



doi: 10.21037/acs-2024-etavr-0103

**Cite this article as:** Fukuhara S, Suzuki T, Deeb GM, Ailawadi G, Patel HJ, Yang B, El-Dalati S. Surgical management is associated with improved survival for endocarditis after transcatheter aortic valve replacement. *Ann Cardiothorac Surg* 2024. doi: 10.21037/acs-2024-etavr-0103

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# Surgical management is associated with improved survival for endocarditis after transcatheter aortic valve replacement

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**Background:** Prosthetic valve endocarditis is a rare yet devastating complication following transcatheter aortic valve replacement (TAVR). This study aims to investigate the outcomes of surgical versus medical management of post-TAVR endocarditis.

**Methods:** Between 2011 and 2024, 67 patients with post-TAVR endocarditis were identified, comprising 24 (35.8%) patients managed surgically and 43 (64.2%) managed medically. All cases were reviewed by our multidisciplinary endocarditis team to determine the optimal treatment strategy.

**Results:** The overall incidence of post-TAVR endocarditis was 1.4%. The number of endocarditis cases increased over time from 1–2 in 2015–2018 to 18 in 2023. The most frequent source of endocarditis was unknown (32.8%), and the predominant causative organism was enterococcus species (25.4%). Notably, among the 43 medically managed patients, 19 (44.2%) exhibited surgical indications, predominantly due to large vegetations with or without embolic complications (n=11; 57.9%). The medical management group had a higher proportion of females and more frequent use of self-expandable valves compared to the surgical group. The time interval between TAVR and endocarditis diagnosis was similar across both groups. In the surgically managed cohort, isolated aortic valve replacement was uncommon, with most patients undergoing complex TAVR explantations coupled with concomitant procedures, most frequently aortic root repair (n=11; 45.8%). The 30-day and 1-year mortality rates for the three groups (surgical, medical without surgical indications, and medical with surgical indications) were 0%, 4.2%, and 31.6% (P=0.002), and 4.2%, 20.8%, and 73.7% (P<0.001), respectively.

**Conclusions:** Surgical management was associated with significantly improved survival compared to medical management for post-TAVR endocarditis. The poor clinical outcomes in the medically managed group were primarily due to patients who did not undergo surgery despite having surgical indications. Prudent clinical judgment and timely surgical intervention when indicated are critical to enhancing the overall clinical outcomes of this challenging condition.

**Keywords:** transcatheter aortic valve replacement (TAVR); surgical aortic valve replacement (SAVR); prosthetic valve endocarditis; aortic root abscess

Submitted Jul 18, 2024. Accepted for publication Oct 01, 2024. Published online Nov 12, 2024.

doi: 10.21037/acs-2024-etavr-0103

View this article at: <https://dx.doi.org/10.21037/acs-2024-etavr-0103>

## Introduction

Transcatheter aortic valve replacement (TAVR) is an established alternative to surgical aortic valve replacement (SAVR) for patients with severe aortic stenosis and suitable

anatomy (1-4). With the substantial growth in TAVR usage, previously unrecognized issues have been gradually revealed, including the excessive risk of reoperations after TAVR (5), challenges related to redo-TAVR and coronary

re-access (6), and endocarditis (7). Endocarditis is a rare but devastating complication of TAVR, with an incidence reported to range from 0.5% to 4.4% (8-12) and a 1-year mortality rate as high as 75%. Notably, the vast majority of post-TAVR endocarditis patients in prior studies were treated nonoperatively (11,13,14). Furthermore, previous investigations have predominantly relied on registry-based studies lacking granular data. Two recent registry studies, each with an extremely small number of surgically managed patients and lacking detailed clinical data, indicated that surgery was not associated with improved survival compared to medical management (13,14). These study results may mislead timely selection of optimal management practices for TAVR endocarditis. The concern for possible amplified risk of reoperation after TAVR and the lack of evidence on surgical management underscore the importance of addressing this knowledge gap. The objective of this study is to elucidate the implications of timely surgical and medical management for post-TAVR endocarditis, guide future management recommendations, and improve clinical outcomes for this challenging condition.

## Methods

The University of Michigan Institutional Review Board approved all aspects of the study (HUM00190884; approved on August 6th, 2020). The approval included a waiver of informed consent.

### Patients and study design

We retrospectively reviewed 2,659 consecutive patients who underwent TAVR at our institution between July 8th, 2011, and December 30th, 2023. Four patients with intraoperative death and five patients with intraoperative SAVR conversion were excluded. Among these, 38 (1.4%) patients were diagnosed with endocarditis. Additionally, 29 patients who received a TAVR procedure at a different center were admitted to our institution for endocarditis. We retrospectively reviewed the clinical details of these 67 patients with post-TAVR endocarditis, comprising 24 (35.8%) patients with surgical management and 43 (64.2%) patients with medical management, who were hospitalized at University of Michigan Hospital between January 2015 and June 2024. Therefore, the observation period of the study groups was between 2015 and 2024, while all original TAVR implantation procedures were performed between 2011 and 2023. The flow diagram of the patient cohort

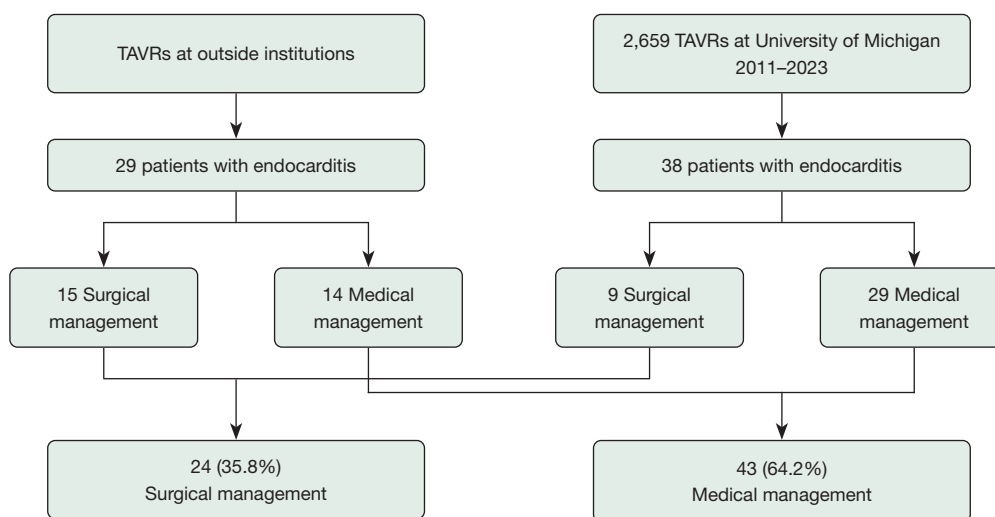
is summarized in *Figure 1*. All patients were reviewed by our multidisciplinary endocarditis team (15) for treatment options. Abstracted data included the following: patient demographic, clinical, and treatment variables, perioperative and follow-up adverse events, and survival.

The details of endocarditis diagnosis are described elsewhere (16). In brief, the Modified Duke Criteria were used for the diagnosis of endocarditis. Only definite endocarditis cases, which included a combination of clinical, microbiological, and echocardiographic findings, were included in the study. This diagnosis requires the presence of at least two major criteria, one major and three minor criteria, or five minor criteria. Major criteria include positive blood cultures with typical microorganisms consistent with infective endocarditis and evidence of endocardial involvement seen in echocardiographic imaging, such as vegetations, abscesses, or new valvular regurgitation. Minor criteria encompass predisposing heart conditions or intravenous drug use, fever, vascular phenomena, immunologic phenomena, and microbiological evidence not meeting major criteria (16).

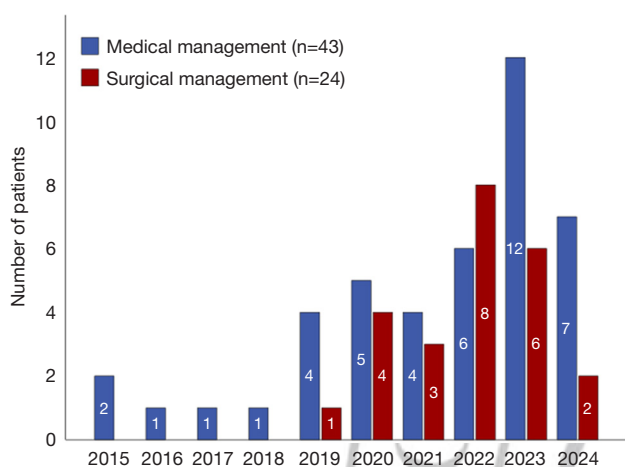
Surgical indications are in accordance with consensus guidelines (17). In brief, surgical intervention is indicated in several clinical scenarios; (I) severe valve dysfunction that cannot be managed with medical management alone; (II) persistent bacteremia or fungal infection that does not respond to appropriate antimicrobial therapy; (III) the presence of perivalvular extension complications such as abscesses, fistulas, or pseudoaneurysms around the TAVR valve; (IV) new complete heart block; (V) endocarditis relapse despite treatment completion; (VI) embolic events such as strokes or other systemic emboli, despite adequate antimicrobial therapy; (VII) >10 mm mobile vegetations; (VIII) evidence of other native or prosthetic valve involvement with associated complications.

### Statistical analysis

Continuous variables are expressed as mean  $\pm$  standard deviation for normally distributed variables and medians with interquartile range (IQR) for non-normally distributed variables. Categorical variables are presented as proportion and absolute number. Differences between groups were detected using the  $\chi^2$  test or Fisher's exact test for categorical variables and Student's *t*-test or Mann-Whitney *U* test for continuous variables. Survival data was depicted using the Kaplan-Meier method and the log-rank test with corresponding 95% confidence intervals (CIs). The date of



**Figure 1** Flow diagram of patient cohort. TAVRs, transcatheter aortic valve replacements.



**Figure 2** Trends of post-TAVR endocarditis cases by year. TAVR, transcatheter aortic valve replacement.

the endocarditis diagnosis was set as day 0 for the survival curves. A P value of  $<0.05$  was considered statistically significant. All P values were the result of 2-tailed tests. The statistical analyses were performed using SPSS 28.0 (IBM-SPSS Inc., Armonk, NY, USA) and Stata 14.2 (StataCorp, College Station, TX, USA).

## Results

### Patient demographics

The number of post-TAVR endocarditis cases increased over time from 1–2 in 2015–2018 to 18 in 2023. All patients were

medically managed until 2018, with surgical management appearing in 2019 (Figure 2). Patient demographics and baseline clinical characteristics are shown in Table 1. Patients in the medical management group were more likely female and more frequently had a self-expandable valve than those in the surgical group. Additionally, there was a trend towards older age in the medical management group. The time interval between TAVR and endocarditis diagnosis was similar between groups. Notably, 41.7% and 32.6% of patients in the surgical and medical management groups had a permanent pacemaker at baseline.

Among the medically managed patients, 19 (44.2%) demonstrated surgical indications, most commonly due to large vegetation with or without embolic complications ( $n=11$ ; 57.9%). Other common indications included severe valvular dysfunction ( $n=3$ ; 15.8%), other prosthetic valve infection ( $n=3$ ; 15.8%), and persistent bacteremia despite antibiotic usage ( $n=3$ ; 15.8%). Six (31.6%) patients in the medical management group did not undergo surgical intervention due to embolic disabling stroke from the infected TAVR valve and subsequent debilitation of the patient's condition. Other reasons for continued medical management despite meeting surgical criteria included excessive surgical risk ( $n=11$ ; 57.9%) and patient refusal ( $n=2$ ; 10.5%).

### Source of endocarditis and causative microorganisms

The most common source of endocarditis was unknown in 41.7% and 27.9% of patients in the surgical and medical

Table 1 Patient demographics			
Variables	Surgical management (n=24)	Medical management (n=43)	P value
Age (years)	71 [60–81]	76 [68–83]	0.063
Time interval between TAVR implant and endocarditis diagnosis (days)	367 [97–1,056]	285 [135–1,099]	0.91
TAVR valve type			0.040*
Balloon-expandable valve	14 (58.3)	14 (32.6)	
Self-expandable valve	10 (41.7)	29 (67.4)	
TAVR valve size (mm)	29 [26–29]	29 [26–34]	0.15
Female gender	3 (12.5)	17 (39.5)	0.020*
Dyslipidemia	19 (79.2)	29 (67.4)	0.31
Diabetes	15 (62.5)	19 (44.2)	0.15
Coronary artery disease	9 (37.5)	20 (46.5)	0.48
Chronic kidney disease	16 (66.7)	22 (51.2)	0.22
Dialysis dependent	5 (20.8)	8 (18.6)	0.83
Chronic atrial fibrillation	13 (54.2)	22 (51.2)	0.81
COPD	6 (25.0)	7 (16.3)	0.39
History of stroke	6 (25.0)	5 (11.6)	0.16
Pulmonary hypertension	4 (16.7)	6 (14.0)	0.77
Permanent pacemaker	10 (41.7)	14 (32.6)	0.45
Previous sternotomy	9 (37.5)	10 (23.3)	0.22
SAVR	4 (44.4)	2 (20.0)	0.35
Aortic root repair	3 (33.3)	3 (30.0)	1.00
CABG	1 (11.1)	3 (30.0)	0.58
Mitral repair/replacement	1 (11.1)	2 (20.0)	1.00
Source of endocarditis			
Unknown	10 (41.7)	12 (27.9)	0.25
Oral	6 (25.0)	3 (7.0)	0.060
Skin	2 (8.3)	6 (14.0)	0.70
Gastrointestinal tract	0	8 (18.6)	0.043*
Spinal infections (discitis/osteomyelitis)	2 (8.3)	1 (2.3)	0.29
Other osteomyelitis	0	5 (11.6)	0.15
Urinary tract infection	0	5 (11.6)	0.15
Dialysis line infection	3 (12.5)	3 (7.0)	0.66
Peritoneal dialysis catheter infection	1 (4.2)	0	0.36

Table 1 (continued)

Table 1 (continued)

Variables	Surgical management (n=24)	Medical management (n=43)	P value
Presence of surgical indications <sup>†</sup>	24 (100.0)	19 (44.2)	<0.001*
Valvular dysfunction	12 (50.0)	3 (15.8)	0.026*
Large vegetation with or without embolic phenomenon	7 (29.2)	11 (57.9)	0.058
Aortic root abscess	8 (33.3)	2 (10.5)	0.15
Other valve/prosthetic infection	3 (12.5)	3 (15.8)	1.00
Persistent bacteremia	3 (12.5)	3 (15.8)	1.00
Fungal infection	0	1 (5.3)	0.44
Complete heart block	2 (8.3)	0	0.50
Reasons for no surgical management			
Neurological complications	N/A	6 (31.6)	N/A
Patient sickness	N/A	11 (57.9)	N/A
Patient refusal	N/A	2 (10.5)	N/A

Variables are expressed as numbers (percentages) or medians [IQR], as appropriate. <sup>†</sup>, some patients had more than one reason. Therefore, the sum of all percentages is greater than 100%; \*, indicates statistically significant (P<0.05). TAVR, transcatheter aortic valve replacement; COPD, chronic obstructive pulmonary disease; SAVR, surgical aortic valve replacement; CABG, coronary artery bypass grafting; N/A, not applicable; IQR, interquartile range.

management groups, respectively. An oral source was more common in the surgical group, while a gastrointestinal tract source was more common in the medical management group.

Causative organisms in each group are summarized in Table 2. Staphylococcus species (37.5%) were the most common microorganisms in the surgical management group. In contrast, among patients with medical management, enterococcus species were the most frequent causal microorganisms (30.2%), followed by streptococcus (20.9%) and staphylococcus species (20.9%).

### Operative data

The operative data is summarized in Table 3. The interval between endocarditis diagnosis and surgical intervention was 13 (IQR, 9–19) days. Isolated SAVR was performed only in 3 (12.5%) patients, and the majority of patients underwent concomitant procedures. The most common concomitant procedure was aortic root repair (n=11; 45.8%), consisting of total root repair (n=6) and partial root repair (n=5). All patients with preoperative permanent pacemakers (n=10; 41.7%) underwent device and lead extraction. Despite the high complexity of these reoperations, there was no in-

hospital mortality or newly diagnosed stroke. Two (10.5%) patients developed renal failure requiring dialysis, and both demonstrated eventual renal recovery. The length of stay was 14 (IQR, 11–20) days in patients with surgical management.

### Follow-up

The Kaplan-Meier survival curve showed the estimated 1-year survival to be 94.4%±5.4% and 50.1%±8.3% in the surgical and medical management groups, respectively (P<0.001) (Figure 3). Furthermore, the medical management group was stratified into medical management without surgical indications (n=24) and with surgical indications (n=19). A subgroup analysis among the three groups (surgical management group, medical management without surgical indications, and medical management with surgical indications) showed that the 30-day and 1-year mortality rates were 0%, 4.2%, and 31.6% (P=0.002) and 4.2%, 20.8%, and 73.7% (P<0.001), respectively (Figure 4). Furthermore, 3 out of 5 survivors in the medical management with surgical indications subgroup suffered severe valvular dysfunction needing valve interventions. One patient has already undergone redo-TAVR and 2 other

**Table 2** Identified causative organisms in each group

Organisms	Surgical management (n=24)	Medical management (n=43)	P value
Enterococcus species	4 (16.7)	13 (30.2)	0.22
<i>Enterococcus faecalis</i>	3	12	
Vancomycin-resistant <i>Enterococcus faecium</i>	1	1	
Staphylococcus species	9 (37.5)	9 (20.9)	0.14
<i>Staphylococcus lugdunensis</i>	1	0	
Methicillin-sensitive <i>Staphylococcus aureus</i>	5	5	
Methicillin-resistant <i>Staphylococcus epidermidis</i>	2	1	
Methicillin-resistant <i>Staphylococcus aureus</i>	1	3	
Streptococcus species	7 (29.2)	9 (20.9)	0.45
Group B streptococcus	1	2	
Group G streptococcus ( <i>dysgalactiae equisimilis</i> )	0	1	
<i>Streptococcus anginosus</i>	0	1	
<i>Streptococcus bovis</i>	0	2	
<i>Streptococcus mutans</i>	1	0	
<i>Streptococcus oralis</i>	0	1	
<i>Streptococcus gallolyticus</i>	1	0	
<i>Streptococcus viridans</i>	2	1	
<i>Streptococcus sanguinis</i>	2	1	
Gram negative species	1 (4.2)	5 (11.6)	0.41
<i>Pseudomonas</i>	0	1	
<i>Klebsiella</i>	0	1	
<i>Haemophilus parainfluenzae</i>	1	0	
<i>Escherichia coli</i>	0	3	
Culture-negative	3 (12.5)	5 (11.6)	0.92
Fungal	0	1 (2.3)	1.00
<i>Candida</i>	0	1	
Others	0	1 (2.3)	1.00
<i>Corynebacterium</i>	0	1	

Variables are expressed as numbers (percentages) or numbers.

patients will be undergoing surgical interventions in the near future.

## Discussion

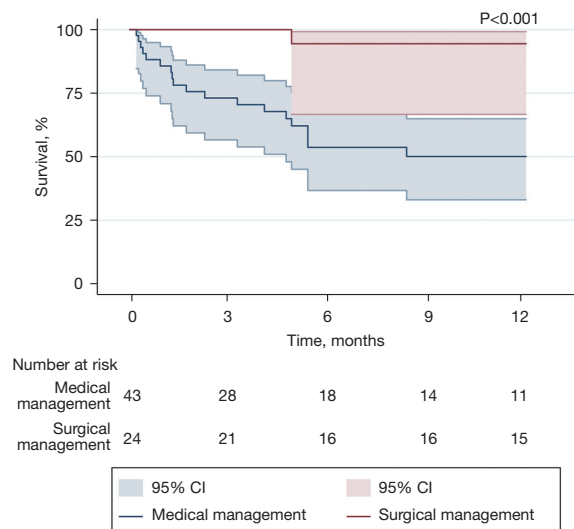
While evidence regarding post-TAVR endocarditis has

accumulated in recent years, these investigations have predominantly relied on registry-based studies lacking granular data. It is critically important to note that these studies consistently lacked a description of surgical management, which is the most fundamental aspect of prosthetic valve endocarditis treatment. Prosthetic valve

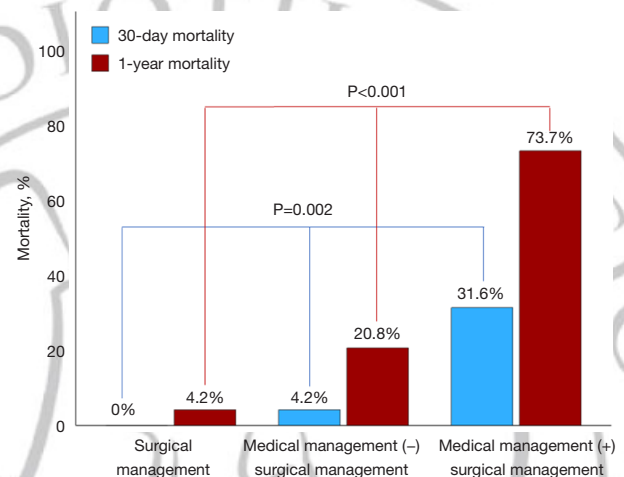
Table 3 Operative data and early postoperative complications in patients with surgical management	
Variables	Surgical management (n=24)
Interval between endocarditis diagnosis and surgery (days)	13 [9–19]
Cardiopulmonary bypass time (minutes)	169 [97–218]
Aortic cross-clamp time (minutes)	118 [79–177]
Any aorta repair	14 (58.3)
Aortic root repair	11 (45.8)
Total aortic root repair	6 (54.5)
Partial aortic root repair	5 (45.5)
Ascending aortic repair	4 (16.7)
Mitral procedures	3 (12.5)
Mitral repair	2 (66.7)
Mitral replacement	1 (33.3)
Commando procedure	1 (4.2)
Tricuspid repair or replacement	4 (16.7)
CABG	1 (4.2)
Gerbode defect repair	1 (4.2)
Pulmonary valve replacement	1 (4.2)
Pacemaker generator and lead removal	10 (41.7)
In-hospital mortality	0
Newly diagnosed stroke	0
TIA	1 (4.2)
Renal failure requiring dialysis <sup>†</sup> (n=19)	2 (10.5)
Reoperation for bleeding	1 (4.2)
Respiratory failure requiring tracheostomy	1 (4.2)
New permanent pacemaker <sup>‡</sup> (n=14)	1 (7.1)
Length of stay (days)	14 [11–20]

Variables are expressed as numbers (percentages) or medians [interquartile range], as appropriate. <sup>†</sup>, among patients without preoperative dialysis; <sup>‡</sup>, among patients without permanent pacemaker preoperatively. CABG, coronary artery bypass grafting; TIA, transient ischemic attack.

endocarditis is more invasive than native valve endocarditis and more refractory to cure with antibiotics alone. Biofilm formation represents a biological basis for the more frequent need for surgery in the presence of prostheses (18).



**Figure 3** Kaplan-Meier survival curve depicting the estimated survival of each group up to 1 year. CI, confidence interval.



**Figure 4** The 30-day and 1-year mortality among 3 groups (surgical management group, medical management group without surgical indications, medical management group with surgical indications).

The present study, providing background between surgical and medical management from the same institution, represents a valuable addition to the evidence for post-TAVR endocarditis, unlike previous studies with limited understanding related to each treatment among allcomers. The primary findings of interest in this study were: (I) the overall incidence of post-TAVR endocarditis among



patients who received a TAVR at University of Michigan was 1.4%; (II) the number of post-TAVR endocarditis cases is gradually increasing; (III) 35.8% received surgical management and 64.2% received medical management; (IV) 44.2% of medically managed patients had surgical indications and did not undergo surgery for various reasons; (V) surgical management involved complex reoperations with excellent short-term results; (VI) survival after surgical management was significantly superior compared with medical management; (VII) the dismal outcomes of medical management were attributable to patients managed medically despite the presence of surgical indications.

The historic extreme rarity of surgical management for post-TAVR endocarditis is not surprising, but highly concerning. The present study results were partially in line with these previous studies, as there were no surgically managed patients prior to 2019. Bansal *et al.* examined the Nationwide Readmission Database (13). Among 906 hospitalizations for TAVR-related endocarditis, only 20 patients (2%) received surgical interventions. Mangner *et al.* investigated their international registry data (14). Similarly, only 19% (n=111) received surgery. Importantly, 25 out of 111 patients (22.5%) in the surgical cohort did not have the infected TAVR valves removed, with only pacemaker device extraction performed. Therefore, the true surgical cohort represented only 14.7% (n=86) of the entire cohort. Authors from both studies concluded that surgery was not associated with improved survival compared with medical management. These study conclusions can be misleading in the absence of granular data. In the present study, the overall 1-year mortality after medical management was approximately 50%, which was similar to the registry study data by Mangner *et al.* (14). However, the surgical management group demonstrated strikingly superior outcomes with complete removal of infected TAVR valves, unlike the previous registry-based studies. Several reasons for the more favorable surgical outcomes in the present study are postulated. First, the surgical intervention was more timely. In the study by Mangner *et al.*, the time to surgery was 17.5 (IQR, 6–41) days from “hospitalization”. In contrast, the time to surgery was 13 (IQR, 9–19) days from the day of “endocarditis diagnosis” in our study. This relatively short time interval from diagnosis to surgery allowed effective timely treatment. Having explanted TAVR valve specimens allows for broad range 16S ribosomal RNA polymerase chain reaction (PCR) testing (19) to identify unknown causative microorganisms in patients with negative blood cultures and more optimized antibiotic

therapy postoperatively. Second, there is rich experience with reoperations after TAVR at our institution. As of the first half of 2024, we have performed over 120 TAVR explants, with outcomes improving over time. In contrast, TAVR explant remains very rare for the majority of centers and surgeons. The unfavorable surgical outcomes in these registry studies were likely attributed to the surgeons’ learning curve, in addition to patient sickness and/or possible reluctance for surgery. Although small in number, there were patients who refused surgical intervention despite our recommendation in the present study. None of them survived at 1 year. Third, our institution has a strong multidisciplinary endocarditis team (15), which allows for more organized and timely patient management, including post-hospital discharge follow-up. Our overall endocarditis clinical outcomes demonstrated significant improvement after the multidisciplinary endocarditis team was implemented (15).

### Study limitations

This study has several inherent limitations, including its retrospective nature with a small sample size at a single institution. A number of patients were initially admitted to outside hospitals prior to transfer to the University of Michigan Hospital, and some clinical information from outside centers was unavailable. Additionally, there may be survivorship bias for those who were able to be transferred to University of Michigan. This may have resulted in the favorable outcomes in the surgical management group.

In summary, the present study demonstrated that surgical management of post-TAVR endocarditis is associated with favorable clinical outcomes, despite the high-risk profile of the cohort with complex reoperations. Additionally, timely surgical intervention effectively prevents catastrophic endocarditis-related complications, such as systemic emboli, which significantly contributed to the loss of opportunity for surgical management in some patients in this study. As the role of TAVR continues to expand, a substantial increase in the incidence of post-TAVR endocarditis is expected in the next decade. In this context, more prudent clinical judgment and prompt surgical management, supported by a strong multidisciplinary endocarditis team, are critical to improving the clinical outcomes of this challenging condition. Coordination between referring hospital and centers with multidisciplinary endocarditis teams with experienced surgeons may help to improve access to surgical treatment for patients with TAVR endocarditis.

## Acknowledgments

*Funding:* None.

## Footnote

*Conflicts of Interest:* S.F. serves as a consultant for Terumo Aortic, Medtronic. Edwards Lifesciences and Artivion. G.M.D. is a consultant and investigator for Medtronic. H.J.P. serves as a consultant for Medtronic Inc. G.A. serves as a consultant/advisory board member for Medtronic, Abbott, Edwards Lifesciences, and Cephea. The other authors have no conflicts of interest.

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**Cite this article as:** Fukuhara S, Suzuki T, Deeb GM, Ailawadi G, Patel HJ, Yang B, El-Dalati S. Surgical management is associated with improved survival for endocarditis after transcatheter aortic valve replacement. *Ann Cardiothorac Surg* 2024. doi: 10.21037/acs-2024-etavr-0103

