Early detection of type 2 diabetes and atherosclerotic disease

Björn Fagerberg, MD, PhD

Type 2 diabetes is mainly caused by a combination of genetic factors, unhealthy diet, physical inactivity, and obesity, and is associated with a significantly increased risk of atherosclerosis and cardiovascular death. Atherosclerosis typically takes many years to develop. It involves infiltration of lipids, inflammatory cells, smooth muscle cells and collagen in the artery wall, resulting in fibrous plaques (Figure 1). Plaque formation is closely related to ageing and most plaques do not cause symptoms. However, if the plaque further develops into a complicated lesion, it is prone to rupture and can thus cause myocardial infarction or stroke.

Both type 2 diabetes and atherosclerosis have insidious onset with long clinically silent phases before diagnosis. It is not clear when and how atherosclerosis starts to accelerate in individuals with type 2 diabetes. The aims of our group are to examine the occurrence and development of early atherosclerosis, and to investigate the mechanisms involved in plaque rupture in men and women with diabetes.

Prevalence of diabetes and impaired glucose tolerance in women

It is of particular interest to study the incidence of diabetes in women, as they have a greater relative risk for cardiovascular diseases than men with diabetes. In our diabetes, impaired glucose tolerance in women, and atherosclerosis (DIWA) study, we screened 2595 64-year-old women in Göteborg using repeated oral glucose tolerance tests to avoid misclassification (1). We found that 9.5% of these women had diabetes, and half of these cases were previously undiagnosed. We also showed that 14.4% of the women had impaired glucose tolerance (IGT), which is regarded as a condition signaling risk for future diabetes.
Carotid artery intima-media thickness and atherosclerosis

We use a high-resolution ultrasound technique to determine lumen diameter, intima-media thickness (IMT), and the occurrence, size and characteristics of atherosclerotic plaques in carotid and femoral arteries. Carotid artery IMT is a well-known surrogate measure of atherosclerosis. Plaques with a high content of lipids and inflammation are known to be vulnerable and prone to rupture, which leads to thrombosis and clinical disease. Plaques that are identified as echo-thin at an ultrasound examination are associated with features of plaque vulnerability and increased risk of future cardiovascular disease. Echo-dense plaques are known to contain more calcium and collagen.

In an earlier population-based study in men [(atherosclerosis and insulin resistance (AIR)], we observed that IMT and carotid plaque size increase gradually with advancing loss of glucose control. In the DIWA study, IMT was greatest in the women with known type 2 diabetes and smallest in the group with normal glucose tolerance (2). Echo-thin plaques were observed in almost 60% of women with known type 2 diabetes, and in about 40% of women with newly detected type 2 diabetes or normal glucose tolerance. The majority of plaques were echo-thin, and the ratio of echo-thin plaques to all plaques did not differ between normal women and women with diabetes (2). We are currently examining the relationship between diabetes and plaque rupture in human plaques from the Göteborg atheroma study group (GASG) biobank.

Figure 2. A summary of the studies included in our project. AIR (atherosclerosis and insulin resistance) is a population-based longitudinal study of 58-year-old men with varying degrees of obesity and insulin resistance, re-examined after 3 and 8.6 years. DIWA (diabetes, impaired glucose tolerance in women, and atherosclerosis) is based on screening 2595 64-year-old women. GASG (Göteborg atheroma study group) is a biobank containing carotid plaques from patients with symptomatic carotid atherosclerosis.

It has previously been shown that coronary arteries enlarge at the early stages of atherosclerosis development to prevent luminal narrowing when wall thickness increases due
to the atherosclerosis process, a concept known as vascular remodeling. In the DIWA study, we observed that the remodeling process is already evident in women with screening-detected type 2 diabetes (2).

We did not observe associations between IGT and increases in carotid IMT or in plaque occurrence in the DIWA study. However, we showed that IGT is associated with a small increase in IMT when comparing results in a meta-analysis of all published studies in this field (3).

**Conclusions**

Given the increased risk of cardiovascular disease associated with diabetes, early detection is of utmost importance. Our screening process identified previously undiagnosed type 2 diabetes in half of the 64-year-old women who were investigated. With conventional clinical routines, their diabetes would probably have remained undetected for many years, although there was already evidence of vascular remodeling in the carotid arteries with increased IMT and lumen diameter. These results indicate that a dedicated screening strategy for diabetes is needed.

**References**

