

# **Non-invasive assessment of coronary flow velocity: Clinical and experimental studies**

## AKADEMISK AVHANDLING

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i Hjärtats aula, Sahlgrenska Universitetssjukhuset, Göteborg den 7 december, klockan 13.00 av

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### **Avhandlingen baseras på följande delarbeten**

- I. Wittfeldt A, Jeppsson A, Gan LM. Effects of nitroglycerine on coronary flow velocity before and during adenosine provocation. Submitted.
- II. Gan LM, Svedlund S, Wittfeldt A, Eklund C, Gao S, Matejka G, Jeppsson A, Albertsson P, Omerovic E, Lerman A. Incremental value of transthoracic Doppler echocardiography-assessed coronary flow reserve in patients with suspected myocardial ischemia undergoing myocardial perfusion scintigraphy. Submitted.
- III. Haraldsson I, Gan LM, Svedlund S, Wittfeldt A, Råmunddal T, Angerås O, Albertsson P, Matejka G, Omerovic E. Noninvasive evaluation of coronary flow reserve with transthoracic Doppler echocardiography predicts the presence of significant stenosis in coronary arteries. *Int J Cardiol.* 2014 Sep;176(1):294–7.
- IV. Wittfeldt A, Emanuelsson H, Brandrup-Wognsen G, van Giezen JJ, Jonasson J, Nylander S, Gan LM. Ticagrelor enhances adenosine-induced coronary vasodilatory responses in humans. *J Am Coll Cardiol.* 2013 Feb;61(7):723–7.

**SAHLGRENKA AKADEMIN  
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# **Non-invasive assessment of coronary flow velocity: Clinical and experimental studies**

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## **BACKGROUND AND OBJECTIVES**

Coronary flow velocity (CFV) and coronary flow velocity reserve (CFVR) evaluated by transthoracic ultrasound is a promising method to assess ischemic heart disease. CFVR is the ratio between CFV during maximal hyperemia and baseline. A reduced CFVR indicates an increased risk for cardiovascular events. The aims of this thesis were 1. To evaluate the effect of nitroglycerine administration on CFV and CFVR. 2. To investigate if CFVR provides prognostic information about cardiovascular events, in addition to myocardial scintigraphy, in patients with suspected coronary artery disease. 3. To investigate the relationship between CFVR and significant coronary stenosis. 4. To assess the effects of ticagrelor on CFV and dyspnea.

## **METHODS**

In study I, CFV and CFVR and coronary artery diameter were assessed before and after sublingual nitroglycerine administration in 26 healthy subjects. In study II, CFVR was measured in 371 patients undergoing scintigraphy due to suspected coronary artery disease. CFVR and scintigraphy results were related to cardiovascular events (cardiovascular death, myocardial infarction, acute revascularization) during a mean follow-up of 4.5 years. In study III, CFVR and coronary angiograms were evaluated in 123 patients from study II. Study IV was a double-blind placebo-controlled cross-over study randomizing 40 healthy subjects to ticagrelor or placebo. CFV and dyspnea were assessed at baseline and during increasing doses of adenosine.

## **RESULTS**

Nitroglycerine increased CFVR due to a reduction in baseline CFV. Adenosine-induced CFV remained unchanged. A  $CFVR \leq 2$  was independently associated with cardiovascular event rate (adjusted hazard ratio 3.02 (1.51-6.04,  $p=0.002$ )) and added prognostic information in addition to scintigraphy. There was a significant association between CFVR and the presence of coronary stenoses. Ticagrelor augmented CFV and dyspnea during adenosine administration.

## **CONCLUSIONS**

Nitroglycerine increases CFVR which indicates that adenosine alone causes a submaximal hyperemia. The associations between CFVR and cardiovascular events, and between CFVR and significant coronary stenosis supports routine assessment with CFVR in patients with suspected ischemic heart disease. The results indicate that adenosine is involved in the systemic effects of ticagrelor.

**Keywords:** ischemic heart disease, coronary flow velocity, ultrasound