Relevance of Indications for CABG in Evaluating the Effect of Dual Antiplatelet Therapy

The secondary analysis of the FREEDOM (Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease) study data (1) leaves unanswered the question of whether patients with acute coronary syndromes (ACS) undergoing coronary artery bypass grafting [CABG] derive benefit from dual antiplatelet therapy (DAPT). However, the subgroup analysis stratified by the indications (ACS or stable angina) that demonstrated no significant benefit in either subgroup provides an additional insight into whether the ongoing distinction between ACS and stable ischemic heart disease in evaluating the effect of DAPT in patients post-CABG is meaningful. This distinction by the clinical indication is largely derived from the historical sequence of trials that initially demonstrated benefits of DAPT use in patients presenting with ACS with or without further percutaneous coronary intervention, culminating in the subgroup analysis of the CABG cohort in the CURE (Clopidogrel in Unstable Angina to Prevent Recurrent Ischemic Events) trial (2). Whether the presenting symptoms would translate into clinical differences relevant to antiplatelet therapy following CABG, however, is questionable.

Potential benefits of DAPT in patients undergoing CABG are derived from stabilization of existing plaque, improving vein graft patency, and continued protection of existing stents (3). Revascularization with CABG alters the coronary perfusion architecture with bypassing grafts. Therefore, although patients with ACS may be more susceptible to subsequent plaque rupture and stent thrombosis, the event may not be as clinically significant in the bypassed coronary anatomy. On the other hand, the benefit of DAPT in preserving vein graft patency has been demonstrated in small trials (4), perhaps implying that the myocardial territory perfused by the vein grafts may be an important baseline parameter in evaluating outcomes of DAPT post-CABG in the future. Clarification of the relevance of the indication would aid in future trial designs, as recent trials have enrolled mixed populations of ACS and non-ACS patients (4).

REFERENCES

REPLY: Relevance of Indications for CABG in Evaluating the Effect of Dual Antiplatelet Therapy

We thank Drs. Mori and Geirsson for their interest in our FREEDOM (Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease) study secondary analysis (1) examining aspirin monotherapy versus dual antiplatelet therapy (DAPT) in diabetic patients with multivessel coronary artery bypass grafting (CABG). We concur with the authors that the postulated benefits of DAPT after CABG include stabilization of the culprit lesion and preservation of both coronary stent and vein graft patency. In addition, DAPT treatment can theoretically: 1) reduce the risk of acute coronary syndrome (ACS) recidivism in nonculprit arteries irrespective of bypass grafting; 2) augment platelet inhibition in aspirin nonresponders; 3) reduce the risks of associated noncoronary conditions (e.g., stroke in patients not receiving anticoagulation for atrial fibrillation); and 4) mediate improved outcomes through nonplatelet receptor interactions (e.g., decreased infarct size via ticagrelor erythrocyte adenosine reuptake inhibition) (2–4).

However, as the authors have astutely highlighted, the evidence supporting routine DAPT post-CABG for...
the prevention of clinical events is based primarily on nonrandomized evidence with substantial inherent limitations, and the small randomized studies published to date have only demonstrated improved graft patency (5). Nonetheless, some clinical practice guidelines recommend 1 year of DAPT for ACS after CABG, thus we felt it was imperative to report results stratified by ACS and stable coronary artery disease.

Given the substantial clinical efficacy and safety uncertainty of DAPT for on-pump CABG, we believe a large randomized controlled trial adequately powered for mortality, graft patency, and safety outcomes should be a research priority for the cardiovascular community.

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http://dx.doi.org/10.1016/j.jacc.2017.04.063

Please note: The authors have reported that they have no relationships relevant to the contents of this paper. Deepak L. Bhatt, MD, MPH, served as Guest Editor-in-Chief for this paper; and Faisal Bakaeen, MD, served as Guest Editor for this paper.

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Hypertension Treatment in the Elderly

Individualized Target or Intensive Blood Pressure Lowering?

The meta-analysis by Bavishi et al. (1) showed that in older hypertensive patients, intensive blood pressure (BP) control decreased major adverse cardiovascular events, whereas the risk of renal failure maybe increased. We wish to discuss some of our views.

First, meta-analysis is considered as the highest level of evidence for guiding clinical practice by professional societies. However, in Bavishi’s analysis, only 4 studies were included, and these studies were with significant heterogeneity, such as differences in trial design, inclusion criteria, and baseline characteristics (2). If clinical heterogeneity cannot be well settled in a meta-analysis, the results should be interpreted with caution.

Second, in the recent clinical practice guideline from the American College of Physicians (3), data from 6 studies showed that lower systolic BP targets (<140 mm Hg) showed no statistically significant reduction in all-cause mortality or cardiac events. In patients with a history of stroke or transient ischemic attack, treating to a systolic BP of 130 to 140 mm Hg reduced stroke recurrence. The different conclusions in the 2 studies may be caused by a difference in the studies included for analysis.

Third, older people are with multiple chronic conditions, such as coronary heart disease, diabetes, chronic kidney disease, and frailty. However, there are little data for determining the optimal BP target (4). Furthermore, to achieve the target BP in elderly patients with chronic conditions, it should be achieved by careful titration of medications and monitoring for side effects.

In conclusion, considering the great clinical heterogeneity among the trials included in Bavishi et al.’s analysis, the results should be interpreted with caution. Emphasizing an individualized target BP weighing side effects and treatment effort may be much more proper than advocating intensive BP lowering.

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http://dx.doi.org/10.1016/j.jacc.2017.04.062

Please note: This work is supported by the Key Specialist Department Training Project of Foshan City, Guangdong, China (No:FSPY3-2015034). The authors have reported that they have no relationships relevant to the contents of this paper to disclose. F.K. Shah, MD, served as Guest Editor-in-Chief for this paper; and Stanley Franklin, MD, served as Guest Editor for this paper.