Ask the Experts: What Is Your Institution's Approach to CAD in TAVR Patients?

Several institutions share their methods for treating patients with coronary artery disease who undergo transcatheter aortic valve replacement.

Determining the relative contribution of coronary artery disease (CAD) to symptoms in patients with severe aortic stenosis (AS) is challenging. Stress testing has poor diagnostic accuracy and is contraindicated in severe AS, and there are limited data on the use of fractional flow reserve in the setting of AS.

All randomized clinical trials for transcatheter aortic valve replacement (TAVR) excluded patients with untreated, clinically significant CAD. In fact, trials mandated percutaneous coronary intervention (PCI) be performed at least 1 month before the TAVR procedure, and thus it has become standard practice for TAVR patients to undergo revascularization first, independent of symptoms or physiologic testing. This approach creates a dilemma because it is at odds with current PCI appropriate use criteria. In the absence of clear guidelines, the Interventional Section Leadership Council of the American College of Cardiology released a position statement in December 2016, recommending PCI for major coronary arteries with significant proximal stenosis before TAVR. Figure 1 summarizes the proposed algorithm for the management of CAD in TAVR patients.

Optimal timing of PCI remains uncertain. Combining PCI and TAVR into one procedure may seem appealing to treat both AS and CAD with a single hospitalization. However, there is an important tradeoff because of the higher risk of contrast-induced nephropathy, longer procedure times, and potential need to interrupt dual antiplatelet therapy in the presence of bleeding or a vascular complication. In a recent analysis of the United States Nationwide Inpatient Sample, patients who underwent TAVR and PCI in the same hospitalization had significantly higher mortality (10.7% vs 4.6%; P < .001) than patients who underwent TAVR alone. Mean hospital length of stay and cost were also significantly higher.

Although early evidence suggested that coexisting CAD negatively impacts procedural outcomes and long-term survival in TAVR patients, procedures have become less invasive with increased use of conscious sedation, lower-profile delivery systems, and less rapid pacing. Altogether, these advances have led to less hemodynamic instability during TAVR, which in turn reduces ischemic consequences.

An additional consideration regarding the timing of PCI is the impact of TAVR on the anatomy of the aortic root. The TAVR valve frame and the displaced native aortic valve leaflets can obstruct the coronary ostia after implantation, rendering PCI after TAVR technically challenging. Other factors to consider include the type of TAVR device, depth of implantation, length of the native aortic valve leaflets, and location of the coronary ostia. Simply engaging the coronary ostia...
through the frame of a self-expanding TAVR device can be difficult, if not impossible. Figure 2 illustrates a case we recently encountered. An 88-year-old man presented with non-ST elevation myocardial infarction, 9 months after TAVR with a self-expanding device. A nuclear stress test yielded positive findings, with inducible ischemia in the lateral wall. Selective coronary angiography was performed through the open cells of the TAVR device using a 6-F, Judkins left 4 guide catheter. De novo focal stenosis in the proximal left circumflex artery was identified and treated with deployment of a drug-eluting stent (DES). If timing, renal function, and clinical presentation permit, we have found that contrast-enhanced cardiac computed tomography can be very useful to identify the relationship of the TAVR valve frame, the displaced native aortic valve leaflets, and the coronary ostia to plan the PCI. If PCI is deferred before TAVR, but is believed to be likely required in the future, a shorter balloon-expandable TAVR device may be preferable to a self-expanding device to facilitate subsequent access to the coronaries.

The final challenge is the requirement for new revascularization strategies in intermediate and low-risk patients. Although limited PCI with TAVR may be appropriate for a high-risk or inoperable patient, a low-risk patient with AS and CAD may be better served with concomitant surgical aortic valve replacement and coronary artery bypass. Currently, low-risk TAVR clinical trials exclude patients with unrevascularized CAD in the same way as the pivotal trials did in the past, and have not been designed to address this important question. In the absence of clinical trial data to determine the optimal management strategy for low-risk patients with AS and CAD, decision making will need to be individualized, bearing in mind these patients may have a life expectancy measured in decades rather than years.

In summary, our approach is as follows:

1. PCI for all proximal epicardial vessels with > 70% stenosis
2. Avoid PCI for distal and branch vessel stenoses
3. Avoid PCI in complex lesion subsets, specifically chronic total occlusions
4. Consider staging the TAVR procedure 1 month after PCI, unless the lesion is type A and there is no renal insufficiency
5. Use DESs rather than bare-metal stents, as the rate of target lesion revascularization is consistently low
6. For complex CAD in low- or intermediate-risk patients, reconsider coronary artery bypass and surgical aortic valve replacement


Figure 2. Percutaneous coronary intervention of the left anterior descending artery 9 months after transcatheter aortic valve replacement (TAVR) with a self-expanding CoreValve system (Medtronic). A 6-F Judkins left 4 guide engaged in the left main ostium through the cells of the self-expanding TAVR device. Arrow indicates a stenosis in the proximal left circumflex (A). After predilatation with a 3-mm balloon, a 4-mm X 12-mm DES was successfully deployed (B; arrow). The final angiographic result showed no residual stenosis (C; arrow).

Jubin Joseph, MA, BMBCh
King’s College London British Heart Foundation Centre of Excellence
The Rayne Institute
St. Thomas’ Hospital Campus
London, United Kingdom
Disclosures: None.

Simon R. Redwood, MD
Professor of Interventional Cardiology
Cardiovascular Department
Kings College London
St Thomas’ Hospital
London, United Kingdom
+44 (0) 207 188 1083;
simon.redwood@gstt.nhs.uk
Disclosures: None.

CAD and senile AS frequently coexist, not only because they share common risk factors, such as diabetes mellitus and hypertension, but because they share a similar underlying pathologic mechanism.1

In patients undergoing surgical aortic valve replacement, untreated CAD increases the risk of perioperative myocardial infarction associated with poor short- and long-term outcomes.2 Current guidelines recommend complete revascularization with coronary artery bypass grafting for CAD (coronary stenosis > 70%, level I; coronary stenosis > 50%, level IIa) to improve long-term outcomes.3-4 There is a greater prevalence of CAD in patients undergoing TAVR compared with surgical aortic valve replacement, however the prognostic implication of this remains unclear.5-7

Given that patients undergoing TAVR tend to be older, with greater comorbidity, it has been debated
whether CAD has any additional adverse effect on clinical outcomes beyond that of severe valvular heart disease and other comorbidities. It is not clear if whether, in this high-risk population, the potential added risk can be ameliorated through revascularization. At our institution, we have attempted to navigate these clinical uncertainties to provide a clear management strategy for CAD in patients undergoing TAVR based on the available evidence and clinical experience.

**IDENTIFYING SIGNIFICANT CORONARY DISEASE IN TAVR PATIENTS**

**Noninvasive Functional Assessment**

In patients with severe AS, the identification of coronary stenosis responsible for myocardial ischemia is not straightforward because stress testing can often show signs of myocardial ischemia in the absence of substantial CAD. Nonetheless, noninvasive stress testing might be considered useful if an area of myocardium subtended by a stenosed coronary artery does not show

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**Figure 1.** An algorithm to help decide whether to perform PCI in patients undergoing TAVR. Considering the clinical presentation, anatomic features, and burden of angina, this algorithm, with the expertise of a heart team approach, can help identify patients in whom revascularization before TAVR may be beneficial.
stress induced dysfunction or hypoperfusion, thereby identifying coronary lesions that are unlikely to benefit from revascularization.

**Invasive Functional Assessment**

Although fractional flow reserve is the gold standard for invasive physiologic assessment of CAD, there is significant uncertainty in interpreting these results in the setting of severe AS. This is, in part, due to the unequal changes that AS has on proximal pressure waveforms, the effect of left ventricular hypertrophy on microvascular function, and the hemodynamic effect of the uncoupling of an aortic valve closure from a fall in left ventricular pressure. Fractional flow reserve before TAVR is not used to help guide revascularization decisions in our institution.

**Anatomic Assessment**

Given the lack of reliable physiologic assessment, the identification of what coronary disease to treat in patients undergoing TAVR is currently driven by anatomic and clinical factors.

Patients with a high SYNTAX score have an increased risk of adverse events during TAVR. A review of the available data and current literature suggests that PCI may be beneficial only in severe proximal stenotic lesions, which places a substantial area of myocardium at ischemic risk. Patients with significant left main stem (LMS) stenosis, or an equivalent, are considered for PCI before TAVR, even in the absence of angina symptoms.

In patients with significant coronary disease (e.g., > 70% in a major epicardial vessel, > 50% in a saphenous vein graft), our decision to consider revascularization depends on the symptoms. Patients with Canadian Cardiovascular Society (CCS) grading of angina III to IV, unstable angina, or a presentation with acute coronary syndrome proceed to PCI if the heart team considers their anatomy suitable. If patients with significant, non-LMS CAD have a CCS angina score of 0 to II, then PCI is deferred (Figure 1).

This approach has been supported by recent guidelines that recommend PCI in patients undergoing TAVR with a coronary stenosis > 70% diameter in proximal coronary segments (class IIa, level of evidence C). There is currently no prospective evidence to support this decision-making process. ACTIVATION is the first ongoing randomized controlled trial of elective PCI before TAVR, which will help define the optimum revascularization strategy and help form evidence-based guidelines on this controversial issue.

**WHEN TO TREAT CAD IN PATIENTS UNDERGOING TAVR**

The decision on when to best undertake PCI is based on clinical, anatomic, and technical factors that are routinely considered by the heart team when contemplating revascularization. Three key considerations are:

**Pre-TAVR (Staged Procedure)**

The advantages of this approach include a reduction in the time taken for a contrast load of the implantation procedure, together with a reduced risk of PCI-related hemodynamic instability that may complicate TAVR. In our practice, most TAVR patients undergoing PCI have had a staged procedure before TAVR.

**Pre-TAVR (Hybrid Procedure)**

Due to the increased contrast load and procedural time, rates of hybrid PCI-TAVR are low. Nevertheless, performing PCI and TAVR during the same invasive session may be a more practical strategy that avoids the risks associated with an additional invasive procedure. As part of a recent meta-analysis, a concomitant approach was found to confer an increased risk of renal failure together with a trend toward higher rates of myocardial infarction and stroke compared to a staged approach.

**Post-TAVR**

The advantage of waiting until after TAVR to perform PCI is that patients can be reassessed for exertional symptoms without the uncertainty that symptoms are attributable to their stenotic valve. Although coronary access is achievable after implantation of all commercially available TAVR prostheses, it may add complexity to the procedure. Given the technical challenges that this strategy brings, it is only considered when the CAD is thought to be unlikely to contribute to the symptoms pre-TAVR.

**HOW TO TREAT CAD IN PATIENTS UNDERGOING TAVR**

The decision concerning coronary stent choice is mostly driven by the subsequent dual antiplatelet therapy requirement and the risk of stent-related complications. When compared to bare-metal stents, DESs have been shown to reduce both the incidence of restenosis and the need for repeat intervention, which has translated into improved clinical outcomes. Given that PCI with DESs has been shown to be safe, and contemporary technology allows for a shorter duration of dual antiplatelet therapy, this is our default option in patients undergoing TAVR.
SUMMARY

The managing of CAD is emerging as an important factor in determining clinical outcomes in patients undergoing TAVR. In the absence of prospective randomized data, our heart team approach is to evaluate potential benefits of revascularization dependent on symptoms, complexity of coronary anatomy, likely ischemic burden, and the comorbidities of each individual patient.

In patients with intrusive angina, or with significant LMS stenosis, we routinely perform revascularization using DESs as a staged procedure before TAVR. Although this seems to be a sensible approach, there is a need for quality prospective randomized data to help inform our decision-making process and add certainty to guideline recommendations.


AS is the most common form of valvular heart disease in the elderly population. TAVR has emerged as a feasible treatment option in patients with symptomatic severe AS at high or intermediate risk for conventional surgical aortic valve replacement. Because the worldwide trend for TAVR is to treat lower-risk patients, considerations on the management of concomitant CAD is of greater importance. The prevalence of CAD in patients referred to TAVR ranges from 40% to 75%. Nevertheless, the impact of CAD on outcomes after TAVR has not been clarified, and the optimal management of concomitant CAD is still debated. Further data are needed to address these issues.

Results from the literature on the impact of CAD on outcomes after TAVR are controversial, mainly due to the heterogeneity of data related to the definition of CAD as well as baseline characteristics and comorbidities of patients, which makes it difficult to evaluate short- and long-term outcomes after TAVR. Some studies have shown that the severity of CAD negatively impacts TAVR outcomes, and the anatomical complexity of the disease leads to a higher risk of death. Conversely, other studies have reported that the presence of CAD does not impact survival after TAVR, the occurrence of major adverse cerebrovascular and cardiac events at 12 months, or the procedural success rates and functional improvement at 30 days after TAVR.

Nevertheless, randomized trials have so far excluded patients with complex CAD, such as unprotected left main (LM) trunk and multivessel CAD. Therefore, the outcomes of TAVR in patients with complex CAD still need to be evaluated appropriately.

Elective PCI can be safely performed in patients with severe AS and in high-risk or inoperable patients in addition to TAVR, without an increased risk of short-term adverse outcomes compared with patients undergoing isolated TAVR. Current guidelines recommend performing PCI before TAVR in patients with a coronary artery diameter stenosis > 70% in proximal segments. However, this recommendation is based on clinical experience rather than clinical studies. Recently, results from a multicenter registry suggest that TAVR plus LM PCI is...
safe and technically feasible and represent a reasonable option for patients at high risk for surgery in the absence of concomitant indication for combined surgical aortic valve replacement and coronary artery bypass graft.\textsuperscript{24}

The potential benefit of complete revascularization is still being debated. However, it has been suggested recently that neither the severity of CAD nor completeness of revascularization is associated with impaired outcomes after TAVR. Considering these results, it seems that complete revascularization is not a prerequisite for success in current TAVR practice and not all patients would require coronary revascularization before TAVR.\textsuperscript{25}

Future randomized studies are required to establish the best treatment strategy for management of CAD in TAVR patients and, until then, the decision for treatment strategy should be made on an individual basis by the heart team based on the specific clinical situation.

**TIMING OF PCI**

When indicated, PCI could be performed either before TAVR as a staged procedure or at the time of TAVR as a single-stage procedure. However, the optimal timing of PCI relative to the TAVR procedure is a subject of debate, and future studies evaluating pros and cons of both these approaches are required.

In a few small observational studies comparing the two strategies, there was a nonsignificant trend toward higher incidence of major access-related complication and renal failure in the staged PCI and TAVR group compared with the single-stage procedure group.\textsuperscript{19-22}

Conversely, PCI after TAVR can often be challenging, and data on its feasibility and safety are limited to only a few case reports.\textsuperscript{26,27} PCI may be technically difficult to perform due to valve struts that may interfere with the cannulation of the coronary arteries. This situation is more likely to occur with balloon-expandable valves, valve-in-valve procedures, and low coronary height.\textsuperscript{28}

**OUR APPROACH**

In our center, a case-by-case approach considering risk-benefit ratio is used to guide patient indication for coronary revascularization in patients referred to TAVR.
CAD screening is always required before TAVR. Although invasive coronary angiography (CA) remains the gold standard for CAD assessment, in our center we use computed tomographic CA (CTCA) as first-line imaging tool for CAD screening.

CTCA is a viable alternative to CA for its proven diagnostic accuracy, noninvasiveness, and low-contrast volume need. However, we prefer to not perform CTCA in patients with severe chronic kidney disease (glomerular filtration rate < 30 mL/min per 1.73 m²) or cardiac tachyarrhythmia not allowing gating. Invasive CA is also indicated in the presence of significant CAD or when coronary anatomy cannot be evaluated after CTCA (e.g. high atrial fibrillation rate, severe calcifications).²⁹

In the presence of hemodynamically significant coronary lesions confirmed by CA, our tendency is to proceed with PCI at the time of TAVR if the risk of the procedure does not outweigh the potential benefits. However, in some selected cases (e.g. patients with severe chronic kidney disease; extremely complex CAD; or complicated PCI) the PCI might be performed also as a stand-alone procedure before TAVR to avoid long and complex procedures with large contrast amount, as there is also a potential increased risk of contrast nephropathy secondary to the additional dye load during the same procedure.

Concomitant PCI in TAVR patients with significant CAD has the potential to reduce the procedural risk of TAVR due to hemodynamic instability related to compromised coronary flow (especially during rapid ventricular pacing and balloon inflation), as well as the need for revascularization after TAVR. We consider concomitant PCI and TAVR for severe coronary stenosis in proximal epicardial coronary vessels that subend a large area of myocardium at risk (e.g. proximal or mid-left anterior descending coronary artery stenosis > 70%; proximal or mid-stenosis > 70% in dominant right coronary artery or left circumflex coronary artery; or LM trunk stenosis > 50%). We don’t recommend PCI in small vessels (< 2.5 mm), distal lesions, and chronic total occlusions. Although recent single-center studies suggest incomplete coronary revascularization may be associated with worse outcomes in patients treated with TAVR and PCI, complete revascularization is not our goal for PCI prior to TAVR, as the rationale to perform PCI is to minimize the risks related to CAD in patients undergoing TAVR procedure.

The advantages associated with a single-stage approach include enhanced resource utilization, patient convenience, and safety due to use of the same arterial access for both the TAVR and PCI procedures on the same day, thereby minimizing the risk of vascular and bleeding complications. We usually use a drug-eluting stent in these cases.

We propose a clinical algorithm (Figure 1) used to assess the need for PCI at the time of TAVR.