

## Complete Revascularization in Patients Before Undergoing Transcatheter Aortic Valve Replacement: Desirable or Superfluous?

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Coronary artery disease (CAD) and aortic valve stenosis (AS) are frequently coexistent in elderly patients.<sup>1,2</sup> Both diseases share a lot of common risk factors such as age, gender, hypercholesterolemia, hypertension, and diabetes mellitus.<sup>3</sup> At the same time, partially similar pathogenesis seems to be responsible for the common clinical occurrence.<sup>4</sup> In addition to degenerative changes, active processes including lipid infiltration, chronic inflammation with lymphocytes and macrophages, fibrosis formation, and osteoblast activation are negatively affecting the diseases progression.<sup>4,5</sup> The fact that both diseases also occur independently from each other, however, suggests that additional parameters such as unfavorable genetics might play a considerable role in pathogenesis.

### See Article by Witberg et al

Current guidelines suggest with a level of evidence C (expert consensus) that patients with a primary indication for aortic/mitral valve surgery and concomitant coronary artery diameter stenosis  $\geq 50\%$  to  $70\%$  should be considered for additional coronary artery bypass grafting at the time of surgical aortic valve replacement (SAVR).<sup>4,6–8</sup> However, combined SAVR and coronary artery bypass grafting carries a higher risk than isolated SAVR. Vice versa, SAVR late after coronary artery bypass grafting is also associated with significantly increased risk so that it has been common consensus to treat both diseases simultaneously to avoid repeated sternotomy.<sup>4,7,8</sup>

Transcatheter aortic valve replacement (TAVR) has become the treatment of choice in elderly patients with severe AS and high or intermediate surgical risk showing a noninferior outcome compared with SAVR.<sup>9,10</sup> In this patient population, the concomitant occurrence of AS and CAD is even more frequent.<sup>4,11</sup> Therefore, the vast majority of TAVR patients is considered for percutaneous coronary intervention (PCI). Combined PCI and transcatheter aortic valve implantation has already been shown to be feasible but requires more data before a firm recommendation can be made.<sup>5,11–13</sup>

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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(*Circ Cardiovasc Interv.* 2018;11:e006556.

DOI: 10.1161/CIRCINTERVENTIONS.118.006556.)

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*Circ Cardiovasc Interv* is available at <http://circinterventions.ahajournals.org>

DOI: 10.1161/CIRCINTERVENTIONS.118.006556

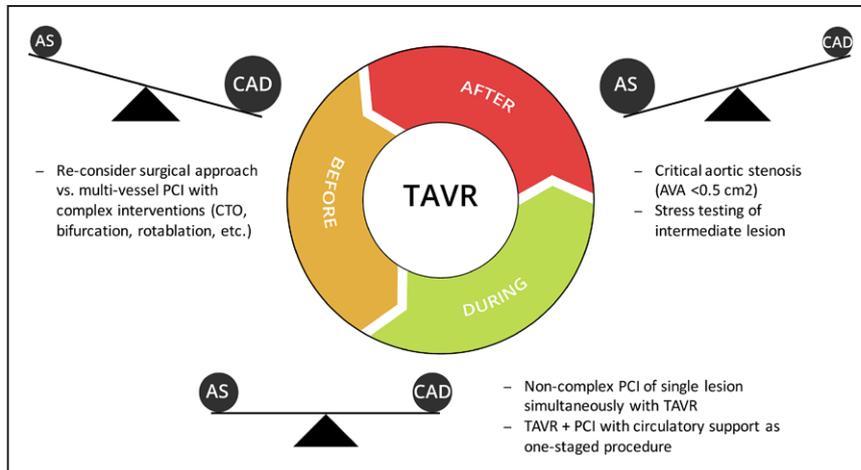
The chronology of interventions is subject of individualized discussion based on the patient's clinical condition, extent of CAD, and myocardium at risk and, therefore, the following questions remain unanswered:

1. What should be the preferred timing for PCI in patients undergoing TAVR?
2. How can prognostically relevant CAD lesions be identified in patients with severe AS?
3. Does CAD have an impact of outcome in TAVR patients and can complete revascularization improve outcome?
4. A staged approach with PCI before the TAVR procedure has the potential to prevent hemodynamic instability because of PCI-related complications and to reduce the risk of ischemia during rapid pacing and balloon inflation during subsequent TAVR, especially in patients with distal left main stenosis and complex bifurcation lesions.<sup>11–13</sup> From a technical standpoint, access to the coronary arteries is less challenging before the valve prosthesis is implanted.<sup>4,13</sup>

Some authors have proposed performing PCI and TAVR during a concomitant procedure, especially single type A or B lesions.<sup>2,11</sup> Potential advantages of this strategy are enhanced resource utilization, patient convenience, and the reduction of vascular and bleeding complications by avoiding separate vascular access.<sup>11</sup> However, disadvantages are a higher amount of contrast dye with an increased risk for acute kidney injury, longer procedure time, and reimbursement issues depending on the health system in the specific country.

But also a third option remains as performing PCI after TAVR. This strategy might be preferable in patients with critical aortic stenosis and intermediate lesions that would be prone for stress testing. However, this strategy will confront the interventionalist with more challenging access to the coronary arteries (depending on the used transcatheter heart valve type) and that catheter manipulation may potentially dislodge the prosthetic valve.<sup>13</sup> Because evidence-based data on the optimal timing are missing, decision-making should be individualized for each patient focusing on the paramount pathology—CAD or AS—to minimize the periprocedural risk as much as possible (Figure).

1. Significant coronary lesions in patients with concomitant severe AS are basically identified with visual estimation and assessment of vessel size and lesion diameter according to the SYNTAX score. Noninvasive and invasive methods for functional evaluation of ischemia have not been validated properly in elderly TAVR patients to date. The measurement of fractional flow reserve has been shown to be a useful tool for determining functional significance of coronary stenoses and the



**Figure.** Timing of percutaneous coronary intervention in relation to transcatheter aortic valve replacement. AS indicates aortic valve stenosis; AVA, aortic valve area; CAD, coronary artery disease; CTO, chronic total occlusion; PCI, percutaneous coronary intervention; and TAVR, transcatheter aortic valve replacement.

need for revascularization in patients with intermediate CAD lesions.<sup>14–16</sup> The coincidence of a severe aortic stenosis in these patients, however, might influence coronary hemodynamics and these functional indexes consistently.<sup>15,16</sup> Therefore, the applicability of fractional flow reserve measurement under these conditions remains to be elucidated in larger studies: Pesarini et al<sup>17</sup> were able to confirm that fractional flow reserve variations after TAVR were minor and that the measured values seemed to remain stable directly after the procedure.

2. Published studies evaluating the impact of concomitant CAD as assessed with the SYNTAX Score on procedural outcomes and long-term survival after TAVR have yielded conflicting results.<sup>5</sup> In most studies, a SYNTAX Score of >22 at baseline was associated with worse outcome after the procedure. A higher CAD burden was more frequently found in patients with concomitant comorbidities resulting in higher risk scores.<sup>18,19</sup>

Taken together, CAD might reflect a higher comorbidity burden negatively affecting outcome after TAVR. Trying to assess the impact of revascularization using the residual SYNTAX score (rSS), however, several individual studies from different centers could not find a significant improvement of post-TAVR survival in patients undergoing revascularization completeness.<sup>12,19,20</sup>

In this issue of *Circulation: Cardiovascular Interventions*, Witberg et al<sup>21</sup> performed a meta-analysis of studies using the rSS to evaluate the impact of revascularization completeness on outcome in patients undergoing TAVR. The SYNTAX score is known as an angiographic tool to quantify CAD severity and complexity.<sup>22</sup> The rSS quantifies the extent and complexity of CAD remaining after PCI<sup>23</sup> and can be used to describe the degree of revascularization in patients with severe AS and concomitant CAD undergoing TAVR. Six observational studies with a total of 3110 patients met the inclusion criteria and were included in their analysis. The rSS cut off values of the individual studies have been retained to compare clinical outcomes between patients without CAD, patients with a high rSS (considered as incomplete revascularization [ICR]), and patients with a low rSS (considered as reasonable revascularization). Outcome data according to the different baseline SYNTAX Score levels were not reported in this meta-analysis. In their carefully conducted analysis, the

authors found a significant association between ICR and mortality. Importantly, patients undergoing reasonable revascularization before transcatheter aortic valve implantation even had an improved outcome compared with patients undergoing ICR.<sup>21</sup>

Taken together, the authors elegantly show that current data suggest that patients with severe CAD (as defined by the SYNTAX score) are at increased risk for mortality after TAVR. In their analysis, more complete revascularization before TAVR (as assessed by the rSS), mitigated the increased risk exerted by CAD in patients undergoing TAVR. In their TAVR study population, revascularization achieving an rSS <8, was equivalent to complete anatomic revascularization in terms of long-term mortality (similar to what is known in the overall CAD population).

Inhomogeneous definition of ICR (eg, high rSS) and the different rSS cut off values which have been used in the studies are important limitations of the meta-analysis. In addition, it still remains to be elucidated whether ICR (rSS) or CAD severity itself (degree of anatomic complexity reflecting a more advanced disease state; baseline SYNTAX score) reflecting a higher comorbidity burden, in general, is driving the worse outcome after TAVR. In future studies, the delta SYNTAX score, reflecting the difference between baseline SYNTAX score and rSS should be assessed, as a marker for the real CAD burden treated by PCI.

Large prospective and randomized trials such as the ongoing ACTIVATION trial are needed to address this question. This trial will assess the impact of revascularization before TAVR compared with best medical treatment in addition to TAVR.<sup>24</sup> Until then, the key role of the institutional Heart Team with individual assessment of the extent of CAD and the degree of anatomic complexity cannot be emphasized more to find the most appropriate treatment strategy for a specific TAVR patient.

## Disclosures

Dr Sinning has received speaker honoraria and research grants from Medtronic, Edwards Lifesciences, and Boston Scientific.

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KEY WORDS: Editorials ■ aortic valve ■ coronary artery disease ■ hypercholesterolemia ■ SYNTAX score ■ transcatheter aortic valve replacement

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*Circ Cardiovasc Interv.* 2018;11:

doi: 10.1161/CIRCINTERVENTIONS.118.006556

*Circulation: Cardiovascular Interventions* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 1941-7640. Online ISSN: 1941-7632

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