Editorial

Secondary prevention for CABG patients: take two arterial grafts at the time of your coronary operation

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Submitted Apr 06, 2016. Accepted for publication Apr 14, 2016.
doi: 10.21037/jtd.2016.04.18
View this article at: http://dx.doi.org/10.21037/jtd.2016.04.18

Due to its platelets-inhibitory effect, aspirin is one of the cornerstones in the field of prevention of ischemic events, having been widely shown to improve survival in patients with ischemic heart disease (1-4). The main reason explaining the antiplatelet activity of this drug consists in its ability to irreversibly act on thromboxane-A2 (TXA2), by reducing its production. As part of the wide spectrum of patients with ischemic heart disease, aspirin plays a key role also in the cohort of those undergoing coronary artery bypass grafting (CABG) surgery. Vein graft patency has in fact been demonstrated to be strongly influenced by aspirin, with angiographically detected vein graft occlusion occurring up to five times more frequently in patients receiving placebo than in those receiving acetylsalicylic acid (5). Aspirin administration shortly after CABG has been proved to improve survival by reducing the burden of ischemic events (6) and, accordingly, international guidelines recommend aspirin to be initiated within 6–12 hours postoperatively, if not administered preoperatively (7,8).

Although no question arises on the benefit of postoperative aspirin, intense debate exists on its perioperative use. In fact, the preoperative pharmacological management of patients undergoing CABG surgery reflects the need to accurately balance the enhanced risk of bleeding with the potential reduction in the rate of ischemic events. Notably, the use of cardiopulmonary bypass circuit adversely affects the number, function and morphology of platelets which can actually prompt platelet activation via production of TXA2 (9). This, in turn, may lead to thromboembolic events that may compromise graft patency or cause perioperative myocardial infarctions. Furthermore, abrupt discontinuation of chronic aspirin therapy may trigger a pro-thrombotic rebound phenomenon, potentially leading to increased risk of ischemic events in the perioperative period (10).

To date extremely controversial evidences on this topic have been produced. While several studies and pooled analysis have proved the use of preoperative aspirin to increase perioperative bleeding with no reduction in perioperative myocardial infarction (11,12), other studies showed improved outcomes (including mortality) when aspirin was administered up until surgery, with no increase in associated complications (6,9,12,13).

Such a scenario translates into conflicting recommendations. According to the most recent American Heart Association guidelines, aspirin (100 to 325 mg daily) should be administered to CABG patients preoperatively (7). However, some authors suggest discontinuation of aspirin before CABG surgery to decrease the risk of bleeding complications, highlighting the lack of large clinical trials testing the two different therapeutic strategies (14).

An attempt to provide solid data in order to solve this controversy comes from the recently published multicenter, double-blind, randomized trial "Aspirin and Tranexamic Acid for Coronary Artery Surgery" (ATACAS) (15). Patients enrolled in the study were eligible if they had not been taking aspirin regularly before the trial or had stopped taking it at least 4 days before CABG. They were then randomized to receive aspirin or placebo administered 1 to 2 hours before surgery; postoperative aspirin was then given to both groups. The primary outcome was a composite of death and thrombotic complications within 30 days after surgery. No statically significant difference was observed

between the two groups with regard to primary outcomes. The authors conclude that among patients undergoing CABG, the administration of preoperative aspirin results in neither a lower risk of death or thrombotic complications nor a higher risk of bleeding than that with placebo. Briefly, the evidence in favor of continuing *vs*. stopping antiplatelet drugs before CABG in order to improve patients' outcome still remains highly controversial.

Although it may seem self-evident, it is probably worth acknowledging that long-term outcomes/survival after CABG is strictly linked to graft patency. In an angiographic study enrolling 1,829 CABG patients Lopes and colleagues examined the relationship between vein graft failure (12 to 18 months after surgery) and subsequent clinical outcomes through 4 years after angiography. The composite of death, myocardial infarction or revascularization occurred more frequently among patients who had any vein graft failure compared with those who had none (adjusted hazard ratio, 1.58; 95% confidence interval, 1.21–2.06; P=0.008) (16).

It is now clear that graft patency is in turn intimately related to the type of conduit used for CABG, with arterial grafts showing significantly superior patency rates. In a meta-analysis of all angiographic controlled randomized trials comparing the saphenous vein with all the arterial conduits for CABG, the use of venous grafts was associated with a 4-fold (1.67–16.00) and 3-fold (0.78–22.20) increased risk of late graft occlusion when compared to the right internal mammary artery and the radial artery, respectively (17). In another meta-analysis including almost 80.000 CABG patients a clear survival benefit was found for those receiving two *vs*. one arterial graft (hazard ratio, 0.78; confidence interval, 0.72–0.84; P<0.0001) (18). Recently, Tranbaugh *et al*. estimated that an increase in the rate of bilateral internal thoracic arteries use at 80% has the potential to prevent over 10,000 deaths annually and add >64,000 person years of life over the course of 10 years in the United States (19). Despite that, arterial grafts are still clearly underused on both sides of the Atlantic (20,21).

Early after it was first isolated, the widespread use of acetylsalicylic acid in the prevention of ischemic events was certainly not expected. Nevertheless, it has become a key element in the management of ischemic patients. The results of the ATACAS trial suggest that single patient's risk profile is pivotal when choosing between continuing *vs*. stopping aspirin before CABG. Patients at high ischemic risk (e.g., unstable patients) may benefit most from preoperative aspirin administration while in those at high hemorrhagic and low ischemic risk (e.g., stable patients with a previous history of gastric ulcer) stopping aspirin before surgery may be advisable.

The use of arterial grafts at the time of CABG has the potential to play a new Copernican revolution, being able to dramatically change graft patency rate and, therefore, long-term survival in both high and low risk patients.

It is the time for a change in surgeons' habits and attitudes, in order to translate current evidence into everyday clinical practice. Arterial grafts should be part of the standard treatment of CABG patients, not differently from postoperative aspirin.

Acknowledgements

None.

Footnote

Provenance: This is an invited Editorial commissioned by the Section Editor Kai Zhu (Department of Cardiac Surgery, Zhongshan Hospital Fudan University, Shanghai, China).
Conflicts of Interest: The authors have no conflicts of interest to declare.

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Cite this article as: Gaudino M, Di Franco A, Crea F, Girardi LN. Secondary prevention for CABG patients: take two arterial grafts at the time of your coronary operation. J Thorac Dis 2016;8(6):1057-1059. doi: 10.21037/jtd.2016.04.18

