

Platelet inhibition and secondary prevention in cardiac surgery patients

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i Katastrofrummet, Thoraxkliniken administration, Sahlgrenska Universitetssjukhuset, den 1 december, klockan 09.00 av

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Legitimerad Läkare

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Avhandlingen baseras på följande delarbeten

- I. Björklund E, Hansson EC, Romlin BS, Jeppsson A, Malm CJ. *Postoperative platelet function is associated with severe bleeding in ticagrelor-treated patients*. *Interact Cardiovasc Thorac Surg*. 2019 May 1;28(5):709-715.
- II. Björklund E, Nielsen SJ, Hansson EC, Karlsson M, Wallinder A, Martinsson A, Tygesen H, Romlin BS, Malm CJ, Pivodic A, Jeppsson A. *Secondary prevention medications after coronary artery bypass grafting and long-term survival: a population-based longitudinal study from the SWEDEHEART registry*. *Eur Heart J*. 2020 May 1;41(17):1653-1661.
- III. Björklund E, Malm CJ, Nielsen SJ, Hansson EC, Tygesen H, Romlin BS, Martinsson A, Omerovic E, Pivodic A, Jeppsson A. *Comparison of midterm outcomes associated with aspirin and ticagrelor vs aspirin monotherapy after coronary artery bypass grafting for acute coronary syndrome*. *JAMA Netw Open*. 2021 Aug 2;4(8):e2122597.
- IV. Björklund E, Enström P, Nielsen SJ, Tygesen H, Martinsson A, Hansson EC, Lindgren M, Malm CJ, Pivodic A, Jeppsson A. *Post-discharge major bleeding, myocardial infarction and mortality risk after coronary artery bypass grafting*. Submitted

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Background and objective: Coronary artery bypass grafting (CABG) is the most common cardiac surgery procedure. Dual antiplatelet therapy (DAPT) reduces the risk for ischaemic events in patients with acute coronary syndrome (ACS) but increases the bleeding risk. Statins, beta-blockers, and renin-angiotensin-system (RAS)-inhibitors are commonly prescribed after CABG but the scientific evidence for their use after CABG is scarce. The objective of this thesis is to investigate how pharmacotherapy are associated with short- and long-term risk for adverse events after CABG.

Methods: Study I: Platelet function before and after cardiac surgery was analysed using impedance aggregometry in patients treated with acetylsalicylic acid and ticagrelor. Associations between pre- and postoperative platelet function and risk for severe postoperative bleeding were investigated.

Study II-IV: Data from several nationwide registries was merged to obtain data on procedural aspects, baseline comorbidities, adverse events and mortality after CABG. Study II investigated use of statins, beta-blockers, RAS-inhibitors and platelet inhibitors and mortality risk. Study III investigated DAPT with ticagrelor vs ASA monotherapy after CABG in ACS patients. Study IV investigated the mortality risk associated with post-discharge major bleeding and myocardial infarction respectively.

Results: Postoperative ADP-induced platelet function predicted severe bleeding with moderate accuracy. Ongoing use of statins, RAS-inhibitors and platelet inhibitors were associated with reduced mortality risk after CABG. Use of beta-blockers was not associated with lower mortality risk. DAPT with ticagrelor was not associated with lower risk for ischaemic events but increased the bleeding risk compared with ASA monotherapy. Post-discharge major bleeding was associated with a marked increase in mortality risk, comparable to the increase in mortality risk associated with post-discharge myocardial infarction.

Conclusions: Adding a postoperative test of platelet function did not improve the accuracy in predicting severe bleeding. Improving long-term utilization of statins, RAS-inhibitors and platelet inhibitors poses an opportunity to improve long-term survival after CABG. Clinical trials are warranted to establish the outcome of DAPT with ticagrelor after CABG in ACS patients, especially considering the increased mortality risk associated with post-discharge major bleeding.

Keywords: coronary artery bypass grafting, secondary prevention, bleeding complications, impedance aggregometry