“Evaluation of ischemic heart disease with non-invasive methods: Aspects on the diagnostic and prognostic performance”.

Introduction

Ischemic heart disease (IHD) is the leading cause of mortality worldwide and includes a wide spectrum of clinical presentation from acute coronary syndrome (ACS) to stable angina pectoris.

In the current ESC/EACTS guidelines for myocardial revascularization (1) in patients with suspected coronary artery disease (CAD), it is strongly recommended to assess the presence and degree of stress-induced ischemia before the decision regarding revascularization therapy is made. This is because it has been shown that the relationship between the degree of coronary stenosis and the severity of stress-induced ischemia is weak (2) and that the amount of stress-induced ischemia is of importance for patient prognosis (3-5). Currently, there are several methods available for assessing stress-induced myocardial ischemia, such as bicycle exercise testing (EST), myocardial perfusion single photon emission tomography (MPS), cardiac magnetic resonance imaging (CMR), cardiac positron emission tomography (PET) and invasive coronary pressure measurements. These methods reflect different aspects of the pathophysiology associated with CAD. Nevertheless, they are used for clinical decision making in the same way. We have preliminary data showing that these different methods show different results when applied in the same patient, which may lead to different treatment depending on what method is being used. We currently lack understanding of what these differences mean with regards to clinical significance and patients prognosis, especially when it comes to gender differences. The only way to determine how different pathophysiological aspects of stress-induced ischemia such as regional myocardial dysfunction, mitochondrial dysfunction, distorted myocardial microcirculation, decreased coronary flow reserve and electrophysiological abnormalities are related is to examine all these aspects in the same patient close in time. Furthermore, in order to understand how these different pathophysiological aspects can predict the outcome of revascularization therapy they have to be examined before and after intervention in the same patient. This has never been done before and would improve our understanding of when revascularization is appropriate (6-7) in this large patient group.
Aims and Methods

Project 1: To assess the pathophysiological correlate of stress-induced ST elevation and stress-induced ST depression on an exercise stress test, specifically with regard to the presence, amount and location of myocardial ischemia as determined by MPS, in patients with suspected or established coronary artery disease.

Project 2: To determine the diagnostic accuracy of stress-induced ST segment changes as a biomarker for stress-induced myocardial ischemia as assessed by MPS, with a special focus on gender differences, in patients with suspected stable IHD.

Project 3: To investigate the ability of both automated and visual assessment of CEI to distinguish ST deviations caused by coronary occlusion by balloon inflation in patients with stable IHD from those that represent normal variation, and those caused by other pathophysiologic conditions.

Project 4: To investigate factors influencing quantification of absolute MBF by cardiac PET including different positions of left ventricular (LV) blood pool volume of interests (VOI), different compartment models, different reconstruction methods as well as inter- and intra-observer variability in patients and in a phantom experiments.

Project 5: To investigate if the change in global myocardial perfusion quantified by cardiac PET as well as the change in regional myocardial perfusion assessed by cardiac MR and MPS reflect the change in VO₂ peak, before and after revascularization, in patients with stable IHD. (Inclusion ongoing).

Results and Conclusions

Project 1: Stress-induced ST elevation, with or without concomitant ST depression is predictive of the presence, location and amount of myocardial ischemia assessed by MPS whereas stress-induced ST depression without concomitant ST elevation is not.
**Project 2:** ST-segment changes at stress is a poor biomarker for stress-induced myocardial ischemia as determined by MPS, especially in females. The diagnostic accuracy of EST is improved in both gender, especially specificity and PPV, by considering other variables in the EST interpretation in addition to the ST response.

**Project 3:** Visual assessment of CEI is a promising method for increasing the accuracy of ECG based triage to PCI or conservative care in patients with suspected ACS.

**Project 4:** Preliminary results show that the absolute myocardial blood flow determined with dynamic cardiac $^{13}$N-NH$_3$ PET gave similar results for the two reconstruction algorithms (OSEM and FBP) with low intra- and inter-observer variability. Calculation of absolute MBF is, however, dependent on the position of the blood pool VOI. The VOI should, according to the phantom study, be kept constant preferably in the basal part of the LV blood pool, to enable accurate comparisons between examinations and patients.

**Project 5:** 24 patients have been included so far. Preliminary results suggest no significant difference in VO$_2$ peak, global absolute myocardial blood flow and stress-induced ischemia by MPS at baseline and follow-up, in the revascularized and in the non-revascularized patients.

**Manuscript list**

Akil S., Sunnersjö L., Hedeer F., Hedén B., Carlsson M., Gettes L., Arheden H., Engblom H. Stress-induced ST elevation with or without concomitant ST depression is predictive of presence, location and amount of myocardial ischemia assessed by myocardial perfusion SPECT, whereas isolated stress-induced ST depression is not. (*submitted*)

Akil S., Hedén B., Pahlm O., Carlsson M., Arheden H., Engblom H. Stress-induced ST changes during exercise stress test is a poor biomarker for stress-induced myocardial ischemia as determined by myocardial perfusion SPECT: aspects on gender differences. (*Early manuscript*)

Akil S., Hedeer F., Oddstig J., Engblom H., Hindorf C. Investigation of how the activity quantification using different blood pool volume of interests and reconstruction methods influence the absolute myocardial blood flow determined with $^{13}$N-NH$_3$ cardiac PET. (Early manuscript/abstract)

Akil S. et al. Maximum oxygen uptake, global and regional myocardial perfusion before and after revascularization in patients with stable ischemic heart disease. (Abstract)

References


