Management of Coronary Artery Disease in Patients with Aortic Stenosis Undergoing Transcatheter Aortic Valve Implantation: A Single Center Experience in Japan

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Objective: Coronary artery disease (CAD) frequently coexists with aortic stenosis (AS). During surgical aortic valve replacement, concomitant coronary artery bypass grafting is recommended in patients with significant CAD. However, the management of CAD in patients undergoing transcatheter aortic valve implantation (TAVI) is undetermined. Materials and Methods: We analyzed 120 consecutive patients who underwent TAVI between April 2010 and February 2015 in our hospital. Significant CAD was defined as unrevascularized significant coronary artery stenosis. Results: Of 120 patients, 34 (28%) had significant CAD. Thirty-day outcomes were similar between patients with CAD and those without CAD. Among 34 patients with CAD, 15 (44%) underwent percutaneous coronary intervention (PCI). PCI was performed safely, except one case of coronary dissection necessitating additional coronary stenting. The clinical outcomes at 30 days were the same in TAVI+PCI group and isolated TAVI group. Ischemic burden evaluated by SYNTAX score (SS) and Duke Myocardial Jeopardy Score (DMJS) were significantly alleviated by PCI (SS: 7.2 ± 2.9 vs 0.5 ± 1.1, p<0.01. DMJS: 5.3±2.8 vs 0.4±0.8, p<0.01). Conclusion: Significant CAD was found in 28% of patients undergoing TAVI. PCI can be performed safely, and significantly alleviates the ischemic burden of CAD.

KEY WORDS: transcatheter aortic valve implantation, percutaneous coronary intervention, coronary artery disease

I. Introduction

Coronary artery disease (CAD) and aortic stenosis (AS) have similar risk factors and pathophysiology.1-3 In managing patients with AS, we often encounter CAD.2-3 Several studies have reported the adverse impact of CAD in patients with AS.4-5 During surgical aortic valve replacement (SAVR), concomitant coronary artery bypass grafting (CABG) is recommended in patients with significant CAD.4-6 However, the best strategy for CAD in patients undergoing transcatheter aortic valve implantation (TAVI) has been undetermined. There is no consensus on the indication, method and timing of revascularization. We reviewed our patients with severe AS who had undergone TAVI at our hospital, aiming to assess the prevalence of coexisting CAD, and to find the optimal strategy for CAD in patients undergoing TAVI.

II. Materials and methods

1. Population

Between April 2010 and February 2015, we performed TAVI in 120 patients with severe AS. Severe AS was defined as meeting at least one of the following: aortic valve area less than 0.75 cm², transvalvular peak pressure gradient higher than 64 mmHg and/or transvalvular mean pressure gradient higher than 40 mmHg. Among patients with symptomatic severe AS, inoperable patients or high surgical risk patients, for whom TAVI rather than SAVR was preferred, were selected by a multidisciplinary heart team. Patients with radiated chest wall, severe pulmonary dysfunction, malignant tumor, or porcelain aorta were considered to be inoperable. High surgical risks included a Logistic EuroSCORE for isolated SAVR higher than 20, a Society of Thoracic Surgeons (STS) score for isolated SAVR higher than 10 or equivalent, and other surgical risks including severe frailty and cirrhosis. In patients with complex multi-vessel CAD or left main disease with an indication for CABG, the option of SAVR with concurrent CABG was selected.
2. Procedures

We performed TAVI using a 20, 23 or 26-mm SAPIEN XT valve (Edwards Lifesciences, Irvine, CA, USA) via a transapical or transfemoral approach. Cardiac catheterization with coronary angiography, transthoracic echocardiography, transesophageal echocardiography (TEE), and cerebral magnetic resonance angiography were generally performed before TAVI. Based on these results, we determined the access route, prosthetic valve size, balloon volume, and need for prevention of coronary obstruction.

In principle, TAVI was performed under general anesthesia and TEE guidance. As standard technique, we placed a temporary pacemaker at the right ventricular apex. For aortic valve preparation and prosthetic valve sizing, we performed balloon aortic valvuloplasty under rapid ventricular pacing and deployed a SAPIEN XT valve. Generally, single antiplatelet therapy with aspirin 100 mg per day was started from the first postoperative day. For patients who were receiving oral anticoagulants for atrial fibrillation or any other conditions, we used bridging therapy with unfractionated heparin, and did not administer antiplatelet drug after TAVI. For patients who underwent concurrent percutaneous coronary intervention (PCI), dual antiplatelet therapy with aspirin (loading dose of 200 mg, maintenance dose of 100 mg per day) and clopidogrel (loading dose of 300 mg, maintenance dose of 75 mg per day) was started before TAVI. For patients who had undergone PCI before TAVI, single or dual antiplatelet therapy was continued at TAVI at the discretion of the operator. During TAVI, activated clotting time was maintained within 250 seconds by unfractionated heparin.

3. Coronary artery disease and percutaneous coronary intervention

Significant CAD was defined as unrevascularized significant coronary artery stenosis (greater than 50% at the left main trunk or greater than 75% at other sites by visual assessment) and graftability demonstrated on a cineangiogram. In patients with significant CAD, a multidisciplinary heart team decided the indication of revascularization based on cardiac function, perfusion area, suitability for percutaneous coronary intervention, access route for TAVI, and predicted negative hemodynamic effect of rapid ventricular pacing. For patients who were indicated for revascularization, in principle we performed PCI concurrently with TAVI. Stent types were selected by the operator taking into account the characteristics of coronary lesion, need for anticoagulants, and risk of bleeding.

4. Data collection and definitions

Clinical, laboratory, echocardiographic and procedural data were prospectively collected from the institutional database. For patients with CAD, the SYNTAX score (SS) and the Duke Myocardial Jeopardy Score (DMJS) were calculated before and after PCI. Clinical outcomes following TAVI were assessed in accordance with the Valve Academic Research Consortium (VARC-2 criteria). The 30-day composite safety endpoint comprised all-cause mortality, all stroke, acute kidney injury (stage 2 or 3), coronary artery obstruction requiring intervention, major vascular complication, and valve-related dysfunction requiring repeat procedure.

5. Statistical analysis

Data analysis was performed using JMP Pro 11 (SAS Institute Inc., Cary, NC). Categorical variables are expressed as number and percentage, and were compared using the chi-square and Fisher’s exact tests. Continuous variables are expressed as mean and standard deviation, and were compared using a two-sided student’s t-test. A p value of <0.05 was considered statistically significant.

III. Results

1. Clinical, laboratory, echocardiographic and procedural characteristics

We retrospectively analyzed 120 consecutive patients who underwent TAVI at our hospital between April 2010 and February 2015. Baseline clinical, laboratory and echocardiographic characteristics are presented in Table 1. A cineangiogram detected significant CAD in 34 patients (28% of all patients, 52 coronary stenotic lesions) (CAD group). The locations of coronary lesions were the right coronary artery in 14 lesions (27% of all coronary lesions), left main trunk in 2 (4%), left anterior descending artery in 14 (27%), diagonal branch in 3 (6%), left circumflex artery in 14 (27%) and saphenous vein graft in 5 (10%). Compared with the non-CAD group, the CAD group had more males (47% vs 23%, p=0.01), higher prevalence of hypertension (94% vs 77%, p=0.04), carotid artery stenosis defined as more than 75% diameter stenosis on magnetic resonance imaging or echography (27% vs 4%, p<0.01), peripheral artery disease (41% vs 14%, p<0.01), previous myocardial infarction (21% vs 1%, p<0.01), previous PCI (41% vs 9%, p<0.01), previous CABG (32% vs 8%, p<0.01), and higher Logistic EuroSCORE (22.3 ± 15.2 vs 16.6 ± 9.0, p=0.03).

Procedural data of TAVI are listed in Table 2. One hundred and nineteen TAVI (99%) were elective procedures, and 116 (97%) were performed under general anesthesia. Trans-femoral approach was used in 84 patients (70%). Device success rate as defined by VARC-2 criteria was 93%. Procedural data did not differ between the CAD group and non-CAD group.

Thirty-day outcomes are presented in Figure 1. There were no differences between the CAD group and the non-CAD group for all the clinical outcomes examined, including the 30-day composite safety endpoint (18% vs 16%, p=0.86).
Patients with coronary artery disease and percutaneous coronary intervention

Among 34 patients with CAD, 15 patients (44%) underwent PCI (TA VI+PCI group) according to the above revascularization strategy. Staged PCI (PCI on an earlier date separate from TA VI) was performed in 7 patients (47% of revascularized patients) owing to the regulation of clinical trial or matter of antiplatelet drug, and concurrent PCI (PCI with TA VI in the same session) was performed in 8 patients (53%). The clinical characteristics of TA VI+PCI group and isolated TA VI group were similar, except the rate of previous CABG (7% vs 53%, p<0.01) (Table 3). Fifty percent of the lesions (12 lesions) were types A and B1 as defined by AHA/ACC classification (Table 4). Angiographic success rate was 100%. Procedural success rate was 96%, with one case of coronary dissection necessitating additional coronary stenting. Coronary stents were used in 24 of 25 lesions (96%; total 25 stents). Forty-six percent of all implanted coronary stents were bare metal stents and 54% were drug-eluting stents (cobalt-chromium everolimus eluting stents 21%, platinum-chromium everolimus eluting stents 17%, and biolimus eluting stents 17%). Procedural data of TA VI was not different between the TA VI+PCI group and the isolated TA VI group. As for 30-day outcomes, there were also no significant differences between two groups (30-day composite safety endpoint: 13% vs 21%, p=0.67).

SYNTAX score and Duke Myocardial Jeopardy Score

The SS and DMJS before and after PCI are presented in Figures 2 and 3. In the TA VI+PCI group, SS was 7.2±2.9 before PCI, and decreased significantly to 0.5±1.1 after PCI (p<0.01). SS in the isolated TA VI group was 6.8±6.1, and was significantly higher than that in the TA VI+PCI group after PCI.
The proportion of patients with SS>9 in the TA VI+PCI group was 20% before PCI, and decreased significantly to 0% after PCI (p<0.01).

In the TAVI+PCI group, the DMJS before PCI was higher than that in the isolated TAVI group (5.3 ± 2.8 vs 2.7 ± 1.0, p<0.01), but became significantly lower after PCI (0.4 ± 0.8 vs 2.7 ± 1.0, p<0.01).

IV. Discussion

Among 120 consecutive patients who underwent TAVI in our hospital, unrevascularized significant CAD was found in 34 patients (28%). Our multidisciplinary heart team decided indication of revascularization with PCI based on several factors including perfusion area and suitability for PCI. Among 34 patients with CAD, we performed PCI in 15 patients (44%) as a staged or combined procedure. PCI was uneventful and alleviated the ischemic burden of CAD.

1. Coronary artery disease in patients undergoing transcatheter aortic valve implantation

Previous studies have reported the presence of CAD in 34 to 64% of the patients undergoing TAVI. The range of prevalence reflects the difference in definition of CAD. Gasparetto et al. defined CAD as any previous coronary revascularization or present coronary stenosis of at least 50%, while Khawaja et al. defined significant CAD as coronary artery stenosis of ≥70% by quantitative coronary angiography.
Patients with AS and coexisting CAD have been reported to be more frequently males, with higher prevalence of peripheral artery disease, previous myocardial infarction, previous PCI, previous CABG, and higher surgical risk.\textsuperscript{11-13} The clinical characteristics of our patients are consistent with previous reports.

2. Indication and effectiveness of percutaneous coronary intervention

In spite of some controversial reports, CAD is generally considered a negative prognostic factor for patients with aortic stenosis.\textsuperscript{4} However, there is no consensus on the management of CAD in patients with aortic stenosis; especially, the indication of revascularization in patients undergoing TAVI remains undetermined.

Many reports have indicated that the ischemic burden of CAD correlates with prognosis and warrants revascularization.\textsuperscript{15, 16} In patients without aortic stenosis, we decide the indication of revascularization based on abnormal findings suggestive of significant ischemia on echocardiography, single photon emission computed tomography, or fractional flow reserve. For patients with aortic stenosis, however, it is difficult to use the exercise stress test or vasodilator drugs that are indispensable for the above assessments, because of possible negative effects on hemodynamics.

The SS indicates the complexity and extent of CAD. A significant correlation between SS and outcome after TAVI has been reported.\textsuperscript{12, 14} Higher SS is associated with worse prognosis following TAVI. An SS higher than 9 was identified as the optimal cut-off, with an independent association with mortality.

Using staged or concurrent PCI, we were able to decrease the
Table 4 Data of percutaneous coronary intervention

<table>
<thead>
<tr>
<th>Lesion type (AHA/ACC)</th>
<th>Type A: 5 lesions, Type B1: 7 lesions, Type B2: 7 lesions, Type C: 5 lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>SYNTAX score</td>
<td>7.2 ± 2.9</td>
</tr>
<tr>
<td>DMJS</td>
<td>5.3 ± 2.8</td>
</tr>
<tr>
<td>TRI/TFI</td>
<td>4 (27%)/11 (73%)</td>
</tr>
<tr>
<td>Stent type</td>
<td>BMS: 11 stents (46%)/DES: 13 stents (54%)</td>
</tr>
<tr>
<td>Angiographic success</td>
<td>24/24 (100%)</td>
</tr>
<tr>
<td>Procedural success</td>
<td>23/24 (96%)</td>
</tr>
<tr>
<td>Complications</td>
<td>Death 0%, myocardial infarction 0%, stroke 0%, coronary perforation 0%, coronary dissection 4%, CIN 0%, shock 0%</td>
</tr>
</tbody>
</table>

AHA; American Heart Association, ACC; American College of Cardiology, DMJS; Duke Myocardial Jeopardy Score, TRI; trans-radial intervention, TFI; trans-femoral intervention, BMS; bare metal stents, DES; drug eluting stents, CIN; contrast induced nephropathy

SS (pre-PCI vs post-PCI: 7.2 ± 2.9 vs. 0.5 ± 1.1, p<0.01) and the proportion of patients with SS>9 (20% vs. 0%, p<0.01).

The DMJS indicates the area of ischemic myocardium, and predicts outcomes of CAD. To score the DMJS, coronary arteries are divided into 6 segments [the left anterior descending artery, the major anterolateral (diagonal) branch, the first major septal perforator, the left circumflex artery, the major circumflex marginal branch, and the posterior descending artery], and 2 points are assigned to each segment. The DMJS, which is the total score for the 6 segments, has been reported to provide prognostic information. The DMJS is a simple and convenient method for estimating the amount of myocardium at risk. In this study, PCI was able to reduce the DMJS (pre-PCI vs post-PCI: 5.3 ± 2.8 vs. 0.4 ± 0.8, p<0.01), which would probably improve the prognosis of patients with CAD in the long term. The SS and DMJS are useful in deciding the indication of revascularization for significant CAD in patients undergoing TAVI.

A number of studies have evaluated combined TAVI and PCI therapy. In these studies, the short-term and long-term outcomes of the combined therapy were comparable to those of isolated TAVI. Our results are similar to these previous studies. PCI combined with TAVI was relatively safe and was effective to alleviate the ischemic burden of CAD. However, patients undergoing TAVI have limited life expectancy and daily activities, and the effect of combined revascularization on long-term outcome has not been determined. Interventional studies including randomized controlled trial are warranted to assess the true effectiveness of PCI combined with TAVI.

3. Timing of percutaneous coronary intervention

In our hospital, we generally perform PCI at the same time as TAVI, because there are some concerns about the safety of performing isolated PCI in the presence of severe AS. On the other hand, staged PCI is thought to minimize the contrast material load, radiation time, and procedural time for each
session. The optimal timing of PCI is also undetermined. In this study, the amount of contrast material used and the radiation time were significantly greater in the TAVI+PCI group than in the isolated TAVI group (contrast material: 187 ± 86 vs. 111 ± 39 ml, p<0.01, radiation time: 31 ± 15 vs. 21 ± 6 min, p<0.05).

Regarding the safety of PCI in the presence of severe AS, Goel et al. reported that PCI can be performed in patients with severe symptomatic AS and CAD without increased risk, except in patients with low cardiac function (left ventricular ejection fractions less than 30%) and high surgical risk (STS score higher than 10). With careful selection, staged PCI may be more acceptable to patients undergoing TAVI than concurrent PCI.

4. Other revascularization method

When screening for the suitability of TAVI, we selected SAVR for patients with complex multi-vessel CAD or left main disease that were indicated for CABG. Our patients who underwent TAVI had relatively simple CAD with low SS (7.1 ± 4.9). However, an additional option of CABG by the minimally invasive coronary surgery (MICS) approach is now available. For patients who are contraindicated for SAVR or conventional CABG, a novel therapeutic option of TAVI with MICS-CABG instead of SAVR with conventional CABG may be selected. However, many issues remain to be solved, such as the access route of TAVI, optimal antithrombotic therapy, the order of TAVI and MICS-CABG, safety of MICS approach in hypertrophic patients, and prolonged procedural time.

5. Limitation

The present single-center observational study included only a limited number of patients. In addition, we did not assess long-term outcomes. The findings should be interpreted with caution. It is necessary to examine the effectiveness of PCI with a prospective and long-term study.

V. Conclusion

Significant CAD was found in 28% of our patients undergoing TAVI. We were able to perform PCI relatively safely in these patients, and alleviated the ischemic burden of CAD. The SS and DMJS may be useful in estimating prognosis and making decision on treatment modality for CAD in patients undergoing TAVI.

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Disclosure Statement

All authors declare no conflict of interest.

References

artery disease defined by quantitative coronary angiography and SYNTAX score upon outcome after transcatheter aortic valve implantation (TAVI) using the Edwards bioprosthesis. EuroIntervention 2015; 11: 450-455


