Editorial

Dual antiplatelet therapy post CABG?—perhaps, but… why not a radial artery instead?

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Comment on: Zhao Q, Zhu Y, Xu Z, *et al.* Effect of Ticagrelor Plus Aspirin, Ticagrelor Alone, or Aspirin Alone on Saphenous Vein Graft Patency 1 Year After Coronary Artery Bypass Grafting: A Randomized Clinical Trial. JAMA 2018;319:1677-86.

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In a recent issue of the *Journal of the American Medical Association*, Zhao and colleagues report their results from a recently completed randomized trial assessing the efficacy of dual antiplatelet therapy (DAPT) in patients undergoing coronary artery bypass graft (CABG) surgery (1). The authors enrolled a cohort of 500 patients with a follow-up time of 1 year. Patients were randomized to receive either aspirin alone, ticagrelor alone or ticagrelor plus aspirin in a 1:1:1 fashion. The primary outcome, saphenous vein graft (SVG) patency at 1 year, was assessed via either coronary angiography or computed tomographic angiography. In the study, which was restricted to patients undergoing isolated, elective CABG, the authors found a significantly higher rate of SVG patency when using DAPT compared to aspirin alone (88.7% *vs.* 76.5%, P<0.001), while the results comparing ticagrelor alone to aspirin alone did not reach statistical significance (82.8% *vs.* 76.5%, P=0.10). While the authors are encouraged by these results, they do not endorse the use of DAPT post-CABG but instead suggest that further research is warranted to assess bleeding risks between the cohorts.

CABG remains the best treatment for patients with left main disease and complex multi-vessel coronary artery disease (2). SVG is still the most widely used conduit and further research to optimize its patency is warranted. SVG failure has been shown to occur in up to 25% of patients within the first 12 months after surgery (3) and has a key role in the not negligible incidence of post-CABG major adverse cardiovascular events (MACE). Such events [including death, myocardial infarction (MI), stroke, and need for re-intervention] occur at a rate greater than 10% in the first year following surgery (4,5). Additionally, patients who have undergone CABG are at a higher risk of delayed thromboembolic stroke secondary to MI, atrial fibrillation and/or progression of existing atherosclerotic disease, all potentially reduced by DAPT (6).

The current standard for antiplatelet therapy following bypass surgery is aspirin alone (7). While there are recommendations for DAPT for patients who have had acute coronary syndrome, off-pump surgery and/or coronary interventions, there has been no randomized trial primarily focused on CABG patients. Previous trials, such as the CURE (Clopidogrel in Unstable angina to prevent Recurrent ischemic Events) trial and the PLATO (Platelet Inhibition and Patient Outcomes) trial examined patients with acute coronary syndrome and analyzed post-hoc the results of the subgroup of patients who underwent CABG (8,9).

Zhao and coauthors must be commended for their work and thought-provoking outcomes. However, their trial, while sufficiently powered to detect a difference in angiographic patency, did not involve enough subjects to comment on differences in clinical outcomes when using DAPT versus aspirin alone.

The authors make no mention of their algorithm for the choice of the second and third graft following the standard

left internal mammary to the left anterior descending artery primary conduit. Given that 95% of CABG surgery performed in China does not utilize more than one arterial graft (1), it can be assumed that nearly all 500 included subjects only had SVGs as their other bypass conduits.

While it is important to optimize the patency of vein grafts following CABG, and DAPT may be the proper way to do this, it would simplify matters dramatically if this were a non-issue. Previous studies have shown that arterial graft patency is both higher than that of SVGs and remains high even in the absence of antiplatelet therapy (10,11). Thus, to avoid adding to an already complex post-operative medication regimen, patients would be best served with multiple arterial grafts at the time of surgery (we know that the number of medications to be taken daily is inversely related to patient compliance) (12).

The RADIAL (Radial Artery Database International ALliance) group recently published the results of an individual patient-level meta-analysis examining the difference in clinical outcomes between the radial artery and SVG as the second conduit for CABG (13). In the analysis of more than 1,000 patients from 6 randomized controlled trials, the group found that the incidence of MACE was significantly lower in patients with radial artery grafts when compared to those with SVGs [hazard ratio (HR) 0.67; 95% confidence interval (CI), 0.49–0.90] at a mean follow-up time of 5 years. Additionally, though not novel, the study found that there was a higher rate of arterial patency at 5 years (91.9% *vs.* 80.1%, HR 0.44; 95% CI, 0.28–0.70).

The Randomized comparison of the clinical outcomes of single versus multiple arterial grafts (ROMA) trial will evaluate the outcome difference between single and multiple arterial grafts in CABG (14). The trial is already open to enrollment and the pilot phase (10% of the sample size) will be completed in autumn 2018.

While the final results of ROMA won't be completed for another decade, the existing evidence lends support to the concept of multiple arterial grafts at the time of CABG (15). In so doing, the question of aspirin alone compared with DAPT will become a moot point. However, for those patients who cannot receive multiple arterial grafts, due to relative or absolute contraindications, it is reasonable to explore the effect of DAPT post-CABG based on the study by Zhao *et al.* Further research is necessary to validate the benefit of DAPT over the potential harm caused by a possible increased bleeding risk.

In the meantime, we all need to take heart and action in order to translate into everyday clinical practice the "paradigm shift" concerning the widespread use of multiple arterial grafts over venous grafting, as advocated in International Guidelines; it would be unfortunate to have our patients pay the cost of us ignoring the compelling amount of available evidence.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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