

Platelet Inhibition and Bleeding Complications in Cardiac Surgery Patients

Clinical and experimental studies

AKADEMISK AVHANDLING

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Avhandlingen baseras på följande delarbeten

- I. Hansson EC, Rexius H, Dellborg M, Albertsson P, Jeppsson A.
Coronary artery bypass grafting-related bleeding complications in real-life acute coronary syndrome patients treated with clopidogrel or ticagrelor.
Eur J Cardiothorac Surg. 2014 Oct;46(4):699-705.
- II. Hansson EC, Jidéus L, Åberg B, Bjursten H, Dreifaldt M, Holmgren A, Ivert T, Nozohoor S, Barbu M, Svedjeholm R, Jeppsson A.
Coronary artery bypass grafting-related bleeding complications in patients treated with ticagrelor or clopidogrel: A nationwide study.
Eur Heart J 2016 Jan 7;37(2):189-197.
- III. Hansson EC, Shams Hakimi C, Åström-Olsson K, Hesse C, Wallén H, Dellborg M, Albertsson P, Jeppsson A.
Effects of ex vivo platelet supplementation on platelet aggregability in blood samples from patients treated with acetylsalicylic acid, clopidogrel or ticagrelor.
Br J Anaesth. 2014 Mar;112(3):570-575.
- IV. Hansson EC, Malm CJ, Hesse C, Hornestam B, Dellborg M, Rexius H, Jeppsson A.
Recovery of platelet function and effects of ex vivo platelet transfusion after discontinuation of ticagrelor in serial blood samples from patients awaiting coronary artery bypass grafting.
Submitted
- V. Hansson EC, Dellborg M, Lepore V, Jeppsson A.
Prevalence, indications and appropriateness of antiplatelet therapy in patients operated for acute aortic dissection: Associations with bleeding complications and mortality.
Heart. 2013;99:116-121.

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BACKGROUND AND OBJECTIVE: Dual antiplatelet therapy (DAPT) with acetylsalicylic acid and a P2Y₁₂ inhibitor (clopidogrel, ticagrelor, or prasugrel) reduces thrombotic events in patients with acute coronary syndrome (ACS), but it is also associated with an increased risk of bleeding complications. The aim of this project was to investigate the prevalence and effects of platelet inhibition in the context of cardiac surgery, the bleeding problems that may occur, and treatment of bleeding complications.

METHODS: Studies I and II investigated the incidence of CABG-related bleeding complications with DAPT in relation to time from discontinuation. Study I was a regional pilot study and Study II was a nationwide registry analysis. Studies III and IV were experimental *ex vivo* studies of platelet function in patients treated with platelet inhibitors, as measured by multiple-electrode aggregometry. Study III investigated the effects of platelet transfusion in patients with different platelet inhibitors, and Study IV examined the effects at time points after discontinuation. Study IV also investigated the recovery of platelet aggregability after discontinuation of ticagrelor. Study V examined the role of platelet inhibition in patients operated for acute aortic dissection.

RESULTS: The incidence of CABG-related major bleeding was high when DAPT was discontinued < 24 hours before surgery. Discontinuation 3 days before surgery, as opposed to 5 days, did not increase the incidence with ticagrelor, but increased the risk with clopidogrel. The overall risk of major bleeding was lower with ticagrelor than with clopidogrel. Platelet supplementation improved platelet aggregability independently of antiplatelet therapy. However, the effect on ADP-induced platelet aggregation was limited, and it was reduced further with ticagrelor compared to clopidogrel. Platelet concentrate did not improve aggregation at later time points after discontinuation of ticagrelor. Platelet aggregation recovered to levels not associated with bleeding 72 hours after ticagrelor, but with large inter-individual variation. The indication for antiplatelet therapy in patients operated for acute aortic dissection was weak or absent in most cases. Patients with ongoing platelet inhibition at the time of aortic repair had more bleeding complications, and DAPT was associated with increased early mortality.

CONCLUSIONS: DAPT with ticagrelor allows shorter discontinuation time before surgery than clopidogrel, and timing of surgery may be aided by platelet function testing. In case of bleeding, platelet transfusion can be expected to improve platelet function, but less so in ticagrelor-treated patients than in clopidogrel-treated patients. It is important to carefully consider the indication for DAPT before treatment is started in patients who may undergo surgery.

KEYWORDS: Acute coronary syndrome, bleeding complications, cardiac surgery, platelet aggregation inhibitors, platelet transfusion