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Editorial

Editorial: Antiplatelet Therapy Post-Transcatheter Aortic Valve Replacement — Less Is More but Is There a Better Option Than Aspirin?

Anita w. Asgar, MD, MSc *

Division of Cardiology, Universite de Montreal, Montreal, Canada

Transcatheter aortic valve replacement (TAVR) has become the treatment of choice for many patients with isolated severe aortic stenosis and is currently recommended by the American College of Cardiology/American Heart Association as a 1A recommendation.[1] The risks of TAVR can be categorized into early and late and include primarily stroke, myocardial infarction, bleeding, and valve thrombosis or prosthetic valve dysfunction. As TAVR has matured, medical therapy has been evaluated in order to establish optimal concomitant treatment to prevent such complications. The rates of stroke have decreased steadily over the past decade with little benefit demonstrated from direct thrombin inhibitors given during the procedure or the use of cerebral embolic protection devices. Experience from coronary stenting led to the rapid adoption of dual antiplatelet therapy (DAPT) to avoid the risk of myocardial infarction post-TAVR, however, recent studies have suggested that the theoretical benefit is outweighed by the bleeding risks in this patient population.

The POPular TAVI trial randomized patients without an indication for anticoagulation or a recent percutaneous coronary intervention to a strategy of single antiplatelet therapy with aspirin (ASA) (lifelong) vs. DAPT with ASA (lifelong) and clopidogrel for 3 months.[2] The primary outcomes were all bleeding and nonprocedural-related bleeding at 12 months. At 1 year, the incidence of bleeding and the composite of bleeding or thromboembolic events were significantly less frequent with aspirin monotherapy than with aspirin plus clopidogrel administered for 3 months. As a result of this trial and other smaller studies, there has been a shift to aspirin monotherapy for patients following TAVR in patients without a recent PCI.

The late risks of TAVR have focused on the occurrence of hypoattenuated leaflet thickening (HALT) which may lead to valve thrombosis and prosthetic valve dysfunction. The mechanisms underlying HALT are unclear and likely multifactorial; however, there is a suggestion that the TAVR procedure may trigger platelet activation and immune system activation contributing to an inflammatory response. In a study of 331 patients, Nuhrenberg et al[3] evaluated the incidence of HALT in patients with variable platelet inhibition responses to clopidogrel, using computed tomography scans. In this study, on-clopidogrel adenosine diphosphate–induced platelet reactivity was not significantly associated with the occurrence of HALT. A study of more potent P2Y12 inhibition with newer antiplatelet agents such as ticagrelor, have been shown to protect against thrombotic events and death in acute coronary syndromes; however, their role in patients post-TAVR is unclear.

In this issue of Structural Heart, Zidar and colleagues present the results of a randomized trial of 2 different DAPT strategies, ASA + clopidogrel and ASA + ticagrelor, and the effects on platelet reactivity and reductions in inflammatory monocytes in patients post-TAVR. In this study of 60 patients, patients were bolused with either clopidogrel or ticagrelor on the day of the TAVR and were given daily doses for 30 days. The primary endpoints were ascertained at 24 hours post-TAVR procedure and included platelet reactivity to adenosine diphosphate, reported as platelet reactivity units using the VerifyNow P2Y12 assay (Accriva Diagnostics, San Diego, California), and the percentage of CD14+CD16+ monocytes relative to total monocytes, measured by flow cytometry. The investigators demonstrated higher platelet inhibition at 24 hours with ticagrelor compared to clopidogrel, but no significant difference in the numbers of circulating inflammatory monocytes, leading them to conclude that a lack of platelet inhibition is likely not an important driver of monocyte activation and the inflammatory response implicated in valve thrombosis. These findings are interesting, particularly considering the study of Nuhrenberg et al.; however, the study lacks clinical or imaging correlation to understand whether the increased platelet inhibition may have an impact on HALT in such patients. This question is currently being studied in the REACTAVI 2 trial randomizing patients to single antiplatelet therapy with aspirin or ticagrelor 60 mg twice a day (NCT05283356) with a primary outcome of safety and secondary outcome of the presence of HALT confirmed on CT imaging.

The implication of such work may be more far reaching than the TAVR procedure alone and perhaps should raise questions on the optimal antiplatelet strategy for PCI prior to TAVR. At present, European Society of Cardiology guidelines recommend DAPT for 6-12 months (I-B) in patients with PCI and TAVR and ACC guidelines suggest DAPT for 3-6

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* Address correspondence to: Anita Asgar, MD, Interventional Cardiologist/Cardiac MR, University of Montreal, Institute of Cardiology of Montreal, 5000 Rue Belanger, Montreal, QC.

E-mail address: anita.asgar@gmail.com.

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months if bleeding risk is low (II-B) post-TAVR.[4] The question is, have we reached a point where we should consider a short course of DAPT post-PCI prior to TAVR and then monotherapy with a more potent antiplatelet agent such as ticagrelor? The TWILIGHT study evaluated a similar question in high-risk patients who underwent PCI. The study results established that ticagrelor monotherapy after 3 months of DAPT was associated with a lower incidence of clinically relevant bleeding than ticagrelor plus aspirin, with no higher risk of death, myocardial infarction, or stroke.[5] Similar findings were published in a subset at high bleeding risk illustrating that ticagrelor monotherapy significantly reduced bleeding without increasing ischemic events, compared with ticagrelor plus aspirin.[6]

DAPT following TAVR is associated with increased bleeding, but the subset of patients requiring PCI will need a DAPT strategy for a certain amount of time. Single antiplatelet therapy may be best for patients following TAVR but perhaps aspirin is not the optimal agent and a more potent antiplatelet agent would be more beneficial.

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