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COMMENTARY

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Ticagrelor monotherapy after CABG—Probably not at all and definitely not forever

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The Ticagrelor Antiplatelet therapy to Reduce Graft Events and Thrombosis (TARGET) trial randomized 250 patients after coronary artery bypass grafting (CABG) to ticagrelor monotherapy or aspirin monotherapy. In a previous issue of this journal, the TARGET investigators reported that among 202 patients (80.8%) who underwent imaging at 1 year, ticagrelor did not significantly reduce the risk of the primary endpoint of saphenous vein graft (SVG) occlusion compared to aspirin (13.2% vs. 17.4%, $p = .30$).[1] In this issue of the *Journal of Cardiac Surgery* Kulik et al.[2] report 2-year outcomes for patients in the TARGET trial that consented to remain blinded and continue their study treatment for an additional year. The rate of SVG occlusion in the 142 patients who consented to the extended study and underwent imaging at 2 years after CABG did not differ significantly between the treatment groups (ticagrelor 13.2%, aspirin 15.7%, $p = .71$). Notably, only 4 new SVG occlusions and 2 new SVG stenoses occurred between years 1 and 2, with no significant differences between the treatment arms ($p = .41$).

The apparent lack of effect of ticagrelor monotherapy compared to aspirin monotherapy on the risk of SVG occlusion in the TARGET trial serves to remind us that that considerable gaps in knowledge still exist as to the optimal antiplatelet strategy after CABG, particularly as it pertains to maintaining graft patency. Aspirin has been shown to reduce the risk of SVG occlusion compared to placebo, and initiation of aspirin therapy within 6 h after CABG and continued indefinitely is therefore endorsed by current guidelines as the preferred antiplatelet agent to prevent SVG occlusion.[3,4] Dual antiplatelet therapy (DAPT), consisting of clopidogrel and aspirin, has been shown to improve SVG patency compared to aspirin monotherapy in aggregate data meta-analyses of small RCTs and observational studies; however, the effect may be limited to specific patient subsets such as those undergoing off-pump CABG.[5] Furthermore, the beneficial effects of DAPT on SVG occlusion risk may come at the expense of increased bleeding risk.[6] A more comprehensive synthesis of the available evidence on the effect of contemporary DAPT with ticagrelor and aspirin on SVG patency has yet to be performed; and the few studies that compared ticagrelor monotherapy to aspirin after CABG all failed to demonstrate a significant benefit in their respective angiographic and clinical endpoints at 1 year.[7,8]

Importantly, whereas there is insufficient evidence available regarding the optimal antiplatelet treatment strategy for the first year after CABG, data pertaining to treatment strategies in the longer term are even more scarce, and the optimal duration of antiplatelet therapy after CABG for prevention of graft failure has not been prospectively addressed until now. The data provided in the present study are therefore important, as they show that the rate of late SCG occlusion among patients with patent grafts at 1 year is low irrespective of antiplatelet regimen. These long-term results are consistent with the pathophysiology of SVG failure; i.e., a much lower risk of graft thrombosis later after CABG than early after CABG, with intimal hyperplasia playing a more important role in late SVG failure.[9] Intensified inhibition of platelet aggregation, therefore, has its greatest conceptual appeal early after CABG. Beyond this initial phase, the role of platelet inhibition for maintaining graft patency is less well defined and its optimal duration remains to be established. Although the 2-year

results of TARGET must be considered observational and hypothesis generating, intensified platelet inhibition to prevent SVG failure beyond 1 year does not appear warranted.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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