Transient Increase in Pressure Gradients After Termination of Dual Antiplatelet Therapy in a Patient After Transfemoral Aortic Valve Implantation

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Transcatheter aortic valve implantation (TAVI) is considered a transformational novel technology for the treatment of severe symptomatic aortic valve stenosis. It has been rapidly adopted in the clinical arena and meanwhile evolved to the standard of care for inoperable and an acceptable alternative for high-risk but operable patients.\(^1,2\) In analogy to the standard of care for inoperable and an acceptable alternative, anticoagulation with vitamin K antagonists is not deemed necessary after TAVI. However, dual antiplatelet therapy with acetylsalicylic acid and clopidogrel is recommended for 6 months\(^2\) after the procedure, although this treatment regimen is not supported by any scientific evidence.

A 72-year-old man with severe symptomatic aortic valve stenosis (aortic valve area, 0.9 cm\(^2\); mean transaortic gradient, 42 mm Hg; New York Heart Association [NYHA] functional class III; chronic kidney disease; logistic EuroSCORE, 19.8%; Society of Thoracic Surgeons score, 5.4%) underwent uncomplicated transfemoral TAVI using the balloon-expandable Edwards-Sapien bioprosthesis (Edwards Lifesciences Inc, Irvine, CA), which resulted in immediate hemodynamic and clinical improvement, especially in view of dyspnea. The patient was discharged after an uneventful postinterventional course with prescription of dual antiplatelet therapy. At 3-month follow-up, he presented with further improvement in heart failure symptoms (NYHA class I-II) and stable transaortic gradients (Figure 1A). At 6-month follow-up, however, our patient had a new, sudden increase of heart-failure symptoms, especially dyspnea (NYHA class III), along with a rise of brain natriuretic peptide (BNP) levels to 397.6 pg/mL. Transthoracic Doppler echocardiography revealed a nearly 4-fold increase in mean transaortic gradient (Figure 1B), and subsequent transesophageal echocardiography demonstrated somewhat thickened leaflet tips with an impression of leaflet adhesion, impairing proper opening, but there was no evidence of thrombi (Figure 1C). Review of the patient’s history revealed that dual antiplatelet therapy was discontinued prematurely by the general practitioner at 4 months. Because no thrombi were found, we decided to resume dual antiplatelet therapy for treatment. This resulted in a continuous decrease of pressure gradients and of BNP levels to postinterventional values within the next 3 months. Consequently, heart failure symptoms declined again to the level gained at 3 months after TAVI (Figure 1D). Recently, the patient presented for 3-year follow-up with a continuously improved clinical status, stable transaortic gradients (Figure 2), and a further drop of BNP values down to 90.8 pg/mL. Lifetime dual antiplatelet therapy was prescribed.

The current case report is hypothesis-generating and raises questions on the administration and duration of dual antiplatelet therapy after TAVI, which is currently a matter of debate.\(^3\) One possible explanation for the functional and structural bioprosthetic valve alterations observed in our patient might be an accumulation of fibrin during the incorporation progress of the foreign-body stent valve, as recently demonstrated histopathologically for the Medtronic CoreValve prosthesis.\(^4\) Microthrombi formation on the nonendothelialized surface of the bovine pericardial tissue leaflets, which were crimped and might therefore have some microfissures that are prone to platelet adhesion, might offer another explanation. Although echocardiography cannot provide a definitive etiologic diagnosis, the positive effect of resumption of dual antiplatelet therapy might favor the latter hypothesis. In addition, microthrombi formation may also offer one potential explanation for the late neurological events observed in the PARTNER trial and may also advocate the necessity of dual antiplatelet therapy to prevent late strokes.

Since we observed similar findings in an additional 3 patients, we currently believe that dual antiplatelet therapy should be administered for at least 6 months after TAVI when patients are in sinus rhythm. For patients presenting with atrial fibrillation, we use a treatment regimen consisting of...
vitamin K antagonist and clopidogrel to account for the increased bleeding risk with triple therapy. Thus far, however, there is no scientific evidence for any anticoagulation and antiplatelet strategy after TAVI, and randomized, controlled trials are needed to elucidate this clinically important issue.

Disclosures
Drs Thielmann and Kahlert serve as clinical proctors for Edwards Lifesciences.

References

Key Words: aortic stenosis • transcatheter aortic valve implantation • antiplatelet therapy
**Figure 2.** Time course of mean transaortic gradient and calculated aortic valve area. DAT indicates dual antiplatelet therapy; AVA, aortic valve area; and $\Delta P_{\text{mean}}$, mean transaortic gradient.
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