Thrombosis and hemostasis in coronary artery bypass grafting surgery

III. Impact Paragraph

This paragraph reflects on the impact of the research presented in this thesis. We will concisely introduce the context of the research performed (1) before we address the research performed itself (2), in order to enable the reader to fully understand the relevance of this research (3) and finally, to whom this research may concern (4).

1. **Context**

As mentioned in the introduction of this thesis, cardiovascular disease remains the leading cause of death worldwide. Surgical treatment of coronary artery disease by coronary artery bypass grafting (CABG) is the most commonly performed cardiac surgery procedure with an incidence of 44 per 100.000 individuals in the modern world, and is still the preferred method of revascularization above percutaneous coronary intervention (PCI) in certain patients.

Retaining the balance between thrombosis and hemostasis in patients undergoing cardiac surgery remains one of the most difficult tasks for treating physicians. Averting both bleeding complications as well as thrombotic complications is vital for we know that the consequences of both are severe. In case of bleeding complications we know that red blood cell transfusions are a risk factor for mortality and that revision for bleeding is associated with mortality. Of course, severe bleeding itself can be fatal. Thrombotic complications include (but are not limited to) postoperative myocardial infarction, stroke, pulmonary embolisms and graft failure. Graft occlusion after CABG on itself presents a whole new set of problems, being associated with new angina complaints, myocardial infarction and long-term survival. Reinterventions for graft failure are associated with morbidity and mortality.

2. **Research**

The main aim om this thesis was to investigate methods to prevent these complications. The first part of this thesis examined the association of certain point-of-care platelet function tests, coagulation parameters and whole blood viscoelastic tests with postoperative blood loss. The second part of this thesis addresses the specific problem of graft failure and the randomized controlled trial we have performed to investigate whether ticagrelor added to the standard aspirin therapy can improve graft patency. The third part of this thesis contains the optimization of long-term postoperative care.

3. **Relevance**

The research presented in the first part of this thesis (prevention of bleeding complications during CABG) was aimed at finding parameters associated with blood loss and bleeding complications, following the notion that the first step towards prevention of postoperative bleeding complications, is predicting in which patients these will occur. Indeed, we were able to identify associations between certain point-of-

care tests and biomarkers. Naturally, the impact of these findings is not yet certain and further investigation is needed to truly determine the use of these tests, but hopefully these findings can provide some foundation for preventing bleeding events in CABG patients.

We conducted the randomized, placebo-controlled POPular CABG trial that is presented in part two of this thesis, in order to answer the question whether the addition of ticagrelor to standard aspirin therapy after CABG could improve graft patency. Although graft occlusion is a surrogate outcome and the trial was not powered for clinical events, we could not establish a discernable effect of the addition of ticagrelor on graft patency. Thereby, based on this trial, we would advise against the standard addition of ticagrelor to aspirin in order to improve graft patency. Ticagrelor is an antithrombotic drug, and can therefore cause bleeding events. The knowledge that it does not improve graft patency can therefore be essential for treating physicians and perhaps prevent some of these bleeding events, and we expect results of this study will be taken into account when international guidelines are composed.

How to deal with the long-term consequences of CABG and thrombosis and hemostasis management is the topic of the last part of this thesis. The finding of the observational study that long-term mortality as well as other adverse events remains higher in elderly patients who undergo PCI as compared with CABG, and the finding that completeness of revascularization was not a predictor of adverse outcomes, might contribute a little to discussion of 'which method of revascularization is best'. It is debatable whether elderly patients value mortality as the most important goal after revascularization, and they are often underrepresented in trials. Therefore, although this study might not provide definite answers to which revascularization method is optimal, it might provide a little more evidence with regard to the elderly.

Lastly, a special mention should be made regarding chapter 7 and 8 of this thesis. No researcher likes to admit mistakes in their research or analysis. However, we hope that by being transparent about these mistakes, we emphasize the importance of wholly and unquestionably ethically conducted research.

4. **To whom this research concerns**

The research described in this thesis has contributed valuable understandings to the subject of thrombosis and hemostasis in patients undergoing CABG. It can aid physicians in their quest of optimally treating their patients, and lays a possible foundation for further research in order to address the still very much encountered problems of thrombosis and hemostasis during CABG surgery.