

Atherosclerosis in 64-year-old women with diabetes mellitus and impaired glucose tolerance

Akademisk avhandling

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Avhandlingen baseras på följande delarbeten:

- I. Carotid artery intima-media thickness in patients with Type 2 diabetes and impaired glucose tolerance: a systematic review**
Brohall G, Odén A, Fagerberg B
Diabetic medicine 2006;23:609-16
- II. Prevalence of diabetes mellitus and impaired glucose tolerance in 64-year-old women.** Experiences of using repeated oral glucose tolerance tests
Brohall G, Behre CJ, Hulthe J, Wikstrand J, Fagerberg B
Diabetic Care 2006;29:363-67
- III. Atherosclerotic plaques and carotid remodelling in a population sample of 64-year-old women with known and newly diagnosed diabetes**
Brohall G, Schmidt C, Pahl-Abrahamsson U, Holdstedt P, Hulthe J, Gustavsson T, Wikstrand J, Fagerberg B
Submitted
- IV. Impaired glucose tolerance and subclinical atherosclerosis in carotid arteries: Results from a study of 64-year-old women and a meta-analysis of available studies**
Brohall G, Schmidt C, Behre CJ, Hulthe J, Wikstrand J, Fagerberg B
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Abstract

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The incidence of obesity and type-2 diabetes (t2D) is rising around the world. T2D is accompanied by an increased risk of macrovascular, atherosclerotic diseases. The timing of the disease process and exact mechanism underlying the association between diabetes and atherosclerotic disease are not known. High-resolution B-mode ultrasound is a non-invasive technique to measure very early atherosclerotic disease as the intima-media thickness (IMT) and to assess occurrence, size and echogenicity of atherosclerotic plaques in superficial arteries such as the carotid arteries. Remodelling, i.e a change in vascular diameter in response to atherosclerosis may also be examined.

The overall aim of this thesis was to examine the occurrence of early atherosclerosis in t2D and impaired glucose tolerance (IGT). Our hypothesis was that there is a gradual enlargement of IMT and an increased occurrence of plaques, especially echolucent plaques, with worsening glucose tolerance, accompanied by a remodelling that might be visible already in subjects with IGT.

In order to summarise current knowledge a systematic review was made in order to identify cross-sectional studies using the ultrasound method. The differences between IMT in t2D or IGT and control subjects were calculated. Meta-analysis using random-effects model was used to calculate summary measures. In a cross-sectional study, the entire cohort of 64 years old women in Göteborg were invited to take part in a screening examination. Of these, 2595 participated and underwent anthropometric measurements and an oral glucose tolerance test (OGTT) that was repeated within two weeks. Ultrasound examinations were made in a cohort of women with known (n=99) and new diabetes (n=106), IGT (n=205) and NGT (n=188).

In the systematic review of 23 studies we found that t2D was associated with an 0.13 mm increase in IMT compared to controls. There was a considerable heterogeneity between the studies that complicated the interpretation of the meta-analysis. This difference can be interpreted as if the diabetic patients were ten years older than the control group and that they had an elevated risk for stroke and myocardial infarction. In patients with IGT, the increase in IMT was about 25% of that observed in diabetes.

The screening examination showed that 10% of the women had diabetes of whom half were newly detected. Without repeated OGTTs 37% of the new diabetes would have been missed. The women with t2D had larger IMT and plaque areas compared to women in IGT and NGT groups. The plaques were most frequently echolucent. In the IGT group, no increase in atherosclerosis was observed, but the result was within the confidence interval of the meta-analysis, indicating that IGT is associated with a small increase in IMT in the CCA (0.03mm). Carotid vascular remodelling with enlargement in IMT and lumen diameter had however occurred already in the women with new t2D. This remodelling process was seen only in women with atherosclerotic plaques and was not associated to t2D per se.

In conclusion, already in screening detected diabetes sub-clinical atherosclerosis with IMT enlargement and occurrence of plaque with vascular remodelling are observed, indicating that a powerful intervention must be initiated in such cases.

Keywords; systematic review, atherosclerosis, type-2 diabetes, IMT, vascular remodelling, IGT.

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