

Cardiac surgery and antiplatelet therapy

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i Förmaket, Sahlgrenska Universitetssjukhuset, Göteborg den 24 mars, klockan 9.00 av

Carl Johan Malm

Legitimerad Läkare

Fakultetsopponent:

Docent Jan Holst

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Avhandlingen baseras på följande delarbeten

- I. Hansson EC, Malm CJ, Hesse C, Hornestam B, Dellborg M, Rexius H, Jeppsson A. Platelet function recovery after ticagrelor withdrawal in patients awaiting urgent coronary surgery. *Eur J Cardiothor Surg*, 2016; doi:10.1093/ejcts/ezw373.
- II. Malm CJ, Hansson EC, Åkesson J, Andersson M, Hesse C, Shams Hakimi C, Jeppsson A. Preoperative platelet function predicts perioperative bleeding complications in ticagrelor-treated cardiac surgery patients: a prospective observational study. *Br J Anaesth*. 2016 Sep;117(3):309-15.
- III. Malm CJ, Singh S, Hesse C, Jeppsson A. Aprotinin but not tranexamic acid improves in vitro platelet function in blood samples from ticagrelor and aspirin treated patients. Submitted.
- IV. Malm CJ, Björklund E, Hansson EC, Wessman C, Rexius H, Nozohoor S, Nielsen S, Jeppsson A. Platelet inhibition and survival after coronary artery bypass grafting in patients with acute coronary syndrome: A nationwide study from the SWEDHEART registry. Submitted.

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Background

Dual antiplatelet therapy (DAPT) with acetylsalicylic acid (ASA) and a P2Y₁₂ inhibitor improves outcome in acute coronary syndrome (ACS). In the subset of ACS patients undergoing urgent cardiac surgery, ongoing or recently discontinued DAPT is associated with increased risk of bleeding. Postoperative DAPT in ACS patients after coronary artery bypass grafting (CABG) may improve graft patency and short-term survival. The aim of this project was to study ACS patients undergoing cardiac surgery and how DAPT with ASA and ticagrelor influences perioperative bleeding risks, how bleeding can be treated, and to investigate if survival after CABG is influenced by antiplatelet therapy.

Methods

In paper I, recovery of platelet function after discontinuation of ticagrelor was investigated using multiple-electrode aggregometry (MEA) in ACS patients awaiting CABG. The effect of platelet concentrate at different discontinuation times was also studied. Paper II was a prospective observational study of patients undergoing cardiac surgery with ongoing or recently discontinued ticagrelor treatment. The relationship between preoperative MEA and postoperative bleeding was investigated. In paper III, MEA was used to investigate the effect of aprotinin and tranexamic acid on platelet function in ACS patients with ongoing DAPT using ASA and ticagrelor. Paper IV was a nationwide study of all ACS patients undergoing isolated CABG surgery during a four-year period. The influence of postoperative antiplatelet therapy on one-year mortality was investigated using propensity score matching.

Results

Mean platelet ADP-induced aggregation increased gradually after ticagrelor discontinuation and reached normal values after 72–96 hours. There was a large inter-individual variability. Platelet concentrate did not improve ADP-induced aggregation at any time, but markedly increased arachidonic acid-induced aggregation at all time points. Preoperative ADP-induced aggregation predicted severe bleeding complications, with an optimal cut-off of 22 aggregation units. Aprotinin, but not tranexamic acid increased ADP-induced aggregation in patients with ongoing DAPT using ASA and ticagrelor. Postoperative treatment with ASA + ticagrelor was associated with a reduced one-year mortality compared to ASA only (hazard ratio 0.42, $p=0.020$).

Conclusions

Platelet function testing improved the assessment of the operative risk in ticagrelor treated patients. Platelet transfusion have no or limited effect in treating bleeding in patients with recent ticagrelor therapy. From a platelet function perspective, aprotinin may be preferred over TA in ticagrelor treated patients. Survival after CABG in ACS patients is likely influenced by postoperative antiplatelet therapy, with improved outcome associated with ticagrelor treatment.

Keywords: Cardiac surgery, Platelets, Acute Coronary Syndrome

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