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The impact of Type 2 diabetes and microalbuminuria on future cardiovascular events in patients with clinically manifest vascular disease from the Second Manifestations of ARTerial disease (SMART) study

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Abstract

Aims Type 2 diabetes mellitus and microalbuminuria are important risk factors for cardiovascular disease (CVD). Whether these two complications are important and independent risk factors for future CVD events in a high-risk population with clinically manifest vascular disease is unknown. The objectives of this study were to examine the impact of Type 2 diabetes and microalbuminuria on future CVD events.

Methods Patients with clinically manifest vascular disease (coronary, cerebral and peripheral vascular disease) from the Second Manifestation of Arterial disease study were followed up for 4 years. Data obtained from 1996–2006 were analysed. At baseline, there were 804 patients with Type 2 diabetes mellitus (mean age 60 years) and 2983 patients without. Incident CVD (n = 458) was defined as hospital-verified myocardial infarction, stroke, vascular death and the composite of these vascular events.

Results Both Type 2 diabetes [hazard ratio (HR) 1.42, 95% confidence interval (CI) 1.16, 1.75] and microalbuminuria (HR 1.86, 95% CI 1.49, 2.33) increased the risk of new cardiovascular events in univariate analyses. From multivariable models, presence of diabetes remained significantly and independently related to incident CVD (HR 1.42, 95% CI 1.11, 1.80). Presence of microalbuminuria also remained significantly independently related to incident CVD (HR 1.38, 95% CI 1.07, 1.77). In diabetes-stratified analyses, the effect of microalbuminuria on CVD risk was observed only in patients with diabetes. In microalbuminuria-stratified analyses, the significant and independent effect of diabetes on CVD risk was shown only in the non-microalbuminuric group.

Conclusions In this high-risk population, both microalbuminuria and Type 2 diabetes are important and independent risk factors for future CVD.

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Keywords cardiovascular disease, microalbuminuria, Type 2 diabetes mellitus

Abbreviations AAA, aneurysm of the abdominal aorta; ACE, angiotensin-converting enzyme; ACR, albumine/creatinine ratio; BMI, body mass index; BP, blood pressure; CHD, coronary heart disease; CI, confidence interval; CVD, cardiovascular disease; DM, diabetes mellitus; GFR, glomerular filtration rate; HR, hazard ratio; SMART, Second Manifestations of ARTerial disease

Introduction

Having Type 2 diabetes is an important risk factor for the development of cardiovascular disease (CVD), with relative risks between 2 and 4 compared with those without diabetes [1–6]. Microalbuminuria is, on the other hand, one of the most important contributors to the increased CVD risk in patients

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with Type 2 diabetes compared with individuals without diabetes [7–10]. In a high-risk population with clinically manifest vascular disease, Type 2 diabetes and microalbuminuria could still be important risk factors for future CVD events. However, the role of both these factors has not been studied in high-risk populations. Could both diabetes and microalbuminuria be equally important in the aetiology of future CVD? It is thought that the three conditions diabetes, microalbuminuria and CVD could all share common antecedents or underlying risk factors in the causal pathway, in the so-called common soil hypothesis [11].

Whether the effects of Type 2 diabetes and microalbuminuria are independent of each other in their relation with future CVD events remains unclear. Hence, our main aim was to examine whether the impact of Type 2 diabetes on the risk of future CVD is independent from that of microalbuminuria and vice versa in a population with clinically manifest vascular disease.

Methods

The Second Manifestations of ARTerial disease (SMART) study is an ongoing prospective, single-centre cohort study in patients with clinically manifest vascular disease or cardiovascular risk factors. The main inclusion criteria are coronary, cerebral or peripheral artery disease, renal artery stenosis, aneurysm of the abdominal aorta (AAA), or risk factors for atherosclerosis comprising dyslipidaemia, diabetes mellitus (Types 1 and 2) and/or hypertension. Excluded are patients with a terminal malignancy, those not able to live independently (Rankin scale > 3) or not sufficiently fluent in Dutch, and those referred back to the referring specialist immediately after one visit.

All participants aged 18–80 years referred to the University Medical Centre Utrecht (UMC Utrecht), the Netherlands, since 1996 have been included. After referral, subjects underwent vascular screening including a questionnaire, blood chemistry and ultrasonography. Eligible patients received written and oral information about the goals and methodology of the study from qualified research nurses or doctors at their first or second visit to the hospital and all patients were asked for written informed consent. The study was approved by the medical ethics committee of the UMC Utrecht. The rationale and design of the SMART study have been described in detail elsewhere [12].

Recruitment to the SMART study is ongoing and approximately 800 patients are enrolled annually. On 1 March 2006, 5822 patients with at least 6 months' follow-up data had been recruited. We restricted the population to those with clinically manifest vascular disease only (excluding 1947 patients who did not have a history of CVD); thus 3875 patients were included. Those patients with diagnosed Type 1 diabetes mellitus (n = 38) were excluded, leaving 3837 patients. Type 2 diabetes was diagnosed by a physician, or defined as a fasting plasma glucose ≥ 7.0 mmol/l or self-reported use of oral glucose-lowering drugs or insulin.

Microalbuminuria was defined as a urinary albumin:creatinine ratio between 2.5 and 25 mg/mmol (men) or between 3.5 and 25 mg/mmol (women) [13]. The glomerular filtration rate (GFR) was calculated using the Cockcroft–Gault formula; in ml/min [(140 – age) × body weight/(serum creatinine × 72) (× 0.85 if female)] [14] and expressed per 1.73 m^2 body surface area.

Follow-up

Patients were asked biannually to complete a questionnaire on hospital admissions and out-patient clinic visits. The follow-up was complete for 98.1%. Events of interest for this study were CVD, comprising ischaemic heart disease, myocardial infarction, ischaemic stroke, vascular death and the composite of these vascular events. When a possible event was recorded by the participant, hospital discharge letters and results of relevant laboratory and radiology examinations were collected. For each event, written standard operating procedures were followed to classify each event accordingly. Based on this information, all events were audited independently by three members of the SMART study Endpoint Committee, comprising physicians from different departments. In case of disagreement, the opinion of other members of the Endpoint Committee was sought and final adjudication was based on the majority of the classifications obtained.

Statistical analyses

Absolute risks were calculated by dividing the number of CVD events by person-years. Cox proportional hazards analyses were performed to estimate relative risks [hazard ratios (HR) and 95% confidence intervals (CI)] for the association between Type 2 diabetes and CVD and microalbuminuria and CVD. If a patient had multiple events, the first was used in the analyses. Multivariate Cox proportional hazards analyses were carried out. Kaplan–Meier survival curves were drawn to illustrate the effects of diabetes, microalbuminuria and the combination of the two on CVD during the follow-up period. The Kaplan–Meier curves were reversed by calculating one minus survival. The proportional hazards assumption was found not to be violated by examining the parallel Kaplan–Meier curves as well as using the Schoenfeld test (P = 0.6 for microalbuminuria and P = 0.9 for diabetes) [15]. Likelihood ratio tests were used additionally to test for an interaction between diabetes and microalbuminuria (comparing a model with diabetes and microalbuminuria with a model with diabetes, microalbuminuria and the interaction term). Adjustments were made for confounders such as age, sex, renal function (using the estimated GFR by Cockcroft–Gault formula), systolic blood pressure, smoking, fasting triglycerides, body mass index (BMI) and the use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor antagonists. We have adjusted for all potential confounding variables which are known to be related to the determinants (Type 2 diabetes or microalbuminuria), but also to the study outcome (CVD). From each risk factor group, one factor was chosen, e.g. fasting triglycerides was chosen from lipids and lipoproteins, BMI was chosen from obesity measures. The analyses were also carried out using diabetes-stratified analyses, microalbuminuria-stratified analyses, and using albumin:creatinine ratio as a continuous variable instead of using a cut-off for microalbuminuria. The statistical packages STATA (STATA 7.0; Stata Corp., College Station, TX, USA) and SPSS (SPSS 11.0; SPSS Inc., Chicago, IL, USA) were used to perform all statistical analyses. A P-value < 0.05 was considered to be statistically significant.

Table 1 Baseline phenotypic characteristics of the SMART cohort by diabetes and microalbuminuria status

	Diabetes (n = 804) Mean ± SD	Without diabetes (n = 2983) Mean ± SD	Microalbuminuria (n = 640) Mean ± SD	Without microalbuminuria (n = 2956) Mean ± SD
Age at baseline (years)	62 ± 9	59 ± 11	64 ± 10	59 ± 10
Duration of diabetes (years)	6.3 ± 7.2	—	—	—
Fasting plasma glucose (mmol/l)	8.9 ± 2.8	5.6 ± 0.6	6.6 ± 2.2	6.2 ± 1.9
Systolic BP (mmHg)	147 ± 21	140 ± 19	149 ± 22	140 ± 19
Diastolic BP (mmHg)	81 ± 10	79 ± 10	82 ± 11	79 ± 10
Pulse pressure	67 ± 17	60 ± 15	67 ± 17	61 ± 16
Cholesterol (mmol/l)	5.1 ± 1.3	5.2 ± 1.2	5.2 ± 1.2	5.2 ± 1.2
LDL-cholesterol (mmol/l)	3.0 ± 1.0	3.2 ± 1.0	3.1 ± 1.0	3.2 ± 1.0
HDL-cholesterol (mmol/l)	1.1 ± 0.3	1.3 ± 0.4	1.2 ± 0.4	1.2 ± 0.4
Fasting triglycerides (mmol/l)*	1.9 (1.3, 2.7)	1.5 (1.1, 2.1)	1.6 (1.1, 2.3)	1.5 (1.1, 2.2)
Non-HDL-cholesterol (mmol/l)	4.0 ± 1.3	4.0 ± 1.2	3.9 ± 1.2	4.0 ± 1.2
Weight (kg) (men/women)	87 ± 14	83 ± 12	83 ± 13	84 ± 13
	79 ± 15	71 ± 13	73 ± 16	72 ± 13
Waist–hip ratio (men/women)	0.96 ± 0.07/	0.93 ± 0.06/	0.95 ± 0.07/	0.94 ± 0.06/
	0.88 ± 0.06	0.84 ± 0.07	0.85 ± 0.06	0.84 ± 0.07
Body mass index (kg/m^2) (men/women)	27.9 ± 3.9/	26.4 ± 3.4/	26.7 ± 3.8/	26.7 ± 3.5/
	29.1 ± 5.2	26.1 ± 4.5	27.2 ± 5.6	26.6 ± 4.6
Glomerular filtration rate, Cockcroft–Gault (ml/min per 1.73 m^2)	77.5 ± 25.1	76.4 ± 21.6	70.6 ± 24.1	78.3 ± 21.1
Albumin creatinine ratio (mg/mmol)*	1.7 (1.0, 3.9)	1.2 (0.8, 2.1)	4.7 (3.3, 8.5)	1.1 (0.7, 1.6)

*Median (IQR).

Results

An overview of the baseline characteristics of the SMART population by diabetes status and by microalbuminuria status is shown in Table 1. There were 804 patients with Type 2 diabetes and 2983 patients without, 640 patients with microalbuminuria and 2956 without. There were 50 missing values for diabetes and 241 missing values for microalbuminuria.

Mean age was 60 years and 75% were male. There was a significant difference in the age (62 vs. 59 years, $P < 0.0001$), but not sex ($P = 0.9$) between those with and without Type 2 diabetes. There were significant differences in the age and sex distribution between those with and without microalbuminuria (63 vs. 59 years, $P < 0.0001$ and 79 vs. 74% men, $P = 0.005$). As expected, those with diabetes had higher baseline fasting plasma glucose levels and were more obese as well as more hypertensive than those without diabetes. In addition, a higher proportion of those with diabetes had microalbuminuria (defined as an albumin:creatinine ratio between 2.5 and 25 mg/mmol in men or 3.5 and 25 mg/mmol in women), with 26 vs. 16% in those without diabetes. The prevalence of Type 2 diabetes in the microalbuminuric population was 30% and 19% in those without microalbuminuria. A considerable proportion of the patients had concomitant cerebrovascular, peripheral arterial disease, coronary artery disease or AAA (Table 2).

During the follow-up period [3.8 ± 2.6 years (mean ± SD)], 458 patients experienced an incident CVD event (121 in the diabetic population, 332 in those without diabetes, 102 in those with microalbuminuria and 318 in those without microalbuminuria). As shown in Fig. 1, the overall absolute risk of CVD was lowest in the non-diabetic and non-microalbuminuric populations and increased significantly for those with microalbuminuria. Those with both Type 2 diabetes and microalbuminuria had an absolute CVD risk of 52/1.000 person-years (95% CI 37, 74). The microalbuminuria effect was no greater in those with Type 2 diabetes than in those without, since the last two bars of Fig. 1 were similar.

Both Type 2 diabetes (HR 1.42, 95% CI 1.16, 1.75) and microalbuminuria (HR 1.86, 95% CI 1.49, 2.33) increased the risk of new cardiovascular events in univariate analyses (Table 3). There was no significant interaction between diabetes and microalbuminuria (likelihood ratio test $P = 0.10$, β coefficient –0.41, 95% CI –0.90, 0.08). To explore whether the presence of Type 2 diabetes or microalbuminuria were independent of each other in relation to CVD, both variables were entered simultaneously into a multivariable model. These analyses showed that both the presence of diabetes and microalbuminuria were significantly and independently related to incident CVD. Analyses were carried out to adjust for cardiovascular risk factors, estimated GFR, systolic blood pressure, smoking, fasting triglycerides and BMI, and use of blood pressure-lowering medication such as ACE inhibitors and angiotensin II antagonists, but these also showed that both diabetes and microalbuminuria are important risk factors for the development of CVD (Table 3, model 5–7).

Table 2 Baseline treatment and clinical characteristics of the SMART cohort by diabetes and microalbuminuria status

	Diabetes % (*n*)	Without diabetes % (*n*)	Microalbuminuria % (*n*)	Without microalbuminuria % (*n*)
Men	75 (604)	75 (2233)	79 (508)	74 (2189)
Ever smoked	80 (641)	82 (2452)	84 (536)	81 (2392)
Ever drank alcohol	75 (595)	82 (2444)	79 (502)	81 (2393)
Hypertension*	85 (681)	72 (2150)	86 (550)	72 (2138)
BP-lowering drugs	54 (430)	38 (1144)	50 (317)	39 (1159)
ACE inhibitors and ATA II use	38 (308)	24 (711)	33 (213)	26 (757)
Lipid-lowering drugs	53 (418)	47 (1408)	48 (305)	48 (1416)
Microalbuminuria	26 (191)	16 (438)	—	—
Diabetes mellitus	—	—	30 (191)	19 (557)
Cerebrovascular disease	19 (155)	22 (655)	23 (147)	21 (626)
Peripheral arterial disease	22 (175)	18 (546)	22 (138)	19 (560)
Coronary artery disease	35 (280)	42 (1242)	30 (194)	42 (1249)
AAA	5 (40)	8 (225)	9 (59)	6 (187)

ATA II, Angiotensin II antagonists.
*> 140/90 mmHg or on BP-lowering drugs.

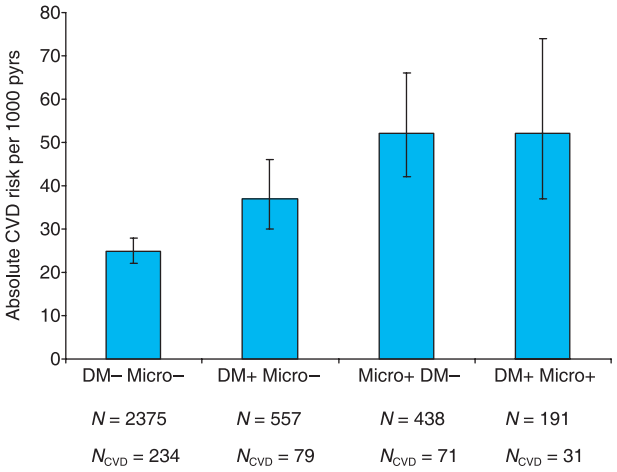


FIGURE 1 Crude absolute risk of cardiovascular disease per 1000 person-years.

Kaplan–Meier curves (Fig. 2) illustrate the effects of Type 2 diabetes and microalbuminuria on CVD across the whole follow-up period. Throughout the whole follow-up period, the presence of both Type 2 diabetes and microalbuminuria at baseline increased the risk of future CVD. As in Fig. 1, Fig. 2 also showed that microalbuminuria increased the risk of developing CVD across the whole period equally in those with and without Type 2 diabetes.

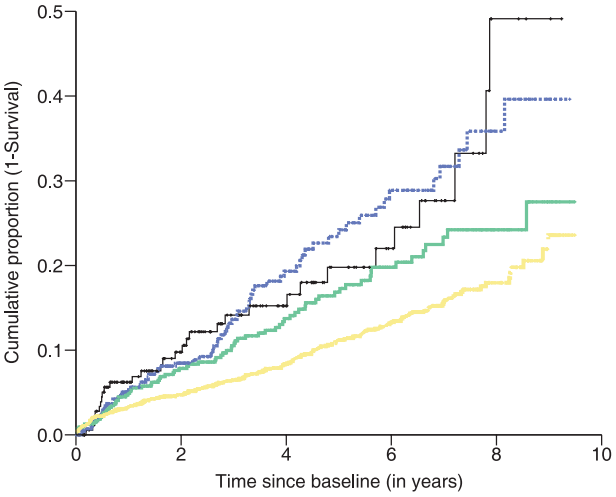
Further stratified analyses were carried out by Type 2 diabetes (Table 4a) and microalbuminuria (Table 4b). These analyses showed that the presence of microalbuminuria was significantly related to an increased risk of CVD in those patients without diabetes, but not in those with Type 2 diabetes. Similarly, the effect of microalbuminuria on CVD was apparent only in those without diabetes.

Table 3 Hazard ratio for future CVD by baseline Type 2 diabetes status or microalbuminuria* status

HR (95% CI)	Type 2 diabetes yes vs. no	Microalbuminuria yes vs. no
Model 1	1.42 (1.16, 1.75)	1.86 (1.49, 2.33)
Model 2	1.27 (1.03, 1.56)	1.46 (1.16, 1.84)
Model 3	1.34 (1.07, 1.67)	1.85 (1.48, 2.32)
Model 4	1.24 (1.00, 1.55)	1.48 (1.18, 1.86)
Model 5	1.32 (1.06, 1.65)	1.38 (1.09, 1.74)
Model 6	1.44 (1.13, 1.83)	1.38 (1.07, 1.77)
Model 7	1.42 (1.11, 1.80)	1.38 (1.07, 1.77)

*Defined by ACR 2.5–25 mg/mmol in men and 3.5–25 mg/mmol in women.
Model 1: Univariate analyses. Model with diabetes related with CVD. Model with microalbuminuria.
Model 2: Model with diabetes, adjusted for age, sex. Model with microalbuminuria, adjusted for age and sex.
Model 3: Model with diabetes, adjusted for microalbuminuria. Model with microalbuminuria, adjusted for diabetes.
Model 4: Model with diabetes, adjusted for microalbuminuria, age and sex. Model with microalbuminuria, adjusted for diabetes, age and sex.
Model 5: Model 4 + renal function.
Model 6: Model 5 + systolic blood pressure, smoking, fasting triglycerides and body mass index.
Model 7: Model 6 + ACE inhibitors and angiotensin II antagonists.

Final analyses were carried out (data not shown) using albumin:creatinine ratio as a continuous variable, instead of microalbuminuria as a categorical variable. The final model with Type 2 diabetes, albumin:creatinine ratio per 10 mg/mmol increase, age, sex, renal function, systolic blood pressure, smoking, fasting triglycerides, BMI, ACE inhibitors and



Persons at risk of developing CVD at 2-year time-intervals starting from baseline

Years since baseline	0	2	4	6	8
No DM, No M	2375	1669	1135	657	155
DM, No M	557	378	242	139	40
No DM, M	438	253	134	69	18
DM, M	191	116	64	32	4

DM = Diabetes, M = Microalbuminuria
DM, M
No DM, M
DM, No M
No DM, No M

FIGURE 2 Kaplan–Meier survival function for cardiovascular disease.

angiotensin II antagonists resulted in HRs for Type 2 diabetes and albumin:creatinine ratio of, respectively, 1.39 (95% CI 1.09, 1.77) and 1.06 (95% CI 1.02, 1.09). These results confirm that Type 2 diabetes and albuminuria are important risk factors for future CVD in patients already at very high risk and that, although they are interrelated, the effects seem independent of each other.

Table 4 (a) Stratified analyses by diabetes status

HR (95% CI)	Type 2 diabetes	No diabetes
Model 1	1.39 (0.91, 2.11)	2.11 (1.62, 2.75)
Model 2	1.31 (0.86, 1.99)	1.54 (1.17, 2.03)
Model 3		1.42 (1.07, 1.87)
Model 4		1.38 (1.02, 1.88)
Model 5		1.38 (1.02, 1.88)

*Defined by ACR 2.5–25 mg/mmol in men and 3.5–25 mg/mmol in women.
Model 1: Univariate analyses. The model with microalbuminuria alone.
Model 2: Adjusted for age and sex.
Model 3: Model 2 + renal function.
Model 4: Model 3 + systolic blood pressure, smoking, fasting triglycerides and body mass index.
Model 5: Model 4 + ACE inhibitors and angiotensin II antagonists.

(b) Stratified analyses by microalbuminuria status

HR (95% CI)	Microalbuminuria	No microalbuminuria
Model 1	1.00 (0.65, 1.52)	1.50 (1.17, 1.94)
Model 2	1.07 (0.70, 1.65)	1.32 (1.02, 1.71)
Model 3		1.41 (1.09, 1.82)
Model 4		1.52 (1.15, 2.02)
Model 5		1.48 (1.12, 1.96)

Model 1: Univariate analyses. The model with diabetes alone.
Model 2: Adjusted for age and sex.
Model 3: Model 2 + renal function.
Model 4: Model 3 + systolic blood pressure, smoking, fasting triglycerides and body mass index.
Model 5: Model 4 + ACE inhibitors and angiotensin II antagonists.

Discussion

In this population with manifest vascular disease it was found that both microalbuminuria and Type 2 diabetes are important and independent risk factors for future CVD. These patients are already at high risk because of their history of CVD, but nevertheless, baseline presence of Type 2 diabetes and microalbuminuria add considerably to the risk of future CVD. An attractive hypothesis is that all three diseases—diabetes, microalbuminuria and CVD—underlie the so-called 'common soil hypothesis' [11] and share common antecedents. A main limitation of this study is that we could not investigate this hypothesis further since we do not have data on the period before the onset of microalbuminuria or Type 2 diabetes. All that is known is that the mean duration of diabetes was approximately 8 years in this study, and the onset of CVD is dependent on duration of diabetes as well as microalbuminuria. We also cannot account for post-baseline development of microalbuminuria, because both Type 2 diabetes and microalbuminuria were assessed at baseline only. On the basis of the data on baseline microalbuminuria and Type 2 diabetes, it can be said, however, that the early presence of both of these abnormalities is related to the development of future CVD.

What could be the underlying pathophysiological mechanism for diabetes and microalbuminuria being independently related to future CVD [16,17]? Several mechanisms have been suggested, such as endothelial dysfunction, low-grade inflammation and oxidative stress, but the nature of the link between diabetes and/or microalbuminuria and cardiovascular risk remains poorly understood. Endothelial dysfunction seems an attractive link and is thought to play an important role not only in the initiation of atherosclerosis, but also in its progression and clinical sequelae. It is not clear to what extent endothelial dysfunction is caused by hyperglycaemia. Type 2 diabetes typically occurs in the context of a cluster of risk factors, notably obesity, hypertension, high triglyceride levels,

low high-density lipoprotein-cholesterol levels, abnormal low-density lipoprotein composition, hyperinsulinaemia, insulin resistance and low-grade inflammation, in addition to microalbuminuria. All these factors may impair endothelial function. Whether endothelial dysfunction induced by diabetes is independent of that induced by microalbuminuria remains to be established. Microalbuminuria is a strong and independent indicator of increased cardiovascular risk. In addition, it has also been shown that microalbuminuria is associated with endothelial dysfunction in the absence of diabetes [18] Speculating further, diabetes could also be associated with endothelial dysfunction, in the absence of microalbuminuria. This is supported by the finding that microalbuminuria occurs in the absence of severe endothelial dysfunction [19]. This is in line with our findings, that the effect of Type 2 diabetes on CVD was shown only in those without microalbuminuria and the effect of microalbuminuria on CVD was shown only in those without diabetes.

Our analyses have shown that microalbuminuria is not related to CVD in patients with Type 2 diabetes. This finding conflicts with results from several studies, which found that the presence of microalbuminuria in patients with diabetes does increase CVD risk [7–10], as in patients without diabetes. Our finding may be due to the high baseline risk of our patients, with at least 40% having a history of coronary heart disease (CHD), precluding further risk increase by presence of microalbuminuria, particularly in those with diabetes mellitus.

Recently, proteinuria has been shown to be an independent predictor of CVD mortality in patients with Type 2 diabetes mellitus in a 18-year Finnish follow-up study, after adjusting for the metabolic syndrome, with a HR of 1.6 (95% CI 1.0, 2.6) [20]. Unfortunately, proteinuria was defined differently as a urinary protein concentration ≥ 0.1 g/l and the effect of Type 2 diabetes itself on cardiovascular mortality was not assessed in this study, but the positive independent relationship between proteinuria and CVD mortality in those with diabetes parallels our results for microalbuminuria.

Previous studies have examined the role of diabetes as an important risk factor for CVD, but not in such a high-risk population as our SMART population, and not after adjustment for microalbuminuria. Much higher relative risks of 3–9 were found in these relatively lower-risk populations [3–5] without adjustment for microalbuminuria. The association between microalbuminuria and cardiovascular mortality in patients with Type 2 diabetes has been studied extensively. A meta-analysis has demonstrated a twofold increased risk of total and cardiovascular morbidity and mortality associated with microalbuminuria [21]. Microalbuminuria also predicts incident CVD in the general population, and many studies have adjusted for diabetes duration or diabetes itself [9,10,22,23]. A Danish study has demonstrated a significant relationship between very low levels of urinary albumin excretion (> 4.8 μg/min) and incident CHD and death, which was also independent of diabetes with a relative risk of 2.0 (95% CI 1.3, 2.9) [24].

Previously, reduced renal creatinine clearance or chronic kidney disease have been shown to be independent predictors of CVD [25–27]. Therefore, we have adjusted the association between microalbuminuria and CVD for renal creatinine clearance and found no confounding influence on the reported association.

In summary, both Type 2 diabetes and microalbuminuria are important independent risk factors for future CVD. It is important to target both Type 2 diabetes and microalbuminuria (or albuminuria in general) as early as possible in order to prevent CVD. In addition, the effect of microalbuminuria on CVD is apparent in those without diabetes, but not in those with Type 2 diabetes. The effect of Type 2 diabetes on CVD risk is apparent in those without microalbuminuria, but not in those with microalbuminuria.

Competing interests

None to declare.

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