Available online at www.sciencedirect.com
SCIENCE DIRECT®
Diabetes Research and Clinical Practice 69 (2005) 262–271
DIABETES RESEARCH AND CLINICAL PRACTICE
www.elsevier.com/locate/diabres

Associations of microalbuminuria and blood pressure with carotid, aortic and femoral atheromatous plaques in elderly Finns

Ulla Rajala [a,c,*], Mauri Laakso [a,c], Markku Päivänsalo [b], Outi Pelkonen [b], Aimo Ruokonen [d], Ilkka Suramo [b], Sirkka Keinänen-Kiukaanniemi [a,c]

[a] *Department of Public Health Science and General Practice, University of Oulu, Aapistie 1, 90220 Oulu, Finland*
[b] *Department of Diagnostic Radiology, University of Oulu, Aapistie 1, 90220 Oulu, Finland*
[c] *Unit of General Practice, Oulu University Hospital, Oulu, Finland*
[d] *Department of Clinical Chemistry, University of Oulu, Aapistie 1, 90220 Oulu, Finland*

Received 24 November 2004; received in revised form 20 December 2004; accepted 11 January 2005
Available online 10 February 2005

Abstract

Aims: To evaluate the possible associations of microalbuminuria (MA) and blood pressure (BP) with the ultrasonographic manifestations of carotid, aortic and femoral atherosclerosis in 65-year-old Finns.
Methods: Ultrasonographic measurements were performed on 54 diabetic subjects, 97 subjects with impaired glucose tolerance (IGT) and 57 normoglycemic subjects (NGT). Urinary albumin and creatinine concentrations were measured from an early morning spot urine sample, and the urinary albumin-to-creatinine ratio (ACR) of $\geq$2.5 mg/mmol in men and $\geq$3.5 mg/mmol in women was used as a measure of MA. Hypertension was defined as either a systolic BP of $\geq$160 mmHg or a diastolic BP of $\geq$95 mmHg or being on antihypertensive medication.
Results: Eighteen subjects were microalbuminuric and 176 subjects normoalbuminuric. MA was associated with diabetes mellitus and high systolic and diastolic BP. The subjects were divided into two groups according to the median total number of carotid, aortic and femoral plaques: $\geq$9 versus 0–8 plaques. A high number of plaques were associated with hypertension, male gender, smoking and MA. When the study subjects were stratified according to hypertension, it turned out that MA was associated with a high number of plaques in hypertensive, but not in nonhypertensive subjects. According to the results of logistic regression analysis with a high number of plaques as the dependent variable, the unadjusted OR for smoking was 6.0 (95% CI 2.4–15.3) in hypertensive subjects. Microalbuminuria was of borderline statistical significance (OR 4.5, 95% CI 0.9–22.9). After adjustment for systolic blood pressure and fasting glucose concentration, the OR for microalbuminuria was reduced to 3.3 (95% CI 0.6–18.4).

Keywords: Microalbuminuria; Atheromatous plaque; Carotid artery; Aorta; Femoral artery; Diabetes mellitus; Hypertension

* Corresponding author. Tel.: +358 8 5375011; fax: +358 8 5375661.
E-mail address: ulla.rajala@oulu.fi (U. Rajala).

0168-8227/$ – see front matter
doi:10.1016/j.diabres.2005.01.001

1. Introduction

Microalbuminuria (MA) has initially been demonstrated to be a predictor of cardiovascular morbidity [1] and mortality [1–7] in patients with diabetes mellitus. Later studies have shown that MA predicts coronary heart disease [8–10] and mortality [4,11] even in nondiabetic populations. The mechanism linking MA with increased cardiovascular morbidity and mortality has been explained by the Steno hypothesis [12]. According to this hypothesis, MA is a marker of generalized endothelial dysfunction, which enhances the penetration of atherogenic lipids into the arterial wall.

If microalbuminuria is a sign of generalized vascular disease, it could be related to atherosclerotic changes in major vessels. Nevertheless, up till now, studies on this topic have been scarce, and they have evaluated only carotid arteries. In a large population-based study, nondiabetic subjects with MA had greater common carotid artery intima-media thickness than those without MA [13]. Some smaller studies on patients with type 2 diabetes [14] and patients with hypertension [15,16] have shown MA to be associated with increased carotid intima-media thickness. In a study by Agewall et al. [17], MA was associated with increased carotid intima-media thickness in hypertensive men with type 2 diabetes. Instead, no such association was found in nondiabetic hypertensive men.

The aim of the present study was to evaluate the possible associations of microalbuminuria and blood pressure with ultrasonographic manifestations of carotid, aortic and femoral atherosclerosis in 65-year-old Finns drawn from a population-based cohort. In addition to intima-media thickness, we focused on atherosclerotic plaques.

2. Materials and methods

The study subjects consisted of 65-year-old Finns drawn from a population-based cohort [18]. In 1998, altogether 60 subjects of the cohort had clinical diabetes, defined as either diabetes diagnosed by a physician before the baseline or as two elevated blood glucose values (either fasting blood glucose values of $\geq$6.1 mmol/l or 2-h OGTT values of $\geq$11.1 mmol/l) during this study in 1992–1998. All subjects with clinical diabetes (except one with cancer) and those with IGT on the basis of the 1996–1998 OGTT results were invited to participate in the present study. In addition, for each diabetic subject, a control subject with normoglycemic test results in OGTTs in 1992 and 1996–1998 was invited to participate. The diabetic and normoglycemic groups were matched for gender, current smoking and BMI class.

This population-based study was started in 1990 in northern Finland, to assess the prevalence of diabetes mellitus (DM) and impaired glucose tolerance (IGT) [18]. All of the 1008 subjects born in 1935 and living in Oulu, a city of 100 000 inhabitants, on 1 October 1990, were invited to participate in the study. Altogether 768 subjects attended the OGTTs, and the participation rate was 78%. In 1994 and 1996–1998, two follow-up studies were carried out [19–21]. OGTTs were performed at these follow-up visits.

Questionnaires, interviews, clinical examinations and laboratory tests were used to collect data during the follow-up study in 1996–1998. Self-reported use of antihypertensive medication was recorded in the questionnaire. Two measurements of blood pressure were made by the radiologist from the right arm, when the subjects had rested for about half an hour after the ultrasound examination. The mean value of these measurements was used in the analyses. Hypertension was defined as either a systolic blood pressure of $\geq$160 mmHg or a diastolic blood pressure of $\geq$95 mmHg or being on antihypertensive medication regardless of the blood pressure values [22].

Height and weight in light clothing were measured in the clinical examination, and the body mass index (BMI) (kg/m^2) was calculated.

A standardized 75-g OGTT was performed according to the instructions of the WHO Study Group [23]. After a 10–12 h fast, a venous blood sample was drawn at 08:00–10:00 h to obtain a fasting value and values for fasting immunoreactive insulin, total cholesterol, high-density lipoprotein (HDL) cholesterol and triglycerides. After that, a 75-g glucose load was given to the participant. At 2 h, a capillary sample was collected for the determination of the 2-h glucose value. Insulin sensitivity index (QUICKI) was determined from the fasting insulin and glucose values according to the equation: $\mathrm{QUICKI} = 1/[\log(I_0) + \log(G_0)]$, where I_0 is the fasting insulin and G_0 is the fasting glucose [24,25].