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COMMENTARY

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Commentary: Ticagrelor monotherapy—Not for CABG?

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Saphenous vein grafts (SVGs) remain the most commonly used conduits in coronary artery bypass grafting (CABG) despite greater rates of both early and late occlusion compared to arterial grafts. In a recent meta-analysis based on aggregate data from 48 studies including 41,530 grafts, the pooled incidence of SVG occlusion within the first year after CABG was estimated at 11%.[1]

The role of aspirin in the prevention of SVG failure has been firmly established. Fremes et al. in a meta-analysis of 17 randomized trials showed that aspirin significantly reduced graft occlusion compared with placebo.[2] A subsequent systematic review of seven studies concluded that administration of aspirin within 6 h of CABG was associated with improved graft patency without increased incidence of bleeding complications.[3] Dual antiplatelet therapy (DAPT) combining aspirin with a P2Y12 inhibitor has since been shown to be the most efficacious treatment regimen to prevent SVG failure, although at the expense of greater bleeding risk.[4] The excess of bleeding events with DAPT has generated interest in the use of antithrombotic approaches that do not include aspirin.

In this issue of *The Journal of Cardiac Surgery*, Kulik et al. present the results of the randomized Ticagrelor Antiplatelet Therapy to Reduce Graft Events and Thrombosis (TARGET) trial.[5] TARGET randomized 250 patients after CABG to receive either aspirin 81 mg twice daily or ticagrelor 90 mg twice daily. The primary outcome of SVG occlusion at 1 year as assessed by computed tomography angiography did not differ significantly between the two groups (aspirin vs. ticagrelor, 17.4% vs. 13.2%, $p = .30$). The secondary outcome of SVG disease, defined as either stenosis >50% or occlusion, also did not show any difference between the randomized treatments (aspirin vs. ticagrelor, 21.5% vs. 22.3%, $p = .88$).

These results are not entirely unanticipated, given previous reports on the lack of a conclusive benefit of ticagrelor monotherapy on SVG patency in the Different Antiplatelet Therapy Strategy after Coronary Artery Bypass Graft Surgery (DACAB) trial,[6] as well as on clinical outcomes in patients undergoing CABG in the Ticagrelor in CABG (TiCAB) trial.[7] The ticagrelor monotherapy arm of the DACAB trial failed to demonstrate a significant difference in SVG patency at 1 year compared with aspirin, although the combination of aspirin and ticagrelor did result in a significant increase in SVG patency.[6] However, 76% of patients in DACAB underwent off-pump CABG (OPCAB), a subgroup for whom a benefit of DAPT using clopidogrel has previously been demonstrated.[8] In the TARGET trial, patients undergoing OPCAB also did not benefit from more potent platelet inhibition provided by ticagrelor. A transient increase in platelet turnover after CABG that limits the duration of platelet TXA_2 inhibition has been proposed as the mechanism for the impaired efficacy of low-dose aspirin observed in the early postoperative period.[9] Multiple daily doses of aspirin may overcome impaired platelet inhibition in response to a conventional once-daily regimen,[10] and may have contributed to a lack of advantage of ticagrelor over aspirin in the current trial. It should be noted, however, that two of the three randomized trials to date evaluating ticagrelor monotherapy (TARGET and TiCAB) were terminated prematurely due to slow enrollment and were individually underpowered to detect a difference in the treatment effect over aspirin, precluding conclusive evidence

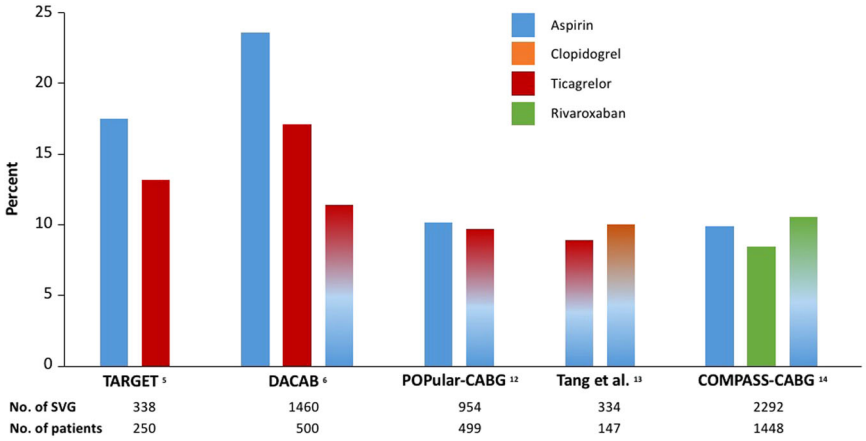

FIGURE 1 Saphenous vein graft occlusion in contemporary randomized trials with computed tomography angiography at 1 year after coronary artery bypass grafting. CABG, coronary artery bypass grafting; DACAB, Different Antiplatelet Therapy Strategy after Coronary Artery Bypass Graft Surgery; SVG, saphenous vein graft; TARGET, Ticagrelor Antiplatelet Therapy to Reduce Graft Events and Thrombosis

on a potential benefit of ticagrelor monotherapy on either SVG patency or clinical outcomes in the setting of CABG.

Prevention of SVG failure requires a multipronged approach, taking into consideration appropriately selected target vessels, atraumatic SVG harvesting technique, use of buffered storage solutions, and postoperative pharmacotherapy including the use of high-intensity statins.[11] Antithrombotic therapy, although a mainstay of therapy, is only one part of the equation. Indeed, the majority of contemporary randomized trials that included imaging follow-up at 1 year have failed to demonstrate a significant benefit of intensified antithrombotic therapy including oral anticoagulation on SVG patency over aspirin[5,6,12–14] (Figure 1). The lack of additional benefit with ticagrelor monotherapy in patients after CABG should also be considered in this context.

The relationship between graft patency, particularly of grafts to non-LAD territories, and clinical outcomes is complex and highly variable.[15] The use of radial artery grafts compared with SVG has been associated with higher patency rates at 5 years,[16] as well as a lower risk of adverse cardiovascular events at 10 years after CABG.[17] Accordingly, a Class I recommendation for the use of radial artery grafts has been issued by both ESC/EACTS[18] and ACC/AHA/SCAI revascularization guidelines.[19] Compared to single antiplatelet therapy, DAPT improved the patency of SVG but not that of arterial grafts in a meta-analysis of five randomized trials.[20] Use of arterial grafts may obviate the need for a more aggressive approach to antithrombotic therapy and should be considered over the SVG in appropriate patients undergoing CABG.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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