Use of Antiplatelet Drugs After Cardiac Operations

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Unfortunately, venous bypass grafts still have a prominent role in operative coronary revascularization (coronary artery bypass graft [CABG]). Venous grafts develop pathologically occlusive disease that limits the effectiveness of CABG, and antiplatelet drugs following operation may limit this problem. The types and indications of antiplatelet drugs following CABG generate some controversy in the recent literature. This review surveys relevant evidence about the use of antiplatelet drugs following CABG to identify the controversial issues, define appropriate questions, and attempt to provide evidence-based interventions that may be helpful in limiting graft occlusion after CABG. Evidence suggests that, in most CABG patients, dual antiplatelet drugs (aspirin and clopidogrel), given after operation, minimizes early (within 1 year) graft failure and improves intermediate-term outcomes, better than single antiplatelet therapy with aspirin alone. There are gaps in the knowledge base that supports this contention, and future clinical trials will likely augment or alter this recommendation.

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QUESTIONS ABOUND ABOUT DUAL ANTIPLATELET THERAPY

The Bleeding Risk of Dual Antiplatelet Therapy and the Effect on Vein Graft Patency

Patients with acute coronary syndromes (ACS) derive long-term event-free benefit from dual antiplatelet therapy. A minority of patients with ACS (10%-20%) require urgent or emergent operation after initial treatment of ACS. Inevitably, some patients on dual antiplatelet drugs will have coronary artery bypass graft (CABG), while on therapeutic doses of these drugs. The effect of stopping dual antiplatelet therapy before operation on vein graft patency is uncertain. This uncertainty is reflected in the diversity of surgeons' preferences about dealing with preoperative antiplatelet drugs.[1]

In the modern era, preoperative clopidogrel is an essential risk factor for blood transfusion, for re-exploration due to bleeding, and for life-threatening bleeding.[2] One study found that, aside from preoperative medications like clopidogrel, there are no strong preoperative multivariate clinical risk factors that predict postoperative bleeding. Contrary to the findings of the post hoc analyses of randomized trials, observational studies showed that recent exposure to clopidogrel before CABG translates to increased risk of postoperative death, reoperations for bleeding, blood loss, and need of blood transfusions.[3] Clopidogrel plus aspirin treatment within 5 days before surgery increased the risk of bleeding and reoperation in all CABG patients, irrespective of whether surgery was performed on- or off-pump.[4] Importantly, stopping clopidogrel for even a few days reduces the bleeding risk in CABG patients.[5] There is an approximate 20% decrease in bleeding risk with each day that clopidogrel is stopped before CABG. However, evidence-based guidelines continue to recommend stopping clopidogrel at least 5 days before CABG and that performing CABG on aspirin alone is associated with postoperative increased bleeding (usually mild) but likely decreases the long-term hazard of coronary events.[6] Figure 1 is a summary of management principles in patients taking clopidogrel and aspirin before operation.

Importantly, there is almost no evidence that addresses the effect of *preoperative* antiplatelet therapy on postoperative vein graft patency. Traditional

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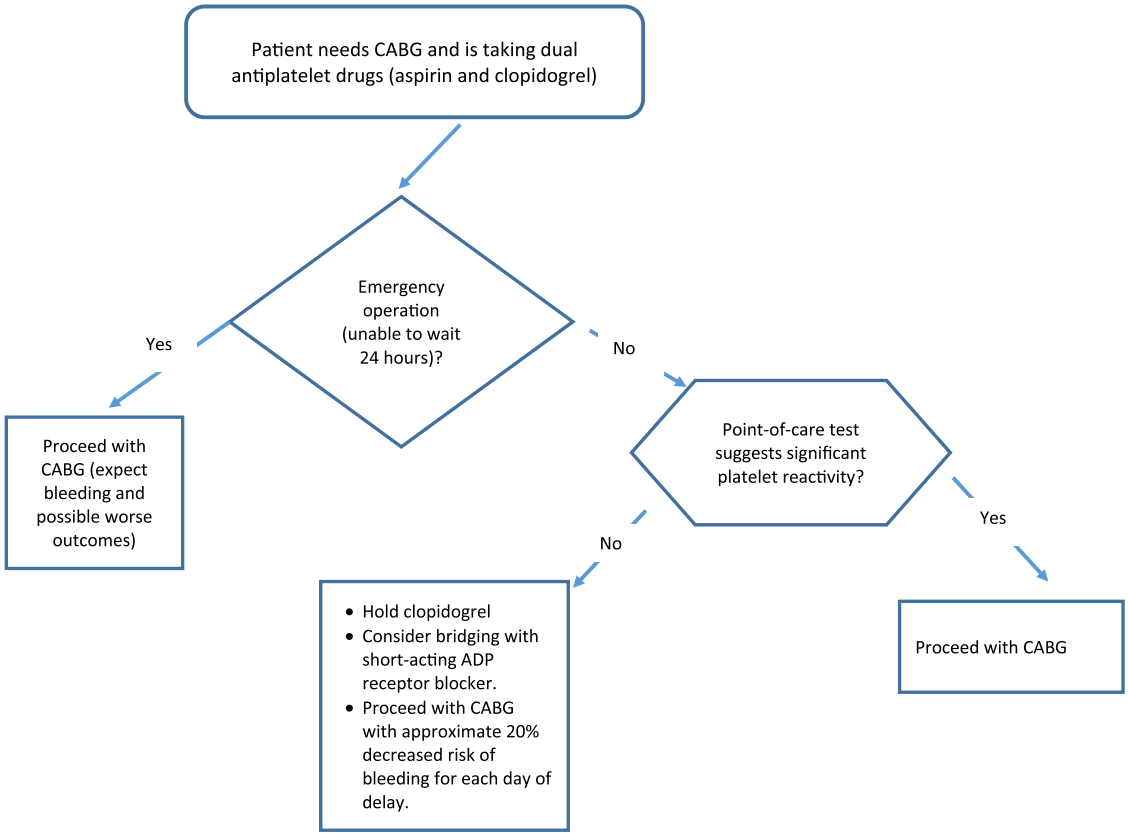

Figure 1. Suggested management of patients taking dual antiplatelet therapy before CABG. (Color version of figure is available online at http://www.semthorcardiovascsurg.com.)

dogma suggests that vein graft patency is independent of the presence of antiplatelet drugs before or during operation. This dogma allowed surgeons to stop antiplatelet drugs before operation without fear of progression of postoperative graft thrombosis as long as antiplatelet drugs were started shortly after operation. Given our current understanding of the pathophysiology of vein graft disease, the optimal time to have an antiplatelet effect for limiting vein graft disease is when the vein graft is harvested. Intimal injury-inducing platelet activation and deposition is the inciting event for the progression of vein graft disease. It makes sense to have an antiplatelet effect while harvesting venous conduit as most platelet-related intimal injuries occur at the time of harvest. Adding antiplatelet therapy after intimal injury is a little like "closing the barn door after the horse has been stolen." It is possible that the best way to minimize vein graft disease is to have an antiplatelet effect on board at the time of vein graft harvest. Of course, the bleeding risk of antiplatelet drugs produces other concerns that argue in favor of stopping antiplatelet drugs before operation. Newer strategies are needed that provide a local antiplatelet effect that minimizes intimal injury to harvested vein grafts while limiting the systemic bleeding risk associated with these drugs.

Postoperative Antiplatelet Drugs and Bypass Graft Patency

Thrombosis of vein grafts limits the benefits of coronary artery operations. There is a continuous annual risk of graft loss, mainly vein grafts, following operative coronary revascularization (CABG). Graft loss is greatest in the first year after operation due to conduit trauma, intimal disruption, and reactive inflammation associated with harvest and implantation into arterial pressure.[7] The re-endothelialization of venous conduits is particularly sensitive to platelet deposition in endothelial-traumatized surfaces with development of neointimal hyperplasia and ultimately atherosclerosis. Based on this pathophysiology, antiplatelet regimens aimed at limiting harmful re-endothelialization make intuitive sense.

Nearly all of the evidence that antiplatelet drugs minimize vein bypass graft disease is limited to 2 drugs: aspirin and clopidogrel. These 2 drugs alter platelet function at 2 different sites in the platelet activation mechanism. Aspirin inhibits the cyclooxygenase