Albuminuria is an Independent Predictor of Carotid Intima-Media Thickness and Atherosclerosis in NIDDM Patients

Much recent research has focused on the measurement of the carotid arterial intima-media thickness (IMT) in diabetes (1–3). IMT has been shown to correlate well with general atherosclerotic status, and epidemiological studies have found that on average, those with diabetes have IMT 0.07 mm thicker than those without diabetes (4). This was also found by Pujia et al. (1) and reported recently in *Diabetes Care*. In addition to duration of diabetes, well-established macrovascular risk factors such as age and systolic blood pressure were positively correlated, and high-density lipoprotein (HDL) cholesterol inversely correlated with IMT in non-insulin-dependent diabetes mellitus (NIDDM) subjects (1). The presence of albuminuria however, is recognized as the most important predictor of prognosis for those with diabetes not only in terms of renal function deterioration but also for risk of macrovascular events. It is one risk factor whose relationship with IMT has not been specifically examined.

We studied 76 NIDDM patients, ages 57.0 ± 0.9 (means ± SE) years and duration of diabetes 7.5 ± 0.7 years, to determine whether the presence of albuminuria was an independent risk factor for increased IMT and therefore, increases the risk of atherosclerosis. Patients attending our Diabetes Complications Assessment Service had their albumin excretion rate (AER) measured from urine collected under standard conditions to determine the presence of albuminuria. Thirty-seven patients with an AER <20 μg/min and 39 with an AER >40 μg/min on two occasions were selected for study. Sixteen patients were treated with diet alone, 47 with tablets, and 13 with insulin therapy. Each patient had fasting blood collected for total cholesterol, HDL cholesterol, triglycerides, and HbA_{1c} determination. Sitting blood pressure after 5 min rest was also measured. Patient characteristics are shown in Table 1.

Using high-resolution ultrasonography (Accuson 128 XP), the right and left common carotid arteries were scanned using a 5-MHz linear array transducer. Measurements were made at the mid-common carotid point and 1 cm up- and down-stream, with IMT determined as the thickest of the three points. Left- and right-sided carotid IMT measurements were meaned. All measurements were made by one observer, who was blinded to the patient's degree of albuminuria. The intermeasurement variation by the same observer was 6%. AER was log-transformed for parametric analysis, and characteristics of those with persistent albuminuria were compared with those having normal albuminuria determined by an unpaired Student's *t* test. Multiple regression analysis was used to determine predictors of IMT.

Both groups were similar in age (57 ± 1.2 vs. 56 ± 1.2 years; nonalbuminuric vs. albuminuric patients, respectively), body mass index (BMI) (30.4 ± 0.9 vs. 30.9 ± 0.9 kg/m^2), total cholesterol (5.6 ± 0.2 vs. 5.8 ± 0.2 mmol/l) and diastolic blood pressure (BP) (77 ± 2.0 vs. 77 ± 1.6 mmHg). However, those with albuminuria had significantly higher duration of diabetes, triglyceride levels, HbA_{1c}, and systolic BP and a significantly lower HDL cholesterol than those with a normal AER (Table 1). Mean IMT was found to be significantly increased in those with albuminuria when compared with those with normal AER (0.8 ± 0.02 vs. 0.7 ± 0.02 mm, respectively; $P < 0.02$), and there was a significant relationship between the degree of albuminuria and IMT ($r = 0.33$; $P < 0.02$). Dependent variables regressed in a stepwise manner against IMT included age, duration, BMI, lipids, HbA_{1c}, BP, log AER, sex, smoking, and diabetic treatment. In the best model, mean IMT was positively associated with age ($t_{69}3.45$; $P = 0.001$) and log AER ($t_{69}2.88$; $P = 0.005$) accounting for 21% of the variance in IMT, with no other factors found to be independently significant predictors.

We conclude that albuminuria is an independent determinant of IMT, and therefore atherosclerosis, in NIDDM patients. Patients with diabetes have IMT measurements higher than those without diabetes of similar age (4). From our regression coefficient, it can be calculated that this thickness is further increased in diabetic patients with persistent albuminuria, resulting in blood vessels that are 13 years more advanced in the atherosclerotic process than those without albuminuria. If we assume that our patient group is similar to that of the population-based study of Folsom et al. (mean age is com-

Table 1—*Patient characteristics*

	Nonalbuminuric patients	Albuminuric patients
n	37	39
Duration (years)	4.2 ± 0.6	10.6 ± 1.1*
Triglycerides (mmol/l)	2.2 ± 0.2	4.1 ± 0.5*
HDL cholesterol (mmol/l)	1.2 ± 0.05	1.0 ± 0.04*
HbA_{1c} (%)	6.8 ± 0.2	8.1 ± 0.3*
Systolic BP (mmHg)	135 ± 2.9	144 ± 3.5†

Data are means ± SE. *$P < 0.005$, unpaired Student's *t* test; †$P < 0.05$, unpaired Student's *t* test.

parable) (4), we estimate that those with diabetes and albuminuria are in effect ~26 years more advanced in this process than those in the general community.

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Eating Attitude and Behavior in IDDM Patients

A case-controlled study

Discordant data have been reported on the prevalence of anorexia nervosa (AN) and bulimia (B) in insulin-dependent diabetes mellitus (IDDM) patients, depending on diagnostic criteria and assessment methods (1–6), while comorbidity of binge eating disorder (BED) with IDDM has not been described so far. Subclinical alterations of eating behavior, which can impair metabolic control (7,8), have been reported to be more frequent in IDDM women than in control subjects (7–9), but the point is controversial (4,5,10). Furthermore, insulin manipulation seems to be used frequently by IDDM women to control body weight (1,2,6).

In order to evaluate eating attitude and behavior, we examined a consecutive series of 118 IDDM patients (62 women, 56 men), aged (means ± SD) 34.4 ± 11.7 years (range 15–60), with duration of diabetes 13.9 ± 11.0 years (range 1–44), HbA_{1c} 7.5 ± 1.7% (range 4.6–11.8), and body mass index (BMI) < 28 kg/m^2. Two patients with BMI > 28 kg/m^2 were excluded as unrepresentative and unsuitable because they were undergoing a weight-reduction program. For the selection of controls, each IDDM patient was asked to indicate at least three nondiabetic subjects of their same sex and approximate age among collegues at work and school and these people were subsequently contacted by the investigators. Subjects with BMI > 28 kg/m^2 were excluded for consistency, obtaining a control sample of 263 (148 women, 115 men).

Patients and controls were examined by a psychiatrist using a structured interview (11), Hamilton rating scale for depression (Ham-D) (12), and Social Adjustment Scale (SAS) (13). BED was diagnosed using the Diagnostic and Statistic Manual-IV criteria (14). Eating attitudes were also investigated using two self-reported questionnaires: Bulimic Investigation Test Edinburgh (BITE) (15) and diabetes-adapted Eating Attitude Test-36 (EAT-36) (9). Finally, anxiety was measured with State Trait Anxiety Inventory (STAI) (16) and, in IDDM patients, quality of life was evaluated with Diabetes Quality of Life (DQOL) (17).

Clinical eating disorders were found in six IDDM patients (5 women, 1 man) and nine control subjects (7 women, 2 men). Among women, prevalence of AN was 1.6% in IDDM patients and 0.9% in control subjects, prevalence of B was 1.6% and 2.7%, respectively; prevalence of BED was 4.9% and 2.7%, respectively. Manipulation of insulin therapy to control body weight was reported by eight patients, all women (12.9%). Subclinical eating disorders (defined as BITE scores ≥ 10 or ≥ 8 with severity score ≥ 2) were found in 33% of IDDM women and 22.5% of control women. Differences in BITE scores and in prevalence of clinical and subclinical eating disorders were not statistically significant. EAT-36 scores were significantly ($P < 0.01$) higher in IDDM women than in control women, but this difference may also be ascribed to diabetes-biased items in the questionnaire. No such difference was found among men. In IDDM patients, BITE scores significantly correlate with STAI-1 ($r = 0.35$, $P < 0.01$), STAI-2 ($r = 0.34$, $P < 0.01$), SAS ($r = 0.23$, $P < 0.05$), and DQOL ($r = 0.21$, $P < 0.05$), but not with Ham-D ($r = 0.12$, P = NS), unlike that observed in control subjects ($r = 0.33$, $P < 0.01$). In IDDM patients, disturbances of eating attitude seem to be related to anxiety more than depression. No significant correlation of BITE with age, IDDM duration, and age at onset of diabetes was observed. BITE scores significantly correlate with HbA_{1c} ($r = 0.40$,