

Antiplatelet Therapy Before Transcatheter Aortic Valve Replacement: Unravelling the Optimal Approach

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This Commentary relates to the article by M. Zhang et al on pages 297-305.

Feeling important makes one heavy, clumsy and vain. To be a warrior one needs to be light and fluid.

Carlos Castaneda

The evolving landscape of transcatheter aortic valve replacement (TAVR) is showing an increasingly safe intervention that can be offered to an increasingly younger and low-risk population. TAVR achieved over time an impressive reduction in procedural complications; despite this, because of age and comorbidities, patients are at very high risk of bleeding and ischemic complications. Periprocedural stroke certainly remains the most fearable, with rates that vary from 1% to 3%.^{1,2} However, despite a notable reduction in the crossing profile of the delivery system and the improved implant technique, periprocedural bleeding still remains an issue, occurring in a significant proportion of patients and adversely affecting prognosis. Appropriate diagnostic preprocedural evaluation, technical optimization in achieving vascular access, and nonmodifiable factors such as age and comorbidities modify overall risk, but certainly appropriate antithrombotic strategy is pivotal in contributing to optimize outcomes. Currently, during TAVR procedures anticoagulation is achieved through weight-adjusted administration of unfractionated heparin, reversed with protamine administration at the end of the procedure, as no indication for long-term anticoagulation exist in these patients.³ Differently from coronary artery disease, where antiplatelet therapy has been thoroughly studied, few certainties are present regarding proper management of antiplatelet therapy in TAVR, with current clinical practice relying mostly on evidence acquired in the coronary field and translated in this clinical scenario. Although after percutaneous coronary intervention dual antiplatelet therapy (DAPT) represents the cornerstone of thrombosis prevention, the adoption of such protocol in TAVR patients might not represent a safe choice. Perhaps, the hemodynamical properties inherent to the implantation site, and the dimension of the stent over which the xenograft leaflets are mounted on the bioprosthesis constitute a very different scenario. Whether to administer DAPT and for how long in the postoperative phase is still matter of debate, and prognostic impact of preprocedural antithrombotic drug administration, because of the paucity of dedicated clinical trials on this topic.

In this issue of the Journal, Zhang et al⁴ report a timely and important study comparing DAPT versus non-DAPT antithrombotic therapy in the preoperative phase in patients undergoing TAVR. To this purpose, authors performed a systematic review of the literature retrieving 5 studies, 1 randomized controlled trial, and 4 observational studies, comprising 2329 patients who underwent TAVR, that were categorized as “non-DAPT” if they received either single antiplatelet therapy (SAPT) or no antiplatelet therapy before intervention or as “DAPT” if they received a preloading dose. The results of the meta-analysis reinforce the concept that a “one-size-fits-all” approach with preoperative DAPT is

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G. Biondi-Zoccai has consulted for Amarin, Balmed, Cardionovum, Crannmedical, Endocore Lab, Eukon, Guidotti, Innovheart, Meditrial, Microport, Opsens Medical, Terumo, and Translumina, outside the present work. All other authors report no conflict of interest.

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not superior in preventing stroke when compared with non-DAPT, causing more minor bleedings [95% odds ratio [OR] 0.58; 95% confidence interval (95% CI), 0.44–0.76; $P < 0.0001$] with no effect on secondary outcomes such as stroke rates (95% OR 1.03, 95% CI, 0.70–1.52) and myocardial infarction (OR 0.76; 95% CI, 0.28–2.08). Among the study limitations, no comparison is possible between SAPT and no antiplatelet therapy because both are categorized as “non-DAPT”; again, whether SAPT with aspirin is superior to clopidogrel should not be inferred because no between-drug comparison is present.

The results, showing an incidence of bleeding of 31.7% in non-DAPT and 43.3% are consistent with data from major trials and demonstrate how hemorrhages still remain a critical issue because risk of death is 1.34 and 2.08 times higher in access-site and non-access-site bleeding, with respect to patients who do not suffer from this complication.⁵ The reduction in delivery sheath size occurred over time and increased operator experience, and routinary adoption of trans-femoral access site certainly contribute to lowering risk, but Zhang et al are to be praised for demonstrating how antithrombotic therapy certainly plays a major role.

The demonstrated lack of efficacy of DAPT in preventing peri-procedural ischemic complications should prompt an appraisal on the pathophysiology of peri-procedural stroke: perhaps, in this context, it is often not directly related to thrombosis, but more to surgical debris and particularly calcium, that is mobilized with high-pressure balloon inflations over diseased valve or while pushing bulky devices through calcified arteries. Hence, only a small portion of strokes can be prevented by platelet inhibition, that, however, notably contributes to increase risk of bleeding. Avoiding postimplantation balloon valvuloplasty and minimizing oral anticoagulant (OAC) interruption in patients with concomitant atrial fibrillation (AF) proved to be safe measures to reduce stroke risk. Furthermore, cardiac embolic protection devices are increasingly used in clinical practice because major trials proved them to be safe and effective in the perioperative period,^{6,7} providing a physical barrier to prevent stroke during intervention. Opportunistic utilization of these devices might represent a valuable alternative to aggressive antithrombotic therapy, especially in very high-risk scenarios such as valve-in-valve, bicuspid valve, severely calcified valve, prior stroke, and patients with atrial fibrillation and CHA₂DS₂VASC >5 .⁸ Notably, these patients were excluded from pivotal trials but exist in every day clinical practice and deserve to be managed on

a case-by-case basis, using all weapons available in current armamentarium.

TAVR constitutes a challenging scenario for antithrombotic therapy. In patients with no recent percutaneous coronary intervention and no concomitant indications to long-term OAC, DAPT is not recommended because it increases bleeding risk with no significant effect on stroke prevention. Preprocedural loading with aspirin, although endorsed by a recent consensus document⁹ and currently representing standard of care, is not backed by consistent data from literature, and its utility should be scrutinized in a dedicated trial. Further studies, including pooled and network analyses,¹⁰ are awaited regarding preprocedural and postprocedural antithrombotic therapy, categorizing patients on the basis of surgical risk and including the potential benefit of cardiac embolic protection devices to prevent periprocedural stroke.

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