Treating Coronary Disease in the TAVR Patient

Making the case for managing CAD in patients undergoing TAVR.

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Transcatheter aortic valve replacement (TAVR) has recently emerged as an attractive, less-invasive therapeutic option compared with traditional surgical aortic valve replacement (SAVR) to treat severe aortic stenosis (AS) in patients with intermediate to high surgical risk. Coronary artery disease (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. Both are characterized by subendothelial accumulation of oxidized low-density lipoproteins and subsequent inflammation with lymphocytes and macrophages, which are responsible for disease progression.

Numerous studies have looked at the management of coexisting CAD in patients undergoing SAVR. In these patients, untreated CAD increases the risk of peri-procedural myocardial infarction causing poor short- and long-term outcomes. As such, current guidelines (the American College of Cardiology and the European Society of Cardiology (ESC)) recommend complete revascularization with coronary artery bypass grafting (CABG) for CAD (coronary stenosis > 70% level I, coronary stenosis > 50% level IIA) to improve long-term outcomes. This is recommended despite some evidence suggesting that concomitant CABG with SAVR is associated with increased perioperative complications as compared with isolated SAVR.

There is a greater prevalence of CAD in patients undergoing TAVR compared to SAVR, however, the prognostic implication of this remains unclear. Given that patients undergoing TAVR tend to be older, with greater comorbidity, it is debated whether CAD has any additional adverse impact on clinical outcomes beyond the effects of severe valvular heart disease and other comorbidities. Furthermore, it is not clear whether in this high-risk population, if that potential added risk can be ameliorated by revascularization.

WHY TREAT CORONARY DISEASE IN THE TAVR PATIENT?

Beyond the conventional risk of CAD resulting in exertional angina and adverse events, the stress of a TAVR procedure can induce ischemia. This is particularly relevant when balloon-expandable valves are implanted that require periods of rapid ventricular pacing that can result in myocardial ischemia and ventricular stunning. Due to this added risk, the effect of CAD on clinical outcomes has been extensively analyzed in retrospective analyses. These studies have used different criteria to define CAD in patients undergoing TAVR, and thus there is no clear consensus of its impact on clinical outcomes.

Groups that have defined CAD by a history of revascularization have found these patients to have a higher perioperative risk. But, importantly, these patients also have a greater prevalence of renal impairment, peripheral vascular disease, and left ventricular systolic impairment, so these findings may not be driven by the presence of CAD alone.

The UK TAVI Registry, defining CAD based on angiographic criteria, did not find this to be an independent predictor of all-cause mortality. This was confirmed in a meta-analysis of seven observational studies by
D’Ascenzo and colleagues that suggested no impact of CAD on mortality after TAVR. These binary definitions of CAD may be too blunt to identify subgroups within the heterogeneous CAD cohort that may have a higher risk of adverse events. Using the SYNTAX score to stratify patients, the Bern TAVI registry showed a higher risk of major adverse cardiovascular events in patients with a SYNTAX score > 22 at baseline compared to those without CAD or a SYNTAX score < 22. Furthermore, in a study of 288 patients at St Thomas’ Hospital in London, there was a higher risk of all-cause mortality in patients with a high SYNTAX score (> 32) when compared to those with intermediate (23–32) or low (< 22) SYNTAX scores.

Overall, there are growing observational data suggesting that the severity of CAD at baseline affects the risk of adverse events among patients undergoing TAVR. The logical question that follows, given the inherent risks of PCI, is what can be done to safely improve clinical outcomes in these patients.

IS IT SAFE TO TREAT CORONARY DISEASE IN THE TAVR PATIENT?

Given the likelihood that complex CAD confers a higher risk of adverse events on patients undergoing TAVR, it is reasonable to suggest that performing PCI to reduce the burden of myocardial ischemia may improve procedural and long-term outcomes. The safety of PCI procedures in TAVR patients was the subject of a recent meta-analysis of nine studies (3,976 patients) comparing clinical outcomes in patients undergoing TAVR versus TAVR with PCI for concomitant significant CAD in severe AS. This analysis demonstrated that PCI, either concomitant or staged, can be safely performed in addition to TAVR for significant CAD in patients with severe aortic stenosis, with no difference in 30-day cardiovascular and 6-month to 1-year mortality between the two groups.

IDENTIFYING WHAT CORONARY DISEASE TO TREAT IN THE TAVR PATIENT

Noninvasive Stress Testing

In patients with severe AS, the identification of coronary stenoses responsible for myocardial ischemia is not straightforward because stress testing can often demonstrate signs of myocardial ischemia in the absence of angiographically substantial CAD. These effects are generally abolished by valve replacement surgery, and no clinical or anatomic factors have been identified to distinguish patients who had symptoms or signs of ischemia due to coronary artery disease as opposed to severe AS.

In patients with known coexisting CAD and severe AS, noninvasive stress testing can be safely performed, but with a lower sensitivity and specificity because of the AS-driven ischemia clouding the picture. There are no data to support the use of noninvasive assessments to guide revascularization in patients undergoing TAVR. Nonetheless, noninvasive stress testing might be considered useful if an area of myocardium subtended by a stenosed coronary artery does not demonstrate stress-induced dysfunction or hypoperfusion, thereby identifying coronary lesions that are unlikely to benefit from revascularization.

Invasive Functional Assessment

Although fractional flow reserve (FFR) is the gold standard invasive physiologic assessment of CAD, there is significant uncertainty interpreting these results in the setting of severe AS. This uncertainty is due, in part, to the unequal changes that AS has on proximal pressure.

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**Figure 1. Algorithm to decide whether to perform PCI in patients undergoing TAVR.** This algorithm, taking into account the clinical presentation, anatomic features, burden of angina, and with the expertise of a heart team approach, can help identify patients in whom revascularization before TAVR may be beneficial.
waveforms, the effect of left ventricular hypertrophy on microvascular function, and the hemodynamic effect of the uncoupling of aortic valve closure from a decrease in left ventricular pressure. These interactions are complex and not fully understood, and as such, there is uncertainty about the interpretation of FFR results in patients before TAVR. After the TAVR procedure and normalization of some of the pathophysiologic effects of severe AS, the FFR results are likely to be more comparable to those values previous but, as yet, there are no methods of predicting the change in FFR due to TAVR.

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.

As previously discussed, patients with a high SYNTAX score are associated with an increased risk of adverse events—a review of the available data and current literature suggests that PCI may be beneficial only in severe proximal stenotic lesions that put a substantial area of myocardium at ischemic risk. As such, patients with significant left main stem stenosis, or equivalent, are considered for PCI prior to TAVR, even in the absence of angina symptoms.

In patients with significant coronary disease (> 70% in a major epicardial vessel or > 50% in a saphenous vein graft), the decision to consider revascularization depends on symptoms. Patients with Canadian Cardiovascular Society (CCS) grading of 3–4 for angina, unstable angina, or a presentation with acute coronary syndrome proceed to PCI if their anatomy is considered suitable by the heart team. PCI is often deferred if patients with significant, non–left main stem CAD, have a CCS angina score of 0–2 (Figure 1).

This approach has been, in part, supported by recently published ESC guidelines on myocardial revascularization that recommend PCI in CAD patients undergoing TAVR with a diameter stenosis > 70% in proximal coronary segments (class Ila, level of evidence C). As yet, there is no prospective evidence base to support this decision-making process, and it is based on personal experience. ACTIVATION (ISRCTN75836930) is the first ongoing, randomized, controlled trial of elective PCI prior to TAVR, which will help define the optimum revascularization strategy in this procedure and help create evidence-based guidelines on this controversial issue.

WHEN TO TREAT CAD IN PATIENTS UNDERGOING TAVR?

Again, there is little evidence to help determine the optimal timing of PCI in patients undergoing TAVR. The decision on when best to undertake PCI is based on clinical, anatomic, and technical factors that are routinely considered by the heart team when considering revascularization.

Pre-TAVR (Staged Procedure)

The advantages of this approach include a reduction in the time taken for, and contrast load of, the implantation procedure, combined with a reduced risk of PCI-related hemodynamic instability that may complicate TAVR. Given these factors, in current practice, most TAVR patients undergoing PCI have had a staged procedure prior to 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 and avoids the risks associated with an additional invasive procedure. As part of a recent meta-analysis, a staged strategy was compared to a concomitant approach, which found an increased risk in renal failure in the concomitant group. Furthermore, although nonsignificant, odds ratios were also higher for myocardial infarction and stroke in the concomitant group.

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. When taking this approach, access to the coronary ostia with the valve device in situ may complicate procedures, and to date, complex PCI procedures requiring significant guide support are reported as single cases. Although coronary access is achievable after implantation of all commercially available TAVR prostheses, there are important considerations to consider if future PCI is anticipated. Newer iterations of TAVR bioprostheses have been designed with reductions in outflow height and wide link spacing to promote access to coronary ostia for future interventions. Given the technical challenges that this strategy brings, it is only considered when the CAD is thought unlikely to contribute to the symptoms prior to TAVR (ie, CCS angina grade 0–2).

HOW TO TREAT CAD IN PATIENTS UNDERGOING TAVR?

The decision concerning coronary stent choice is mostly driven by the subsequent dual antiplatelet therapy (DAPT) requirement and the risk of stent-related complications.
SUMMARY

The management 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 anginal symptoms, complexity of coronary anatomy, likely ischemic burden, and the comorbidities of each individual patient.

With modern technology, there are increasingly few circumstances in which bare-metal stents will be used in preference to drug-eluting stents, and TAVR patients should be treated no differently. Also, once the decision has been made to proceed to revascularization, the procedure can be performed in either a staged or concomitant manner. It is our practice to routinely perform this revascularization as a staged procedure to minimize contrast load and reduce the impact of potential PCI complications on the TAVR procedure.

Although this seems a sensible and practical approach, there is a need for quality prospective, randomized data to help inform our decision-making process and add certainty to guideline recommendations. ■

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