EDITORIALS

The Art and Science of Managing Stable Coronary Artery Disease in Patients Undergoing TAVI

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Transcatheter aortic-valve implantation (TAVI) emerged as a disruptive, revolutionary approach for treating patients with aortic stenosis.[1] However, how we should approach catheter-based therapy in patients with concomitant stable coronary artery disease, which affects approximately 50% of candidates for TAVI, has remained a clinical conundrum. Should we mimic surgical practice and revascularize all obstructive lesions? If so, should we do this before, during, or after TAVI? Or should we not even revascularize at all? After all, would we even know of the presence of coronary artery disease had we not performed coronary angiography as a part of the TAVI workup in the first place? In patients with stable coronary artery disease, percutaneous coronary intervention (PCI) offers symptom relief over medical therapy, without benefits regarding mortality or a risk of myocardial infarction.[2,3] Currently, we exert our best clinical judgment in deciding how to treat patients with concomitant stable coronary artery disease who are candidates for TAVI, without substantial clinical evidence to point us in any clear direction.

Therefore, the third Nordic Aortic Valve Intervention (NOTION-3) trial, the results of which are reported in this issue of the *Journal*,[4] is an eagerly anticipated open-label, randomized, controlled trial that tested the hypothesis that PCI before TAVI in patients with stable coronary artery disease and severe aortic stenosis would be superior to medical management with respect to a primary composite end point of death from any cause, myocardial infarction, or urgent revascularization. Patients with a coronary-artery diameter stenosis of at least 90% on visual assessment or with a coronary-artery diameter stenosis of 50% up to but not including 90%, with a positive fractional flow reserve measurement in vessels that were at least 2.5 mm in diameter, were included. Patients with unstable coronary syndromes or left main coronary-artery stenosis were excluded. Patients were assigned either to undergo PCI or to receive conservative treatment, with all patients also undergoing TAVI.

The median age of the patients was 82 years, the median left ventricular ejection fraction was 60%, and the median number of physiologically significant coronary-artery lesions per patient was one. In the PCI group, the majority of patients underwent PCI either before or concomitant with the TAVI procedure, and a balloon-expandable valve was implanted in 41% of the patients. At a median follow-up of 2 years, the risk of a primary end-point event was 29% lower in the PCI group than in the conservative-treatment group, which came at the expense of a 51% higher risk of the safety end point of any minor, major, or life-threatening or disabling bleeding (with the risk apparently driven mostly by minor bleeding).

The maximal benefit of PCI appeared to be driven by myocardial infarction and urgent revascularization and occurred in patients with angiographic coronary-artery diameter stenosis of 90% or more. The authors and investigators should be congratulated on performing a seminal, potentially practice-changing, large-scale trial that is relevant to daily clinical practice. Should the results of this trial now shift our practice to undertake PCI in physiologically significant lesions with a coronary-artery diameter stenosis of 50% up to but not including 90% or

in non–left main coronary-artery lesions with a diameter stenosis of at least 90% in all patients undergoing TAVI?

No periprocedural harm was noted from TAVI without revascularization per se in the conservative-treatment group. The Kaplan–Meier curves showed the cumulative incidence of myocardial infarction to accrue more commonly in the conservative-treatment group than in the PCI group from approximately 1 year onward, whereas the cumulative incidence of urgent coronary revascularization (which was subject to bias, given patient and operator knowledge of coronary anatomy) accrued earlier. These data suggest that PCI could be delayed in the period after TAVI when one has time to monitor residual symptoms closely, adjust goal-directed medical therapies, and plan a potential PCI (when and if indicated) with a focus on lesions with a coronary-artery diameter stenosis of at least 90%, which are the type of lesions that may have portended incident myocardial infarction in this trial. Post-TAVI PCI may, intuitively speaking, be better undertaken in patients with intact aortic-valve function and unloaded left ventricles and appears to be more advantageous from a bleeding perspective by the avoidance of dual antiplatelet therapy during TAVI that would occur in the context of pre-TAVI PCI.[4-6] The risk of bleeding due to dual antiplatelet therapy use after PCI performed before TAVI is balanced by the difficulty of accessing coronary arteries across an implanted transcatheter heart value when PCI is attempted after TAVI.[7]

The data from the NOTION-3 trial are similar to results from a large, single-center, retrospective analysis by Persits et al. that included patients with high- or extreme-risk coronary anatomy (severe left main or three-vessel coronary artery disease, including those with a reduced left ventricular ejection fraction) and confirmed that the TAVI procedure imparted no added periprocedural risk (relative to the presence of nonobstructive coronary artery disease).[8] Long-term data on all-cause mortality and the risk of unplanned coronary revascularization in that study were also similar to the results in the NOTION-3 trial, which is most likely reflective of the natural history of coronary atheroma burden. An analysis of the coronary-artery lesions in the current trial would also be insightful with regard to understanding the risk of coronary events in the conservatively treated population, which received only TAVI, as would a better appreciation of the use of high-intensity statins during treatment and cholesterol levels, which fundamentally influence the risks of coronary events, even among older patients.[9] On the other hand, some types of lesions, such as ostial lesions that may interact with the valve-stent frame or be deemed difficult to reaccess, may be better treated with PCI before TAVI, with greater attention than usual to the degree of stent extrusion into the aorta. Although this trial has provided the field with much-needed science, the treatment of patients with stable coronary artery disease who undergo TAVI still requires the art of medical and procedural judgment.

Disclosure forms provided by the author are available with the full text of this editorial at NEJM.org.

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