Prognostic impact of coronary microvascular function in patients with ischemic heart disease

Akademisk avhandling

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Inger Haraldsson

Fakultetsopponent: Docent Karl-Henrik Grinnemo Institutionen för kirurgiska vetenskaper, Thoraxkirurgi, Uppsala Universitet

Avhandlingen baseras på följande delarbeten;

- I. <u>Haraldsson, I.</u> Gan, L. Svedlund, S. Wittfeldt, A. Råmunddal, T. Angerås, O. Albertsson, P. Matejka, G., Omerovic, E. *Non-invasive evaluation of coronary flow reserve with transthoracic Doppler echocardiography predicts the presence of significant stenosis in coronary arteries* International Journal of Cardiology 2014 Sep;176(1):294-7
- II. Angerås, O. <u>Haraldsson, I</u>. Redfors, B. Fröbert, O. Petursson, P. Albertsson, P. Ioanes, D. Odenstedt, J. Olsson, H. Witt, N. Ruck, A. Millgård, J. Nilsson, J. Persson, J. Söderbom, M. Wedel, H. Erlinge, D. James, S. Råmunddal, T. Omerovic, E. *Impact of thrombus aspiration on mortality, stent thrombosis and stroke in patients with ST-segment-elevation myocardial infarction: A report from the Swedish Coronary Angiography and Angioplasty Registry Journal of American Heart Association 2018 Jan; 7(1): e007680*
- III. Redfors, B. Dworeck, C. <u>Haraldsson, I</u>. Angerås, O. Odenstedt, J. Ioanes, D. Petursson, P. Völz, S. Albertsson, A. Råmunddal, T. Persson, J. Koul, S. Erlinge, D. Omerovic, E. *Pretreatment with P2Y₁₂ Receptor Antagonists in ST-Elevation Myocardial Infarction: A Report from the Swedish Coronary Angiography and Angioplasty Registry* Submitted
- IV. <u>Haraldsson, I.</u> Gan, L. Svedlund, S. Torngren, K. Westergren, H. Redfors, B. Lagerström-Fermér, M. Angerås, O. Råmunddal, T. Petursson, P. Odenstedt, J. Albertsson, P. Erlinge, D. Omerovic, E. *PROspective Evaluation of Coronary FLOW Reserve and Molecular Biomarkers in Patients with Established Coronary Artery Disease. The PROFLOW trial: Cross-sectional evaluation of coronary flow reserve.* Manuscript

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ABSTRACT

Background: Ischemic heart disease is the leading cause of death globally. Despite recent advances in interventional and medical therapies, survivors of myocardial infarction are at high risk of recurrent cardiovascular events. In recent years, coronary microvascular function has attracted more attention as the main target for risk stratification and as a possible target for pharmacological intervention as a part of multifaceted treatment of ischemic heart disease. Coronary flow reserve (CFR) is one of the central indices that reflex the status of coronary circulatory function.

Aims: To investigate if transthoracic Doppler echocardiography-CFR (TDE-CFR) can predict significant epicardial coronary artery stenosis (paper I); to investigate the prevalence of reduced CFR in high-risk patients with prior myocardial infarction (paper IV). To investigate the impact of thrombus aspiration (paper II) and pretreatment with P2Y₁₂ inhibitors (paper III) on mortality in patients with STEMI undergoing PCI.

Methods: The SCAAR registry was used for data analysis and patient recruitment. CFR was assessed with TDE-CFR in paper I and IV. Regression modelling was used for statistical analysis of data including propensity score adjusted logistic regression (paper I), instrumental variable analysis (paper II), propensity-score adjusted mixed-effects logistic regression (paper III) and multiple linear regression (paper IV).

Results: TDE-CFR predicts significant coronary artery disease (paper I). Thrombus aspiration was not associated with any effect on mortality or stroke but was associated with decreased risk of stent thrombosis (paper II). Pretreatment with $P2Y_{12}$ receptor antagonists was not associated with reduced IRA occlusion at the time of primary PCI or decreased stent thrombosis or improved survival at 30 days (paper III). Impairment of CFR was frequent in a high-risk post infarction population with nearly 40% of patients having CFR<2.5. Incomplete revascularization was the strongest independent predictor of lower CFR (paper IV).

Conclusions: A majority of high-risk patients with previous MI have decreased CFR despite receiving adequate pharmacological treatment as a part of secondary prevention. TDE-CFR is a valuable tool for risk stratification in patients with established ischemic heart disease. High-quality observational studies based on large-scale registries and adequate statistical modelling provide valuable complementary evidence for the external validity of randomized controlled trials.

Keywords: coronary microvascular function, coronary flow reserve, coronary artery disease, acute coronary syndromes, thrombus aspiration, pre-treatment, SCAAR, SWEDEHEART.

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