Clinical Conundrum of Coronary Artery Disease and Aortic Valve Stenosis

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Coronary artery disease (CAD) and severe aortic valve stenosis frequently coexist. CAD is prevalent in >60% of patients undergoing surgical aortic valve replacement (SAVR) and up to 65% of patients undergoing transcatheter aortic valve replacement (TAVR). This strong association is thought to be due to the common pathophysiology involving low-density lipoprotein–mediated inflammatory response resulting in an accelerated atherosclerotic process and shares similar risk factors including age, smoking, hypertension, and hyperlipidemia.

Historically, concomitant CAD in patients undergoing SAVR for aortic stenosis was treated by coronary artery bypass grafting (CABG) at the time of SAVR, although there was the presumption of a significantly increased operative risk with the addition of CAGB. The rationale for concomitant CAGB originates from limited early surgical data in which patients undergoing SAVR with unrevascularized CAD had poorer long-term outcomes compared with those that had CAGB. This rationale has now been reinforced by a recent study showing that coronary artery revascularization at the time of aortic valve replacement was associated with improved long-term survival without affecting operative risk. The survival benefit, however, was seen mostly in the group that received a left internal mammary artery to the left anterior descending artery, whereas this benefit was not seen in those that had bypass grafting of the circumflex and right coronary arteries only. Importantly, there has never been a randomized controlled trial of SAVR with versus without CABG. The current American College of Cardiology and American Heart Association valve guidelines give a class IIa recommendation for revascularization of >70% luminal reduction in major coronary arteries or >50% luminal reduction in the left main coronary artery, based more on opinion than evidence.

The introduction of TAVR has presented a paradigm shift in treating severe aortic valve stenosis. With that came the challenge of optimal management of concomitant CAD. The PARTNER and US CoreValve High Risk Study trials, which led to approval of TAVR by the US Food and Drug Administration, excluded patients with unrevascularized CAD. With further advances in the safety of TAVR, however, attention has turned again to discovering the best approach to treatment. Revascularization with percutaneous coronary intervention (PCI) now, in the early days of TAVR, might be less risky than the addition of CABG was in the early days of SAVR. The potential benefits of revascularization prior to TAVR might include the prevention of myocardial ischemia during periods of hypotension and rapid pacing, especially with increased wall stress, microvascular dysfunction, and impaired coronary blood flow. In contrast, there are risks in performing PCI prior to TAVR. These include periprocedural myocardial infarction; bleeding from antiplatelet agents, especially in patients with atrial fibrillation on anticoagulation; and contrast-induced nephropathy. Again, the long-term benefits of complete revascularization are unclear in this population of patients whose primary problem is the increased afterload from the valve disease.

So far, several observational studies have examined the outcomes of CAD and PCI in patients undergoing TAVR. D’Ascenzo et al published a meta-analysis showing lack of impact of the presence of CAD on mortality in patients undergoing TAVR. This analysis was limited by the heterogeneous definition of CAD in the multiple studies that were pooled. Other studies looked at the outcomes of PCI and completeness of revascularization prior to TAVR and, for the most part, did not reveal any benefit in terms of lowering rates of mortality or major cardiovascular events.

In this issue of JAH, Paradis et al performed a retrospective analysis of 377 patients who underwent TAVR. Using quantitative coronary analysis, they calculated a SYNTAX score (SS) and divided patients into 4 groups: no CAD, low SS, intermediate SS, and high SS. They then analyzed their primary outcome, which was a composite of all-cause mortality, stroke, and myocardial infarction at 30 days and 1 year (primary
outcomes), and found no statistically significant difference between the 4 groups. Interestingly, the patients with no CAD had a higher stroke rate and higher atrial fibrillation burden. They also analyzed echocardiographic data and found no significant improvement in left ventricular ejection fraction after TAVR across all groups. In the second part of the study, they looked closely at the patients who underwent PCI within 6 months and divided them into 2 groups: those with high and low residual SS. They also analyzed those that had CABG and divided them according to their CABG SS. Again, no statistically significant difference was found in the primary outcome at 1 year. The authors concluded that severity of CAD and completeness of revascularization, for either PCI or CABG, did not affect the primary outcome of death, stroke, and myocardial infarction at 30 days and 1 year.

This study is certainly a welcome addition to the literature aimed at unraveling the enigma of managing CAD prior to TAVR; however, some points warrant further discussion:

1. The heterogeneous definition of CAD can add potential confounders to the outcomes. Patients can have stable obstructive lesions found incidentally on pre-TAVR coronary angiogram or unstable lesions with recent myocardial infarction. Such nuances could introduce confounders that can affect outcomes and prognoses.

2. The SS was originally designed to help classify patients with 3-vessel disease or left main disease into PCI or CABG. A cutoff of 50% luminal narrowing was used to define obstructive luminal narrowing. In addition, narrowing in small vessels added to the score. Although it is common practice to surgically bypass lesions with 50% stenosis, this degree of luminal narrowing might not be enough to cause flow limitation during TAVR or even affect long-term outcome. Again, this could present confounders that can attenuate the results of the outcomes and could account for the lack of improvement in the left ventricular ejection fraction observed in this study.

3. The group with no CAD in this study had higher rates of stroke, and this could have driven the higher rates of the primary outcome in that group. Interestingly, this group also had higher prevalence of atrial fibrillation; therefore, these results could have been attributed to periprocedural management of anticoagulation rather than a thrombotic phenomenon.

4. Determining the degree and significance of luminal narrowing in the setting of severe aortic valve stenosis is very challenging. Angina is present in patients with severe aortic stenosis, even in the absence of CAD, and the mechanism is most likely related to failure of increase in coronary blood flow and a shorter diastolic time fraction coupled with an increased demand due to the increased afterload. Consequently, a coronary artery lesion can be a red herring if angina is present. Alternatively, if a patient presents with severe aortic valve stenosis and concentric hypertrophy—or other causes that increase oxygen demand even more—and has obstructive CAD and no angina, then most likely these coronary lesions are not functionally significant. Given inter- and intraobserver variability with visual assessment of the angiographic lesions, quantitative coronary analysis can assist in more objective measurement of the luminal narrowing. This method, however, can be inaccurate in extremely calcified and tortuous vessels, both of which are common in severe aortic stenosis; intracoronary imaging might be a more favorable diagnostic choice in this circumstance. In addition, functional evaluation of lesions using noninvasive testing or fractional flow reserve is not validated in severe aortic stenosis, given the global ischemia and microvascular dysfunction that is present in these patients. Using the instantaneous wave-free ratio in severe aortic valve stenosis shows promise and is under investigation.

History has proven to us on multiple occasions that our approach to revascularizing obstructive lesions has been overenthusiastic. Just like the COURAGE trial showed a lack of benefit over medical therapy in patients with stable CAD and the CARP trial proved that revascularization prior to major elective vascular surgery does not change outcomes, we might not be surprised to find that revascularization prior to TAVR does not improve short- and long-term outcomes. The clinical conundrum of managing CAD in patients undergoing TAVR is in need of randomized clinical trials. As the authors alluded to, the results of the ACTIVATION (percutAneous Coronary inTervention prior to transcatheter aortic VAle implantaTION) trial are closely awaited. In this trial, patients with significant CAD (>70% stenosis in >1 lesion or >50% in vein graft or protected left main coronary artery) will be randomized to PCI or no PCI. Other trials such as PARTNER 2A and SURTAVI will also shed light on the impact of revascularization strategies prior to TAVR. Until then, it would be reasonable to intervene with PCI in patients with proximal left anterior descending or left main CAD prior to TAVR, which has been shown to be feasible without incremental risk compared with TAVR alone, or in patients who present with severe angina symptoms—but not necessarily apply our “oculostenotic reflex” to all visible lesions seen on coronary angiography.

Disclosures
None.

References
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