

Myocardial perfusion and glucose uptake in patients with type 2 diabetes and ischaemic heart disease

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ABSTRACT

The present PhD dissertation is based on three papers and an overview, and was performed at the department of Cardiology, Skejby Hospital, and department of Clinical Pharmacology, Aarhus Hospital, Aarhus University Hospital.

Patients with coronary artery disease (CAD) and type 2 diabetes mellitus (T2DM) have a higher mortality and morbidity than patients with CAD without T2DM, mainly due to congestive heart failure. The mechanisms responsible for this relationship are unknown. Whether reduced myocardial perfusion in macrovascular well perfused regions is combined with an abnormal glucose metabolism in T2DM compared to non-diabetics, and whether this is caused by microvascular changes or an abnormal glucose metabolism caused by insulin resistance (IR) has not been clarified.

The objective of this dissertation was to study insulin's vasodilatory effects in the myocardium as well as mechanisms and regulation of myocardial perfusion (MP) and myocardial glucose uptake (MGU) by positron emission tomography (PET) in healthy volunteers. Furthermore the effect of T2DM on MP and MGU was examined in CAD patients with preserved left ventricular function in regions of the myocardium supplied by a non-stenotic and a stenotic coronary artery. Finally a comparison of quantitative analysis of the image reconstruction methods "Filtered backprojection" and "Iterative reconstruction" for dynamic PET has been performed.

The overall conclusion of the dissertation is that insulin does not seem to have significant vasodilator effects in the coronary vasculature when used in physiological doses. Furthermore insulin stimulated MGU is independent of changes in perfusion. MGU can be stimulated even when perfusion decreases suggesting that autoregulation of MGU is preserved despite uncoupling of vascular autoregulation. When left ventricular function is preserved, myocardial insulin resistance is not an inherent feature of T2DM irrespective of the degree of epicardial disease and whole-body insulin resistance.