



Literature Reviews

Effect of clopidogrel premedication in off-pump cardiac surgery are we forfeiting the benefits of reduced hemorrhagic sequelae?

Kapetanakis EI, Medlam DA, Petro KR, Haile E, Hill PC, Dullum MK, Bafi AS, Boyce SW, Corso PJ. *Circulation*. 2006 Apr 4;113(13):1667-74. Epub 2006 Mar 27

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Abstract: The use of clopidogrel reduces the incidence of thrombotic complications after percutaneous coronary revascularization procedures. However, because of the irreversible platelet inhibition that clopidogrel causes, patients subsequently undergoing surgical revascularization are at increased risk of bleeding complications and transfusion requirements. The purpose of this study was to determine if clopidogrel administration led to increased hemorrhagic complications (hemostatic reexploration, transfusion requirements, morbidity, etc.) in patients undergoing off-pump coronary artery bypass grafting (CABG). Off-pump surgery was selected because of the proposed benefits in reducing hemorrhagic complications versus traditional CABG surgery utilizing cardiopulmonary bypass (CPB). One thousand, five hundred, seventy-two patients who had isolated off-pump CABG surgery were identified and their perioperative course examined retrospectively. Of these 1,572 patients 281 (17.9%) did and 1,291 (82.1%) did not receive clopidogrel prior to their operation. The group receiving clopidogrel had a five times higher likelihood of hemostatic reoperations, a 60% increase in the odds of receiving packed cell transfusions and a 2.5 times higher likelihood of platelet transfusion. Clopidogrel patients also had a higher median length of hospital stay. The mortality rate was not significantly different. The authors conclude that clopidogrel administration in the cardiology suite increased the risk for hemostatic reoperation and requirements for blood products perioperatively for patients subsequently undergoing off-pump CABG surgery.

Comments: Proponents of off-pump CABG surgery cite decreased transfusion requirements as one of the benefits when off-pump surgery is compared to more traditional CABG utilizing CPB. However, the authors of this study demonstrate this potential benefit is mitigated by the use of clopidogrel preoperatively, as these patients required increased blood product transfusions and surgical reexplorations. It should be noted that the retrospective nature of the study presents limitations, one of which is

that physicians were not blinded to the use of clopidogrel in patients and therefore may have had a bias towards more blood product (especially platelet) transfusions. However, this should have had no bearing on the differences seen in surgical reexploration.

These results pose a dilemma for physicians involved in caring for these patients. The benefits of clopidogrel, coupled with its relatively low side effect profile, have led to widespread use by everyone from internists to emergency room physicians in patients thought to be experiencing myocardial ischemia. While the majority of these patients may not need surgical revascularization, those that do may end up requiring more transfusions and their inherent risks (infection, transfusion reactions, etc.), as well as surgical procedures. The authors suggest that perhaps administration of clopidogrel be delayed until it is certain which type of intervention patients will undergo. This, however, may not be realistic. An accompanying Editorial notes that the majority of patients do not go on to have surgical intervention; thus, withholding clopidogrel in all patients may lead to increased risk (Bavry AA, Lincoff AM: Is clopidogrel cardiovascular medicine's double-edged sword? *Circulation*, 2006 Apr 4;113(13):1638-1640). The Editorial also proposes that patients who have received clopidogrel should perhaps have their surgery delayed for five days when possible, or withhold the drug when surgical intervention seems likely rather than withholding it in all patients. This recommendation however, has its own drawbacks, namely not all patients can have their surgery delayed safely with medical management, and not all patients are easily pre-identified as being destined for surgical management.

Previous studies have demonstrated that clopidogrel is associated with increased bleeding risks, but these were mostly in patients undergoing surgery associated with CPB. This is the first study to demonstrate the increased risk of hemorrhagic complications in off-pump CABG surgery in patients on clopidogrel, something many of us have experienced anecdotally. From an anesthesiologist's perspective, we usually inherit the patient who has already received clopidogrel as we are not present during the initial evaluation and/or treatment of most of these patients. However, we can participate in discussion with the cardiologists and surgeons regarding optimal surgical timing for these patients to reduce the use of blood products, possibly avoiding complications associated with increased transfusions, and continue to judiciously allocate our limited blood product resources.