analysed, showed that infective endocarditis is not uncommon and reported a cumulative incidence of TAVI prosthesis infection of 5% during the first 5 years [12, 16, 17]. Several risk factors have been associated with TAVI endocarditis [13–15, 18–20], and alternative imaging tools have been proposed for a prompt and correct diagnosis [11, 14, 21]. Robust evidence for effective treatment strategies that improve the prognosis is still lacking despite a better understanding of the incidence, causes and means of prevention [22].

Most patients with TAVI endocarditis (90%) receive conservative management, resulting in a dismal early outcome with high in-hospital mortality and poor short-term survival [11, 13, 14]. Surgical treatment with explantation of the TAVI prosthesis has not shown superior survival. Experience with treatment remains limited, and most patients are deemed inoperable or at excessive surgical risk in an elective

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P. G. Malvindi (✉) · S. Luthra · S. Sarvananthan · A. Zingale · C. Olevano · S. Ohri  
Wessex Cardiothoracic Centre, University Hospital  
Southampton, Southampton, UK  
[pg.malvindi@hotmail.com](mailto:pg.malvindi@hotmail.com)



setting [13, 18, 23]. Expanding indications to include intermediate- to low-risk patients for TAVI mandate a better understanding of the treatment of TAVI endocarditis, comparison of medical versus surgical options and well-defined treatment pathways.

The aim of our study was to review the patient characteristics, microbiology, underlying causes and outcomes of patients who underwent explantation of TAVI valves due to infective endocarditis.

## Methods

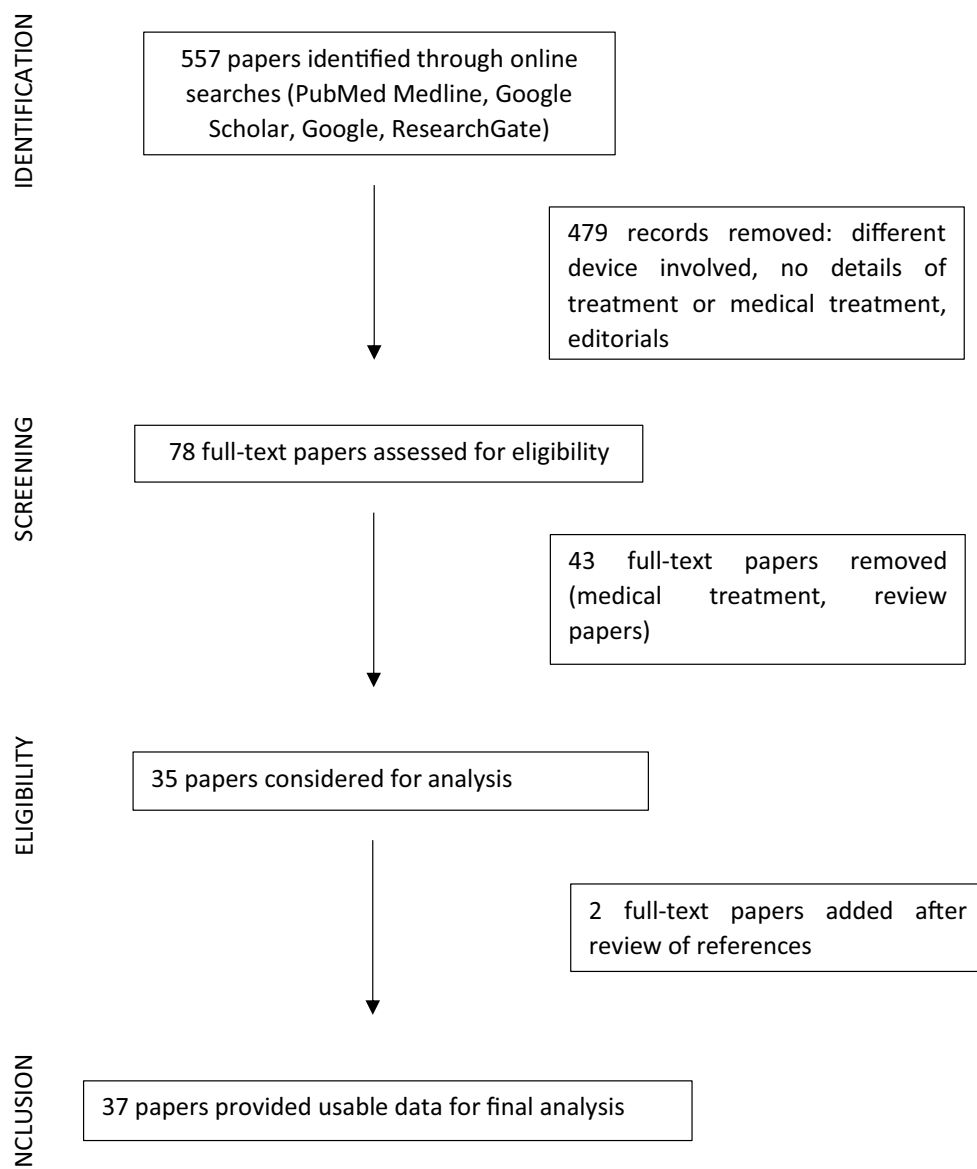
### Literature search

A literature search was performed using online databases and web-based search engines (PubMed, Google Scholar, Google, ResearchGate) to obtain research articles about infection of TAVI prostheses. The following keywords were used: ‘TAVI’, ‘transcatheter aor-

tic valve’, ‘TAVR’, ‘infection’, ‘endocarditis’, ‘explant’, ‘explantation’ and ‘retrieval’.

Two independent reviewers (SS and AZ) identified and assessed the studies for eligibility. We applied the following inclusion criteria: (1) study in adult human subjects who underwent TAVI prosthesis explantation due to infective endocarditis; (2) paper reporting results of TAVI prosthesis explantation due to infective endocarditis; (3) paper written in English; (4) no restriction regarding the date of publication (last search performed in June 2020); and (5) no restriction regarding type of prosthesis. Exclusion criteria were: (1) study in adult human subjects and paper reporting results of TAVI endocarditis treated conservatively; (2) study in adult human subjects and paper reporting results of TAVI endocarditis treated with interventional procedure; and (3) paper not reporting details of patient characteristics or outcomes. All differences

**Fig. 1** Flowchart of literature search strategy, according to rules specified by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)



of opinion and divergences were resolved by consensus after discussion with a third reviewer (PGM).

Eligible full-text papers were cross-referenced, and patient characteristics of interest and relevant outcomes were extracted from the included studies. Extracted data included the following:

- Number of patients, type of prosthesis, and interval time between TAVI implantation and explantation;
- Patient characteristics: age, gender, previous cardiac surgery, clinical presentation, result of cultures, risk score, presence of vegetation(s), presence of annular abscess, involvement of mitral valve, associated complications and type of surgical operation performed;
- Outcomes: in-hospital mortality, details of postoperative course and survival.

Patient characteristics are presented as mean  $\pm$  standard deviation, median (range), or number and percentage. Fig. 1 represents a search flowchart that was created according to the rules specified by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [24]. The PRISMA checklist, including the PubMed search, can be found in the Electronic Supplementary Material.

## Results

### Study selection

A total of 557 papers were screened and, after removal of 479 records, 78 full-text papers were assessed for eligibility. We cross-referenced reports to include any missed studies. Finally, 37 papers (7 series and 30 case reports) provided data on 107 patients, who were included in the study (Fig. 1). A summary of the studies is included in Tab. 1 in the Electronic Supplementary Material.

### Preoperative characteristics

The mean age was  $76 \pm 8$  years. Most patients were male (72%). A previous cardiac operation was per-

formed in 15% of the cases. For 64 patients, the interval time between the TAVI procedure and the reoperation was provided: the mean time was  $10 \pm 10$  months (median 8 months; range 1–52).

Clinical presentation was characterised by persistent fever or sepsis in 74% of cases and by refractory heart failure in 26%. Embolic complications were described in 35% of cases. Echocardiographic evidence of infection was most commonly seen as vegetations (65%), annular abscess (34%) and additional mitral valve involvement (31%). Tab. 1 in the Electronic Supplementary Material details the preoperative, operative and outcome data available for all full-text papers included in the final analysis. The most common organisms were coagulase-positive staphylococci, streptococci and enterococci; no growth was observed in 5% of cases. Details regarding microbiological findings are reported in Tab. 1.

### Surgical treatment and early outcome

All patients underwent TAVI prosthesis explantation and surgical aortic valve replacement; Tab. 2 shows details of the type of TAVI prosthesis. Associate procedures were annular patch reconstruction in 11% of cases, aortic root replacement in 13% and mitral valve replacement in 22% (Tab. 1 in the Electronic Supplementary Material).

Overall postoperative in-hospital mortality was 28%; this percentage was 22% for patients who had not undergone a previous cardiac operation and 33% for patients who needed a redo cardiac procedure. Follow-up data were provided in 12 papers; in the series of 20 patients by Mangner et al. [23], the mortality rate through the first year after surgery was 15%. Eleven case reports reported survival data, with 10 patients being alive at a median time of 12 months (range 6–45).

**Table 1** Microbiological findings<sup>a</sup>

Microorganism	Frequency (%)
<i>Staphylococcus</i> spp	33
– Coagulase-positive/ <i>S. aureus</i>	18
– Coagulase-negative	16
<i>Streptococcus</i> spp	24
<i>Enterococcus</i> spp	23
Fungi	7
<i>Corynebacterium</i> spp	3
Other Gram-positive bacteria	2
Other Gram-negative bacteria	2
Negative	5

<sup>a</sup>Data available for 61/107 patients

**Table 2** Details of TAVI prostheses<sup>a</sup>

Type of valve	Frequency (%)
Balloon-expandable	68
– Sapien	30
– Sapien XT	15
– Sapien 3	12
– Lotus	1
– Not defined	8
Self-expandable	32
– CoreValve	15
– Jena Valve	2
– Symetis	2
– Portico	1
– Not defined	12

TAVI transcatheter aortic valve implantation  
<sup>a</sup>Data available for 59/107 patients

## Discussion

Infection of TAVI prostheses is not uncommon, with a reported incidence of 0.5–1.6% per year in populations followed up to 5 years; the concomitant survival rate is 40–50% [12, 54–56]. Review papers [18, 57, 58] and analyses of national and international registries [11–14, 16] have started delineating the common features of TAVI prosthesis infection and have ultimately highlighted two important findings: patients with TAVI endocarditis suffer a dismal early outcome with a mortality of 40–70% at 1 year after the diagnosis, and surgical explantation of the infected prosthesis was performed in only 2–14% of cases despite clear indications for surgical intervention in more than 80% of patients [11, 13, 14, 16, 41, 59].

Reasons for not operating include a remarkably high clinical or surgical risk, need for additional procedures, advanced age of the patient and limited life expectancy, multiorgan failure, septicaemia and dismal long-term prognosis. Within the limitations of including small series and case reports, we found an early survival rate of more than 70% after surgical retrieval of infected TAVI prostheses. Early postoperative mortality is strictly associated with the risk profile of these patients (active infection, age, 15% needing a redo procedure) and, as per initial TAVI practice, with the coexistence of unfavourable clinical or anatomical features for conventional surgical aortic valve replacement, making these patients already at a high risk for isolated aortic valve disease in an elective setting. Local complications are also common in TAVI endocarditis, as we found evidence of periannular abscess formation and mitral involvement in more than one third of the patients. These findings confirm previous observational studies reporting periannular abscess and mitral valve involvement in about 12–25% and 22–25% of patients with TAVI endocarditis, respectively [11, 58]. A similar rate of periannular complications has been reported for surgical aortic prosthesis infective endocarditis, with 50–60% of patients presenting with an annular abscess, a fistula or a false aneurysm [60]. These cases represent a medical and technical challenge, as they are associated with a more severe or advanced infective process and require a complex surgical repair; we showed that a full root replacement was performed in 13% of cases and mitral valve surgery was required in 22% of patients.

The microorganisms involved in the infective process were the common pathogens found in elderly populations. Both staphylococci and streptococci were isolated in about 30% of cases and *Enterococcus* was found in one-fourth of the patients. These results fully align with previous findings in patients with TAVI infective endocarditis [11, 16, 58, 59].

Follow-up data were provided in 12 out of the 37 papers included in our analysis. The only series reporting the 1-year survival showed 15% of post-discharge

mortality during the first year [23]. Two previous studies compared the survival of patients with TAVI endocarditis who received medical therapy vs surgical operation [18, 23]. Those who underwent medical treatment were older, had a higher Society of Thoracic Surgeons score and more often had severe chronic kidney disease. On the other side, patients who were treated with TAVI prosthesis retrieval and surgical aortic valve replacement more frequently presented with significant aortic regurgitation, annular abscess and mitral valve involvement. No statistical differences were found in terms of mortality and survival between the two treatment options, a result which was confirmed after comparison of matched populations [23]. However, the follow-up time was limited to 3 months [18], and 12 months [23]. Patients operated for surgical prosthetic valve infective endocarditis usually sustain a non-negligible rate of mortality in the early postoperative period, but during the first year, a drop in survival curves is usually seen due to infection relapse or lack of recovery. A longer follow-up period may show a larger difference in survival curves in favour of surgical explantation of the TAVI prosthesis.

## Study limitation

The main limitation of this review is the inclusion of small series and case reports, which could have biased this initial picture of surgical treatment for TAVI prosthesis infection. Long-term survival data were lacking in most case series. Collation and assimilation of data on individual outcomes and a formal meta-analysis could not be carried out, making it difficult to draw meaningful conclusions regarding the effectiveness of the surgical approach. However, we do not believe that our results are far different from reality. They seem to be in line with the more robust findings coming from surgery for infected aortic valve prostheses, for which, due to technical and medical challenges, we could expect an in-hospital mortality rate up to 15–20% [64–66]. Furthermore, a recent preliminary analysis of the Society of Thoracic Surgeons database reported a similar postoperative in-hospital mortality (29.3%) in patients who underwent TAVI prosthesis retrieval and surgical aortic valve replacement for infective endocarditis (oral presentation at 2020 ACC World Congress of Cardiology [67]).

The main reason for denying a surgical procedure in almost 90% of patients with a TAVI prosthesis infection is probably the previous decision to avoid a conventional operation in favour of a transcatheter procedure and the coexistence of important clinical comorbidities and/or anatomical difficulties. Patients' age could have played an important role as well, but the low survival rate registered after medical therapy suggests maximising the effort in providing a surgical solution. The majority of patients requiring TAVI prosthesis explantation would also not need a redo sternotomy; thus, they would have a lower risk of re-

entry complications and bleeding than patients with a previously implanted surgical prosthesis. Local aggressiveness of the infective process results in perianular abscess formation and, more importantly, in the involvement of the anterior mitral valve leaflet and the occurrence of new mitral regurgitation. This last issue is a peculiar finding in TAVI endocarditis and, rather than being considered a further operative risk factor, should result in a prompt indication for a surgical operation.

## Conclusion

The surgical treatment of TAVI infective endocarditis is associated with a high in-hospital mortality rate. However, these initial experiences included elderly and high-risk patients presenting with local and systemic infective complications and often requiring a complex surgical repair. Despite the medical and technical challenges associated with this disease, a radical and prompt surgical treatment with the resolution of sepsis and heart failure can provide acceptable mid-term outcomes and could be the best option for a life-saving procedure.

**Conflict of interest** P.G. Malvindi, S. Luthra, S. Sarvananthan, A. Zingale, C. Olevano and S. Ohri declare that they have no competing interests.

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