Prosthetic Valve Endocarditis After Transcatheter Aortic Valve Implantation

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Background—Transcatheter aortic valve implantation (TAVI) is an advancing mode of treatment for inoperable or high-risk patients with aortic stenosis. Prosthetic valve endocarditis (PVE) after TAVI is a serious complication, but only limited data exist on its incidence, outcome, and procedural risk factors.

Methods and Results—Observational single-center study of 509 consecutive patients treated with a transcatheter implanted self-expandable aortic valve prosthesis (Medtronic CoreValve). We identified 18 patients diagnosed with TAVI-PVE during a median follow-up period of 1.4 years (interquartile range, 0.5–2.5 years; longest follow-up was 6.3 years). TAVI- PVE was most frequent in the first year after implantation (first-year incidence, 3.1% [confidence interval, 1.4%–4.8%]); the overall annualized rate was 2.1% per patient-year (confidence interval, 1.2%–3.3%). Seventeen patients (94%) were treated conservatively and 1 with surgery. Four patients (22%) died from endocarditis or complications to treatment, 2 of those (11%) during initial hospitalization for PVE. An increased risk of TAVI-PVE was seen in patients with low implanted valve position (hazard ratio, 2.8 [1.1–7.2]), moderate or worse postprocedural paravalvular regurgitation (hazard ratio, 4.0 [1.5–11]), implantation of >1 prosthesis (hazard ratio, 5.2 [1.5–18]), and any vascular complication (hazard ratio, 3.8 [1.5–9.8]).

Conclusions—TAVI-PVE occurred at a slightly higher rate than reported for surgically implanted valves. Conservative treatment was associated with an acceptable outcome. Suboptimal valve deployment and vascular complications were associated with an increased risk of TAVI-PVE. (Circ Cardiovasc Interv. 2015;8:e001939. DOI: 10.1161/CIRCINTERVENTIONS.114.001939.)

Key Words: endocarditis ■ transcatheter aortic valve replacement

Transcatheter aortic valve implantation (TAVI) is increasingly used to treat patients with severe symptomatic aortic stenosis who are considered at high or extreme risk for surgical aortic valve replacement.1,2 Continued improvement of the long-term outcome after TAVI will depend on a better understanding of late complications and of their causes.

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Prosthetic valve endocarditis (PVE) after surgical valve replacement (SAVR) occurs in 0.3% to 1.2% per year1 and has an in-hospital mortality of >20%.2 Data on TAVI-PVE are limited and conflicting.3,6 In the randomized Placement of AoRtic TraNsscatheterER Valves (PARTNER) A trial on TAVI versus surgery7 and PARTNER B trial on TAVI versus conservative treatment,8 cumulative 2-year incidence of TAVI-PVE was only 0.6% and 1.4%, respectively. In a recently published case series by Puls et al9 of 180 TAVI-patients, the 1-year occurrence of PVE was 3.4%. TAVI-PVE is often treated conservatively because of the inherent high operative risk of these patients, but the effect of this approach is uncertain. A combined mortality rate of 27% in TAVI-PVE (4 of 15 patients) was reported by Puls et al.9 In TAVI, no procedural factors have yet been shown to be associated with PVE,6 making it difficult to provide recommendations to avoid this complication.

To improve our understanding of the occurrence and optimal management of TAVI-PVE, this study was performed with the following aims: (1) report the incidence of PVE in a well-characterized and large group of consecutive patients treated with TAVI, (2) describe treatment and outcome in terms of in-hospital and overall mortality, and (3) identify procedural risk factors for TAVI-PVE.

Methods

Study Population
Between November 2007 and February 2014, a total of 509 consecutive patients underwent TAVI at Rigshospitalet, Copenhagen, Denmark. Patients had symptomatic severe aortic stenosis and were considered either at extreme or at high surgical risk—the decision to perform TAVI was in all cases taken by the Heart Team. Patients
WHAT IS KNOWN

- Prosthetic valve endocarditis after transcatheter aortic valve implantation is a serious complication.
- Its clinical importance will increase as the number of patients with previous transcatheter aortic valve implantation increases.

WHAT THE STUDY ADDS

- The incidence of transcatheter aortic valve implantation prosthetic valve endocarditis is nontrivial and potentially higher than that after surgical valve therapy.
- With dedicated management, a conservative strategy is often effective.
- Suboptimal valve deployment and vascular complications are associated with a higher risk of transcatheter aortic valve implantation prosthetic valve endocarditis.

with postprocedural PVE were treated at Rigshospitalet in a dedicated endocarditis unit or in select cases at local hospitals in close collaboration with Rigshospitalet. When diagnosed with TAVI-PVE, all patients were reevaluated by the surgical endocarditis team for the possibility of surgical treatment.

Cases of endocarditis were retrospectively identified from electronic health records. All clinical, echocardiographic, procedural, and postprocedural data were retrieved from a prospectively updated clinical database.

Procedure

Before TAVI, all patients underwent dental examination, including x-ray, and any infection focus was treated before the procedure. TAVI was performed under general anesthesia using the Medtronic CoreValve system (Medtronic, Minneapolis, MN—valve sizes 23, 26, 29, and 31 mm). Percutaneous transfemoral access was the first choice, followed by subclavian and direct aortic approaches. In case of transfemoral access, ProStar XL (Abbott Vascular, CA) was used as a closure device. Patients without a permanent pacemaker had a temporary pacemaker lead inserted from the jugular vein which was removed after 4 days if a new permanent pacemaker was not required. Furthermore, all patients had a central venous catheter introducted from the jugular vein which was routinely removed after 24 hours. All patients received antibiotic prophylaxis with cefuroxime 1.5 g IV before the procedure, at 8 hours and at 16 hours after.

Patients were advised to take prophylactic antibiotics before high-risk dental procedures according to European and national guidelines (amoxicillin or roxithromycin in cases of penicillin allergy).

Patients not on oral anticoagulants were treated with dual-antiplatelet therapy (aspirin 75 mg/day+clopidogrel 75 mg/day) for 3 months; after that, they were treated with aspirin indefinitely. Patients on oral anticoagulants (mostly warfarin) were treated with supplementary aspirin indefinitely.

Definitions

Classification into definite or possible PVE was performed according to the modified Duke criteria.26 In all cases, patients with a diagnosis of definite or possible endocarditis were treated for PVE for the full duration of guideline-based antibiotic treatment (26 weeks).

Deaths occurring during the initial hospitalization for TAVI-PVE were regarded as in-hospital PVE-related deaths. Deaths occurring after discharge were individually adjudicated based on patient records and categorized as PVE related if they were associated with evidence of relapse of infection, were caused by complications to treatment for PVE, or were within 1 month of discharge with no other apparent reasons.

TAVI-in-TAVI was defined as the placement of one transcatheter valve within another. Nineteen patients had TAVI-in-TAVI performed at the initial procedure, and 5 patients had a TAVI-in-TAVI implantation performed at a later procedure. Vascular and bleeding complications were defined according to the Valve Academic Research Consortium (VARC)-2 recommendations.11 Depth of final device position in the left ventricular outflow tract was measured using an aortogram in left anterior oblique/cranial projection. We measured the average of the distance from the native aortic annular margin on the side of both the noncoronary cusp and the left coronary cusp to the edge of the stent frame. According to the instructions for use, an average implantation depth of 26 mm was considered a low implantation. Severity of paravalvular leak (PVL) was estimated based on an integrative analysis of transesophageal echocardiography (TEE), angiographic (aortogram), and hemodynamic data. Most weight was given to the color Doppler evaluation in the parasternal short-axis view (just below the valve stent) to quantify the jet arc length (>10% of the circumference characterizing moderate or worse PVL).12

Intracardiac Echocardiography

Intracardiac echocardiography (ICE) was performed from the right atrium and right ventricle, using the AcuNav (Biosense Webster, Diamond Bar, CA) or the ViewFlex Xtra (St. Jude Medical, St. Paul, MN) ultrasound catheter. If visualization was unsatisfactory, ICE from the aortic arch was also performed.

Statistical Analysis

To accurately reflect the risk profile of the population, the 5 patients with repeat procedures were included with both first and second procedures in the baseline table and statistics. These patients reentered the survival analysis at the time of the second procedure. Survival curves were constructed using the Kaplan–Meier method. Patients were censored when they died or survived to the final follow-up in March 2014 with no event. No patients were lost to follow-up. Estimated time-related cumulative incidence is reported, as is the overall annualized person-time event rate using total follow-up time. Risk factors were tested with Cox proportional hazards analysis. Because of the low number of end points, we limited the number of variables used in multivariate modeling. For mortality, simple proportions are reported. Group comparisons of categorical data were performed using the Fisher exact test. Cohen \( \kappa \) was used for inter-rater agreement. Incidences and hazard ratios (HRs) are reported with 95% confidence intervals in parentheses. A 2-sided \( P \) value of <0.05 defined statistical significance. R for Windows, version 3.0.3 (R Foundation for Statistical Computing, Vienna, Austria), was used for all statistical analyses.

Ethics

The study was retrospective and did not influence the treatment of patients. In accordance with institutional guidelines and Danish law, approval from an institutional review committee was not required.

Results

A total of 509 procedures were performed (in 504 individual patients; 5 redo procedures). Total follow-up time was 860 person-years, and median follow-up was 1.4 years (interquartile range, 0.5–2.5 years; longest follow-up was 6.3 years). During this period, 18 patients developed PVE. Characteristics at time of TAVI and their relation to the occurrence of PVE are given in Table 1. Detailed information on each case of TAVI-PVE is given in Table 2.

Presentation

Persistent bacteremia was present in all cases. Causative organisms were enterococci in 6 cases (33%), Staphylococcus aureus...
Incidence and Mortality

The annualized event rate was 2.1% per person-year (1.2%–3.3%). In 5 patients, TAVI-PVE occurred very early (≤30 days), in 8 patients early (30 days to 1 year), and in 5 patients later than 1 year after TAVI. Figure 1 shows the Kaplan–Meier estimate of time free from TAVI-PVE. Estimated incidence of very early TAVI-PVE was 1.0% (0.1%–1.9%). Estimated incidence in the first year was 3.1% (1.4%–4.8%), and estimated incidence in the second year was 1.6% (0%–3.2%).

Two patients died during initial hospitalization for PVE (in-hospital mortality, 11% [2%–36%]). These 2 in-hospital deaths occurred in the only 2 patients with aortic root abscess on TEE. Both were found to be nonoperable. An additional 2 patients died after discharge and were classified as PVE-related deaths, giving a total mortality of 22% [7%–48%]. One died from complications to treatment (liver failure because of long-term Fusidic acid treatment), and the other died suddenly 2 weeks after discharge.

Risk Factors for TAVI-PVE

Of baseline characteristics, only male sex was associated with the occurrence of TAVI-PVE (HR, 1.4 [1.8–10.2]). A low implantation position (HR, 2.8 [1.1–7.2]), at least moderate PVL after the procedure (HR, 4.0 [1.5–11.1]), implantation of >1 valve prosthesis (TAVI-in-TAVI: HR, 5.2 [1.5–18.1]), and any vascular (HR, 3.8 [1.5–9.8]) or bleeding (HR, 3.1 [1.2–7.9]) complication were all procedural risk factors significantly associated with the occurrence of TAVI-PVE in univariate testing (Table 1). Vascular and bleeding complications were highly correlated (94% of all patients with a vascular complication also had a bleeding complication), and vascular complication was the stronger predictor of TAVI-PVE in multivariate testing, why only this variable was retained in the models. Kaplan–Meier plots stratified according to individual procedural risk factors are shown in Figure 2.

When adjusting each of the 4 identified procedural factors for sex, the effect estimates were essentially unchanged (HR, 2.4 [0.9–6.2] for low implantation; HR, 4.3 [1.6–12.3] for at least moderate PVL, HR 4.6 [1.3–16.1] for TAVI-in-TAVI, and HR 4.5 [1.7–11] for vascular complication). Regarding collinearity of risk factors, there was a borderline significant association only between TAVI-in-TAVI and PVL (odds ratio, 2.8 [0.9–7.9]). Neither pairwise adjustment of procedural factors against each other nor inclusion of all procedural factors in the same Cox proportional hazards model revealed evidence of confounding, as effect estimates remained essentially the same.

Vascular complications were strongly associated with very early TAVI-PVE (within 30 days of the procedure; HR, 15 [1.6–133]). On the other hand, low implantation (HR, 1.3 [0.2–7.8]), at least moderate PVL (HR, 0; P=0.28), and TAVI-in-TAVI (HR, 5.9 [0.7–53]) were not associated with very early TAVI-PVE.

In contrast, in TAVI-PVE occurring ≥30 days later, low implantation (HR, 3.8 [1.2–12]), at least moderate PVL (HR, 6.8 [2.3–20]), and TAVI-in-TAVI (HR, 5.0 [1.1–23]) were all associated with TAVI-PVE, whereas vascular complications were not (HR, 2.3 [0.7–7.7]).

In 20 patients, inter-rater agreement was tested for assessing low implantation (agreement 80%; κ, 0.60) and at least moderate PVL (agreement 80%; κ, 0.46).

Discussion

In this observational study of 509 consecutive patients treated with TAVI, we report a nontrivial incidence of TAVI-PVE, an acceptable mortality rate in this very high-risk population after conservative treatment and important procedural risk factors associated with TAVI-PVE.

Incidence

The rate of TAVI-PVE was higher than expected. The incidence of surgical PVE has been reported to be 0.3% to 1.2% per patient-year, and in a pooled analysis of VARC-complying end points in TAVI-studies, Genevraux et al found a reported incidence of TAVI-PVE of only 0.6% per year, similar to the findings from the PARTNER trials.

On the other hand, higher rates have also been reported by others. A study by Puls et al reported a 1-year rate of TAVI-PVE of 3.4%, which is similar to the findings in the present study. Both Puls et al and we included the diagnosis of suspected infective endocarditis (IE) using the modified Duke criteria to define PVE. Duke criteria for definite IE are known to be less sensitive in PVE, and European guidelines on IE therefore emphasize the need for clinical judgment in establishing the diagnosis.

In a study on IE after transcatheter pulmonary valve implantation, McElhinney et al reported a very similar annualized rate of 2.4% for all IE, including cases not obviously related to the valve prosthesis. Transcatheter valve implantation in pulmonary and aortic position may share many risk factors for endocarditis. Residual right ventricle outflow tract stenosis because of incomplete stent expansion or implantation in small conduit, as well as PVL after TAVI, causes turbulence, which predisposes to thrombosis acting as a nidus for seeding by microorganisms. Similarly, the pulmonary and aortic valve prostheses are often deployed into conduit and aortic annulus, respectively, with variable shape, contour, and compliance. This may lead to incomplete apposition, which introduces the potential for pockets of space of variable size and shape with the risk for thrombus formation and endocarditis.

Contributing to the apparent increased incidence compared with surgical PVE could be the facts that PVL occurs more
often after TAVI than after SAVR and that the population treated with TAVI is older with more comorbidities than the surgical population.

The causative organisms identified here were comparable with those seen in PVE after SAVR at our institution and did not include the number of more uncommon organisms.
Table 2. Risk Factors, Presentation, Treatment, and Course of Individual Cases

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, y</th>
<th>Sex</th>
<th>Risk Factors*</th>
<th>Time to PVE, d</th>
<th>Microbiology</th>
<th>Echo Findings</th>
<th>Modified Duke Criteria</th>
<th>Antibiotic Treatment</th>
<th>Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>79</td>
<td>M</td>
<td>Low implant, vascular complication</td>
<td>3</td>
<td><em>Staphylococcus aureus</em></td>
<td>TEE: MV ulcerations and vegetation</td>
<td>Definite</td>
<td>Cefuroxime+Fusidic acid (6 wk) and dicloxacillin+Fusidic acid (long-term)</td>
<td>Conservative treatment; discharged with lifelong Fusidic acid and dicloxacillin; failed to improve, developed liver failure (assumed related to Fusidic acid treatment), and died 5 mo after diagnosis</td>
</tr>
<tr>
<td>2</td>
<td>75</td>
<td>M</td>
<td>TAVI-in-TAVI, vascular complication</td>
<td>8</td>
<td><em>Enterococcus faecium</em></td>
<td>TEE negative, AV vegetation on ICE</td>
<td>Definite</td>
<td>Vancomycin+linezolid</td>
<td>Conservative treatment; full resolution; regression of vegetation on final ICE</td>
</tr>
<tr>
<td>3</td>
<td>62</td>
<td>M</td>
<td>Low implant</td>
<td>11</td>
<td><em>Staphylococcus aureus</em></td>
<td>TEE: AV vegetation</td>
<td>Definite</td>
<td>Cefuroxime+Fusidic acid (6 wk)</td>
<td>Conservative treatment; full resolution, TEE normalized</td>
</tr>
<tr>
<td>4</td>
<td>84</td>
<td>M</td>
<td>Vascular complication</td>
<td>14</td>
<td><em>Streptococcus mitis</em></td>
<td>TEE negative</td>
<td>Possible</td>
<td>Ceftriaxone+rifampicin (6 wk)</td>
<td>Conservative treatment; full resolution</td>
</tr>
<tr>
<td>5</td>
<td>83</td>
<td>M</td>
<td>Vascular complication</td>
<td>17</td>
<td>Nonhemolytic <em>Streptococcus</em></td>
<td>TEE: AV vegetation</td>
<td>Definite</td>
<td>Penicillin+gentamicin (6 wk)</td>
<td>Conservative treatment; full resolution, unchanged small vegetation on final TEE</td>
</tr>
<tr>
<td>6</td>
<td>86</td>
<td>M</td>
<td>Low implant, PVL≥2, vascular complication</td>
<td>41</td>
<td>Nonhemolytic <em>Streptococcus</em></td>
<td>TEE: PM lead vegetations</td>
<td>Definite</td>
<td>Penicillin (13 wk)</td>
<td>Conservative treatment and implantation of new PM; full resolution</td>
</tr>
<tr>
<td>7</td>
<td>85</td>
<td>M</td>
<td>Low implant, PVL≥2, TAVI-in-TAVI</td>
<td>162</td>
<td>HemoLytic <em>Streptococcus</em></td>
<td>TEE: aortic root abscess+atrial vegetations</td>
<td>Definite</td>
<td>Penicillin+Fusidic acid</td>
<td>Conservative treatment; died during hospitalization after 5 wk of antibiotic treatment</td>
</tr>
<tr>
<td>8</td>
<td>75</td>
<td>M</td>
<td>Low implant</td>
<td>163</td>
<td>Coagulase-negative <em>Staphylococcus</em></td>
<td>TEE negative</td>
<td>Possible</td>
<td>Vancomycin+rifampicin (6 wk)</td>
<td>Conservative treatment; full resolution</td>
</tr>
<tr>
<td>9</td>
<td>81</td>
<td>M</td>
<td>Low implant, PVL≥2</td>
<td>184</td>
<td>Nonhemolytic <em>Streptococcus</em></td>
<td>TEE negative</td>
<td>Possible</td>
<td>Penicillin+linezolid (2 wk) followed by ampicillin+rifampicin (4 wk)</td>
<td>Conservative treatment; full resolution</td>
</tr>
<tr>
<td>10</td>
<td>73</td>
<td>M</td>
<td>Low implant, vascular complication</td>
<td>223</td>
<td><em>Enterococcus faecalis</em></td>
<td>TEE negative, AV vegetation on ICE</td>
<td>Definite</td>
<td>Penicillin+rifampicin (6 wk)</td>
<td>Conservative treatment; full resolution</td>
</tr>
<tr>
<td>11</td>
<td>85</td>
<td>M</td>
<td>Vascular complication</td>
<td>257</td>
<td><em>Enterococcus faecium</em></td>
<td>TEE: AV vegetation</td>
<td>Definite</td>
<td>Vancomycin+linezolid (6 wk)</td>
<td>Conservative treatment; full resolution, TEE normalized</td>
</tr>
<tr>
<td>12</td>
<td>67</td>
<td>M</td>
<td>Low implant, PVL≥2, TAVI-in-TAVI</td>
<td>331</td>
<td><em>Staphylococcus aureus</em></td>
<td>TEE: aortic root abscess+MV vegetation</td>
<td>Definite</td>
<td>Dicloxacillin+rifampicin</td>
<td>Conservative treatment; died during hospitalization after 3 wk of antibiotic treatment</td>
</tr>
</tbody>
</table>

(Continued)
Olsen et al  Endocarditis After TAVI

Mortality and Treatment
Our study found PVE-associated mortality to be only 11% in-hospital (22% overall). Considering the high-risk profile of the current population, this mortality rate is low. In comparison, in-hospital mortality from PVE after SAVR was found to be 22% in an analysis of 556 cases from the International Collaboration on Endocarditis Registry. In that registry, mortality was higher in older patients, in health-care associated PVE, and in PVE caused by *Staphylococcus aureus*.

It is reassuring that our primarily conservative treatment strategy was effective in the large majority of cases. Only 1 patient underwent surgery primarily because of severe mitral valve regurgitation after anterior leaflet perforation. In contrast, in PVE after SAVR, ≈50% are treated with redo surgery.

Risk Factors
No previous studies have shown procedural factors to be associated with TAVI-PVE, whereas the present study identified reported in a review of TAVI-PVE case studies. We did not identify a difference between early and late TAVI-PVE in terms of causative organisms.

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### Table 2. Continued

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, y</th>
<th>Sex</th>
<th>Risk Factors</th>
<th>Time to PVE, d</th>
<th>Microbiology</th>
<th>Echo Findings</th>
<th>Modified Duke Criteria</th>
<th>Antibiotic Treatment</th>
<th>Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>76</td>
<td>M</td>
<td>None</td>
<td>351</td>
<td><em>Enterococcus faecalis</em></td>
<td>TEE negative, ICE negative</td>
<td>Possible</td>
<td>Ampicillin+gentamicin (6 wk)</td>
<td>Conservative treatment; full resolution</td>
</tr>
<tr>
<td>14</td>
<td>88</td>
<td>M</td>
<td>Low implant</td>
<td>407</td>
<td><em>Enterococcus faecalis</em></td>
<td>TEE negative, AV vegetation on ICE</td>
<td>Definite</td>
<td>Vancomycin+linezolid (6 wk)</td>
<td>Conservative treatment; full resolution</td>
</tr>
<tr>
<td>15</td>
<td>85</td>
<td>F</td>
<td>PVL≥2</td>
<td>485</td>
<td><em>Staphylococcus aureus</em></td>
<td>TTE: worsened aortic regurgitation†</td>
<td>Definite</td>
<td>Cefuroxime+Fusidic acid (6 wk)</td>
<td>Conservative treatment; full resolution</td>
</tr>
<tr>
<td>16</td>
<td>75</td>
<td>M</td>
<td>None</td>
<td>611</td>
<td><em>Staphylococcus epidermidis</em></td>
<td>TEE: AV vegetations</td>
<td>Definite</td>
<td>Dicloxacillin+rifampicin (6 wk)</td>
<td>Conservative treatment; full resolution</td>
</tr>
<tr>
<td>17</td>
<td>77</td>
<td>M</td>
<td>Low implant, vascular complication</td>
<td>653</td>
<td><em>Enterococcus faecium</em></td>
<td>TEE negative, ICE negative</td>
<td>Possible</td>
<td>Vancomycin+linezolid (6 wk)</td>
<td>Conservative treatment; apparent resolution but died 2 wk after discharge</td>
</tr>
<tr>
<td>18</td>
<td>76</td>
<td>M</td>
<td>Low implant, PVL≥2</td>
<td>888</td>
<td><em>Streptococcus salivarius</em></td>
<td>TEE: thickened AV leaflets+MV vegetation and perforation</td>
<td>Definite</td>
<td>Cefuroxime+ciprofloxacin (6 wk)</td>
<td>Successful surgery‡, full resolution</td>
</tr>
</tbody>
</table>

Cases are sorted based on time to PVE. Cases 1–5: very early PVE, cases 6–13: early PVE, and cases 14–18: late PVE. AV indicates aortic valve; ICE, intracardiac echocardiography; MV, mitral valve; PM, pacemaker; PVE, prosthetic valve endocarditis; PVL, paravalvular leak; TAVI-in-TAVI, transcatheter valve implanted in another transcatheter valve; TEE, transesophageal echocardiography; and TTE, transthoracic echocardiography.

* Presence of significant procedural risk factors identified in this study.
† Only TTE performed.
‡ Surgical aortic valve replacement with insertion of a bioprosthetic valve, mitral valve debridement, and repair with pericardial patch and ring-annuloplasty and tricuspid valve ring-annuloplasty.

Figure 1. Kaplan–Meier estimate of overall transcatheter aortic valve implantation (TAVI) prosthetic valve endocarditis (PVE) incidence. Dashed lines indicate 95% confidence intervals.
both suboptimal valve deployment and access-site complications as important risk factors.

Low implantation, moderate or worse PVL, and implantation of >1 TAVI prosthesis were all associated with an increased and persistent risk of TAVI-PVE. Several case reports have anticipated that a low implantation could be involved in the pathogenesis of TAVI-PVE.20–23 A potential mechanism could be mechanical affection of the mitral valve, which was demonstrated in these cases.

The frequency of moderate or worse PVL was 11.2% in our entire population, and this is similar to the 9.1% reported in the recent CoreValve US Pivotal Trial High Risk Study17 and to the 12.2% in the PARTNER A trial using a balloon-expandable valve.15 In these randomized trials, more than moderate postprocedural regurgitation was more frequent after TAVI-treatment compared with surgery. PVL is related to prosthesis-annulus size mismatch, technical difficult procedures with valve malpositioning, and is more common when treating heavily and asymmetrically calcified aortic valves.24

PVL may increase the risk of endocarditis because the high-velocity regurgitant jet damages or otherwise increases the vulnerability of endothelial surfaces.

Because the use of TAVI-in-TAVI was limited, the uncertainty on our estimate of the associated risk is large. However, it raises a flag of warning that 3 of 24 patients (13%) who had TAVI-in-TAVI performed went on to develop PVE. We speculate that the increased risk of infection stems from the existence of more foreign material and potential pouches and narrow space between the tissue elements of the 2 valves. Most vascular complications and bleeding complications after TAVI relate to the arterial access site, and almost all cases of vascular complications involve bleeding. Local hematoma can be speculated to increase the incidence of bacteremia in a short period after the procedure, resulting in an increased risk of TAVI-PVE during the first month.

Interestingly, neither blood transfusions nor treatment of access-site bleeding with a covered stent was associated with TAVI-PVE.

Our estimated HR for male sex was surprisingly high but with wide confidence limits. Men have in other studies been found to be affected by IE more often than women25; the reasons for this difference are not clear. In a population of elderly TAVI-patients, issues related to dental and urologic hygiene could be speculated to have a larger effect on men.

**Perspectives for Avoiding PVE After TAVI**

After TAVI, compared with surgery, there is an increased risk of endothelial damage from low implantation and from para-valvular regurgitation, which could increase the risk of PVE. Design differences between surgical valves and TAVI valves should also be kept in mind.

Reducing PVL has been a strong motivation in the ongoing development of next-generation transcatheter valves. Improved delivery systems can also be expected to lead to fewer vascular complications, for example by reducing the sheath diameter. Our results raise the hope that improvements in valves and implantation techniques will also result in fewer cases of TAVI-PVE. Our findings should also lead to a heightened focus on sterile techniques during implantation and on potential sources of bacteremia in individual patients.

Although long-lasting antibiotic prophylaxis is not considered appropriate after SAVR,24 a longer regimen of antibiotic prophylaxis could be considered in all TAVI-patients with vascular complications. Cephalosporins are traditionally used, but this choice could be reconsidered if it is confirmed that enterococci are important pathogens in very early TAVI-PVE.

**Intracardiac Echocardiography**

It is an interesting supplementary finding that ICE can provide relevant information in cases with suspected TAVI-PVE and negative TEE. We have in our institution previously found ICE to be valuable for detecting vegetations in transcatheter pulmonary valves,26 and others have found ICE useful in detecting right-sided cardiac device–related endocarditis.27 Sensitivity could be superior to TEE, but the specificity of this approach needs verification.

**Limitations**

Despite analyzing consecutive data, the study was limited by its observational and exploratory nature, with the limitations inherent to this design. Specifically, no final conclusions on causality can be made.

With only 18 events, some significant results may be false positives. For example, using a Bonferroni correction for the
4 significant results, low implantation would no longer be significant.

Patients were treated with 1 valve type only, and the results might not be generalizable to other valves. Especially, the effect of low implantation can be expected to differ with different valve designs. The reliance on data from a single center assured a high degree of internal consistency and control of data quality, but this may also affect the generalizability of findings.

Five patients did not have imaging evidence of endocarditis despite typical clinical signs and symptoms, and they were therefore classified only as possible IE according to the modified Duke criteria. Despite the fact that all patients were treated for the full duration of guideline-based antibiotics based on the evaluation of institutional experts, some may not have had endocarditis, resulting in some overestimation of the risk of TAVI-PVE.

Conclusions

The cumulative incidence of TAVI-PVE was 3.1% at 1 year and 2.1% per patient-year overall. A conservative treatment strategy was associated with an in-hospital mortality of 11%. Male sex, a low implanted valve position, moderate or worse PVL, implantation of >1 TAVI prosthesis, and vascular complications were associated with an increased risk of TAVI-PVE.

Disclosures

Dr Sonnegaard is a proctor for CoreValve, Medtronic.


Prosthetic Valve Endocarditis After Transcatheter Aortic Valve Implantation

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