# Chronic ischaemic myocardial dysfunction in patients with heart failure

*Henrik Wiggers, MD*

This PhD dissertation was accepted by the Faculty of Health Sciences of the University of Aarhus, and defended on November 9, 2007.

Official opponents: Birger Hesse, Christian Hassager, and Kristian Thygesen.

Correspondence: Henrik Wiggers, Rosenvej 24, 8240 Risskov, Denmark.

E-mail: henrikwiggers@dadlnet.dk

Dan Med Bull 2007;54:383

ABSTRACT

This PhD dissertation originates from Department of Cardiology, Skejby Hospital, Aarhus University Hospital, Aarhus, Denmark. It consists of eight published papers and a review. In patients with ischaemic heart disease and heart failure, dysfunctional myocardium can be chronically ischaemic and recover function after revascularization. The aims of the present thesis were to investigate pathophysiology of chronic ischaemic myocardium, compare different diagnostic methods for evaluation of viability of the myocardium, and study the effect of revascularization in patients with heart failure and ischaemic heart disease.

By positron emission tomography (PET) and ambulatory ECG-monitoring we found that both reduced resting perfusion and repetitive episodes of ischaemia contribute to chronic ischaemic myocardial dysfunction. In myocardial biopsies we found no biochemical evidence of ischaemia. Short-term metabolic intervention did not affect contractile function of viable, dysfunctional myocardium in heart failure patients indicating that the ability to generate energy form different substrates is preserved. In a follow-up study, chronic ischaemic dysfunctional myocardium had preserved perfusion, uptake of the glucose tracer $^{18}$F-flouro-deoxyglucose (FDG), and contractile function over time suggesting an adaptation to chronic ischaemia.

FDG PET was the most sensitive method for the detection of chronic reversibly dysfunctional myocardium, whereas low-dose dobutamine echocardiography was more specific. Invasive catheter-based electromechanical mapping (NOGA) differentiated between myocardium with and without improvement of contractile function after revascularization, but this method had inferior diagnostic characteristics as compared with other imaging modalities. If revascularization is feasible FDG PET is recommended as the initial diagnostic test in patients with severe heart failure

Revasularization of major regions of viable, dysfunctional myocardium improved left ventricular ejection fraction and exercise capacity whereas no beneficial effect on heart rate variability was observed.

In conclusion, chronic ishaemic dysfunctional myocardium is exposed to repetitive episodes of ischaemia, but displays no biochemical signs of ongoing ischaemia. It has a preserved ability to generate energy form different substrates and can adapt to chronic ischaemia. The cellular mechanism behind this ability remains unknown. FDG PET was the most sensitive method for diagnosing chronic reversible myocardial dysfunction and is suggested as the initial diagnostic test.

The effect of revascularization of viable, dysfunctional myocardium on different surrogate endpoints is equivocal which underlines the need for large randomized trials in this field.