Renal Impairment Associated With Diabetes in the Elderly

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OBJECTIVE — To characterize renal impairment associated with diabetes in older adults by serum markers of glomerular filtration rate and microalbuminuria tests.

RESEARCH DESIGN AND METHODS — The study population consisted of 187 diabetic and 1,073 nondiabetic subjects (age range 64–100 years) participating in a cross-sectional, population-based survey in southwestern Finland. Renal function was estimated by serum cystatin C (Cys C), serum creatinine (Cr), and the urinary albumin-to-creatinine ratio, and determinants of elevated levels were assessed by multivariate analysis.

RESULTS — Diabetes, compared to hypertension, was a more powerful determinant of elevated Cys C and Cr levels in the very old (age ≥80 years), whereas the impact of hypertension was more pronounced in the younger group (age <80 years). The prevalence of microalbuminuria among diabetic subjects was 29.7%, and 15% had elevated Cr levels, whereas the prevalence of elevated Cys C levels varied considerably depending on whether adult or age-adjusted reference limits were used (64.7 vs. 21.4%). In 64.1% of diabetic subjects with elevated Cys C levels based on age-adjusted reference limits and in 48.2% of subjects with elevated Cr levels, microalbuminuria was absent.

CONCLUSIONS — The impact of diabetes on renal impairment changes with increasing age. Serum markers of glomerular filtration rate and microalbuminuria identify renal impairment in different segments of the diabetic population, indicating that serum markers as well as microalbuminuria tests should be used in screening for nephropathy in diabetic older people. The appropriate reference limit for Cys C in geriatric clinical practice must be defined by further research.

Diabetes Care 27:2648–2653, 2004

Over the past decade there has been considerable interest in the increasing incidence of diabetic nephropathy, predominantly in patients with type 2 diabetes (1). As the treatment of cardiovascular diseases has improved, diabetic nephropathy is increasingly becoming a disease of older people (2). However, our understanding of diabetic nephropathy is primarily based on research done among middle-aged populations, and direct extrapolation of these results to the elderly, especially to the very old, may be inappropriate.

Screening for microalbuminuria, the earliest manifestation of diabetic nephropathy, is recommended for all diabetic patients (3). However, much of the knowledge about diabetic nephropathy is derived from studies concerning type 1 diabetes, while kidney disease in type 2 diabetes may be more heterogeneous and not necessarily manifested as classic diabetic glomerulosclerosis and albuminuria. It has been suggested that clinicians, in addition to monitoring urine albumin excretion, should assess glomerular filtration rate (GFR) to screen for renal disease among patients with type 2 diabetes (4).

Serum creatinine (Cr) is the most widely used marker of GFR in the office setting, although it is an insensitive measure of early renal disease (5). Serum cystatin C (Cys C), a low–molecular weight protein steadily produced by all human nucleated cells, has been claimed to be superior to Cr as an endogenous marker of GFR (6). Cys C is freely filtered in the glomeruli, reabsorbed, and metabolized in the proximal tubule, and thus, the serum concentration is mainly determined by GFR and does not depend on muscle mass or sex (7). It has been suggested (8) that Cys C could be especially useful in the detection of early nephropathy, as demonstrated by increased Cys C levels in patients with hypertension and microalbuminuria, but a GFR still in the normal range. In elderly subjects with Cr concentrations within the normal range, Cys C was found to be a better marker of reduced GFR than Cr (9). Cys C has also been reported to have advantages over Cr in monitoring nephropathy in diabetic subjects (10,11). Glucocorticoid treatment has been recognized as a nonrenal factor increasing Cys C (12).

The objectives of the study were to explore the features of renal dysfunction associated with diabetes in the elderly and, especially, to evaluate possible differences between older people <80 years of age and the very old. Cys C and Cr were used to estimate GFR and albumin-to-Cr ratio (ACR) to assess microalbuminuria.

RESEARCH DESIGN AND METHODS

— The study population consisted of 1,260 elderly residents (533 men and 727 women; mean age 74 years,

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Received for publication 23 March 2004 and accepted in revised form 16 August 2004.

Abbreviations: ACR, albumin-to-creatinine ratio; Cr, creatinine; Cys C, cystatin C; GFR, glomerular filtration rate; NHANES III, Third National Health and Nutrition Examination Survey.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

range 64–100) in Lieto, a semi-industrialized rural municipality in southwestern Finland. During 1998–1999, all Lieto residents born in or before 1933 (n = 1,519) were invited to participate in a community-based, cross-sectional epidemiological survey; 83% gave written consent and were included. Institutionalized individuals constituted 5% of the study population. Information on chronic health conditions and current medications was obtained through standardized interviews, thorough clinical examinations, and review of medical records, extensively available over a maximum time span of >40 years. ICD-10 diagnosis codes were used for documentation. The local Commission of Ethics approved the study protocol.

Measurements and definitions

Early-morning fasting venous blood and spot urine samples were analyzed in the Central Laboratory of Turku University Central Hospital. Cys C concentrations were determined using a particle-enhanced nephelometric immunoassay (N Latex Cystatin C, BN II System; Dade Behring, Marburg, Germany) with an upper reference limit of 0.95 mg/l for adults. Regression-based, age-adjusted reference limits, constructed earlier for the same population (13), were applied year by year. The upper reference limits per age-group were 1.37 mg/l for subjects <80 years of age and 1.63 mg/l for those ≥80 years of age. Serum and urinary Cr were measured using the Jaffé reaction, and serum glucose was measured by the enzymatic hexokinase method (Roche Diagnostics, Mannheim, Germany, and Hitachi 917; Hitachi, Tokyo, Japan). The reference limit for serum Cr was 118 μmol/l for men and 104 μmol/l for women according to the sex-specific reference ranges earlier determined for the study population (13). Urinary albumin was analyzed using an immunoturbidimetric method (Optima Microalbuminuria kit; Thermo Clinical Labsystem, Helsinki, Finland). Albuminuria was defined by the urinary ACR as microalbuminuria (>30–300 mg albumin/g Cr) or macroalbuminuria (>300 mg albumin/g Cr) (14).

A 12-lead resting electrocardiogram was recorded and interpreted using the Minnesota Code (15). Physical functioning was assessed using a questionnaire adapted from the protocol of the Eleven Countries Study and included four items on mobility (capability to walk outdoors, between rooms, in stairs, or ≥400 m) and five items on activities of daily living, i.e., dressing, eating, bathing, going to bed, and toileting (16). The maximum sum score, indicating no limitations in physical functioning, was 27.

Diabetes was defined based on the medical history or one fasting serum glucose concentration of ≥7 mmol/l (17). Individuals were classified as hypertensive if they were using antihypertensive medication or had been diagnosed by a physician. Coronary heart disease was diagnosed based on medical records or electrocardiography. The diagnosis of urinary infection was based on significant bacterial growth in an early-morning urine specimen or documentation of chronic urinary infection.

The clinical examination and review of medical records were complete for all participants, whereas seven blood samples and 26 urine samples were missing, reducing the study population accordingly.

Statistical analyses

All statistical analyses were performed using SAS for Windows, version 8.02 (SAS, Cary, NC). χ^2 test and Mann-Whitney U test were used to analyze univariate associations. Because of skewed distributions, Cys C and Cr concentrations were inversely transformed for statistical analysis. The associations of the independent variables with the continuous dependent variables Cys C and Cr, respectively, were evaluated using multivariate linear models. Multivariate logistic regression analysis was used to assess the association of independent variables with the dichotomous dependent variable microalbuminuria. Analyses were adjusted for potential confounding factors. $P < 0.05$ was considered significant.

The impact of age on the main outcomes was analyzed by dividing the population into a younger (age <80 years, n = 1,010) and an older (age ≥80 years, n = 250) subgroup. Within these subgroups, adjustment for age was performed by multivariate linear modeling with age included as a continuous explanatory variable.

RESULTS — Demographic and clinical characteristics of nondiabetic and diabetic subjects according to age-groups are displayed in Table 1. The prevalence of diabetes (n = 187,14.8%) increased with age, but the difference between age-groups was not significant. In 32 individuals (17.1% of all diabetic subjects), diabetes was newly detected. Six individuals, equally representative of the two age-groups, were treated with insulin only, probably indicating type 1 diabetes. Because the group was small and the classification not verified by laboratory analysis, it was not analyzed separately.

Mean BMI, adjusted for sex, was significantly lower in older subjects compared with younger ones in the diabetic group (P = 0.002) as well as in the nondiabetic group ($P < 0.001$) (Table 1). Mean BMI in newly diagnosed diabetic subjects (27.9 kg/m^2) tended to be lower than mean BMI in previously diagnosed subjects (29.6 kg/m^2), but the difference did not reach significance (P = 0.071). The trend was similar in both age-groups.

The prevalences of hypertension and coronary heart disease were significantly higher in diabetic subjects compared with nondiabetic subjects (Table 1). Among diabetic subjects, the prevalence of hypertension decreased significantly with increasing age (P = 0.025), whereas in nondiabetic subjects, the proportion did not change significantly with age. The prevalence of hypertension in newly diagnosed diabetic subjects was similar to the prevalence in nondiabetic subjects (34.4 vs. 34%).

Impact of diabetes and hypertension on levels of kidney function

The impacts of diabetes and hypertension on the mean levels of Cys C and Cr concentrations differed considerably in the two age-groups (Tables 1 and 2). In the older group, the impact of diabetes was more pronounced, whereas the younger group showed a greater impact of hypertension. In the older group, hypertensive diabetic subjects, compared with diabetic subjects without hypertension, had lower mean levels of Cys C and Cr (Table 2). In the older age-group, diabetes, after adjustment for age, sex, use of glucocorticoids, coronary heart disease, and hypertension, was significantly associated with elevated Cys C (P = 0.011) and Cr (P = 0.004) levels. In the younger age-group, diabetes was not associated with elevated levels of Cys C or Cr, whereas the impact of hypertension was highly significant ($P < 0.001$). In diabetic subjects, hypertension adjusted for confounders

Table 1—*Demographic and clinical characteristics of the study population categorized by diabetes status and age*

	Total study population (n = 1,260)			Subjects <80 years of age (n = 1,010)			Subjects ≥80 years of age (n = 250)		
	No diabetes	Diabetes	P	No diabetes	Diabetes	P	No diabetes	Diabetes	P
n	1,073 (85.2)	187 (14.8)	—	863 (85.4)	147 (14.6)	—	210 (84.0)	40 (16.0)	—
Men	446 (41.6)	87 (46.5)	NS	377 (43.7)	73 (49.7)	NS	69 (32.9)	14 (35.0)	NS
Age (years)	73.9 ± 6.8	74.7 ± 6.9	NS	71.1 ± 4.0	71.9 ± 4.3	0.047	85.0 ± 4.0	84.9 ± 4.5	NS
BMI (kg/m^2)	26.6 ± 4.5	29.3 ± 5.0	<0.001	27.0 ± 4.3	29.9 ± 5.0	<0.001	24.9 ± 4.9	27.3 ± 4.3	0.005
Serum Cys C (mg/l)*	1.07 ± 0.35	1.17 ± 0.44	NS†	1.02 ± 0.28	1.06 ± 0.28	NS†	1.31 ± 0.47	1.56 ± 0.65	0.011†
Serum Cr (μmol/l)*	93.4 ± 18.8	99.1 ± 26.0	NS†	92.3 ± 16.6	95.4 ± 20.1	NS†	97.8 ± 25.6	112.8 ± 38.3	0.004†
Serum glucose (mmol/l)*	5.5 ± 0.6	9.1 ± 3.2	<0.001	5.5 ± 0.6	9.1 ± 3.1	<0.001	5.4 ± 0.6	9.2 ± 3.7	<0.001
Hypertension	365 (34.0)	104 (55.6)	<0.001	290 (33.6)	88 (59.9)	<0.001	75 (35.7)	16 (40.0)	NS
Coronary heart disease	420 (39.1)	96 (51.3)	0.002	308 (35.7)	70 (47.6)	0.006	112 (53.3)	26 (65.0)	NS
Microalbuminuria‡	171/1,049 (16.3)	55/185 (29.7)	<0.001	102/850 (12.0)	42/146 (28.8)	<0.001	69/199 (34.7)	13/39 (33.3)	NS
Macroalbuminuria‡	7/1,049 (0.7)	9/185 (4.9)	<0.001	5/850 (0.6)	7/146 (4.8)	<0.001	2/199 (1.0)	2/39 (5.1)	NS

Data are means ± SD or n (%). *Values missing in 7 nondiabetic subjects; †adjustment for age, sex, use of glucocorticoids, coronary heart disease, and hypertension; ‡albuminuria was not determined in 24 nondiabetic and 2 diabetic subjects.

was not significantly associated with elevated Cys C or Cr levels. In the younger group of diabetic subjects, however, hypertension was associated with elevated levels of Cr (P = 0.035), and the association with Cys C was nearly significant (P = 0.050) (Table 2).

Duration of diabetes and level of hyperglycemia were not associated with elevated levels of Cys C or Cr. In the younger group, the history of diabetes was significantly longer among those with hypertension compared with those without hypertension, whereas a reverse relationship was observed among older diabetic subjects (Table 2).

Microalbuminuria

The prevalences of micro- and macroalbuminuria were significantly higher among diabetic subjects than among nondiabetic subjects in the younger age-group, whereas in the older group, the difference was not significant (Table 1).

Table 3 presents the mean concentrations of Cys C and Cr in diabetic subjects with and without microalbuminuria. In all subgroups, the mean levels of Cys C and Cr were higher in microalbuminuric subjects compared with normoalbuminuric ones. However, microalbuminuria adjusted for confounders was not significantly associated with rising Cr levels in either the diabetic population or the total population, whereas Cys C analysis showed a significant association (P = 0.006) in the total population and a borderline association in older diabetic subjects (P = 0.071).

The mean duration of diabetes was significantly longer in microalbuminuric subjects compared with normoalbuminuric ones. (The trend was similar in the two age-groups, but significance was not reached in the older group [Table 3].) Older age was not associated with microalbuminuria in diabetic subjects, but was associated with elevated levels of both Cys C and Cr ($P < 0.001$).

In the overall population, after controlling for urinary infection, coronary heart disease, and demographic variables, diabetes (odds ratio [OR] 2.15, 95% CI 1.46–3.16; $P < 0.001$) and hypertension (1.47, 1.07–2.02; P = 0.018) were significantly associated with the risk for microalbuminuria. The associations were similar in the younger age-group (diabetes 2.75, 1.76–4.30; $P < 0.001$, and hypertension 1.49, 1.01–2.18; P = 0.042),

Table 2—*Serum Cys C and serum Cr concentrations according to hypertension and diabetes status and age of subjects*

	Age-group					
	<80 years (n = 1,005)*			≥80 years (n = 248)*		
	Hypertension			Hypertension		
	No	Yes	P	No	Yes	P
Total study population	628	377	—	159	89	—
Serum Cys C (mg/l)	0.97 ± 0.23	1.10 ± 0.34	<0.001†	1.30 ± 0.49	1.44 ± 0.55	0.002†
Serum Cr (μmol/l)	90.2 ± 14.5	96.9 ± 20.2	<0.001†	98.4 ± 27.7	103.4 ± 29.7	0.045†
No diabetes	569	289	—	135	73	—
Serum Cys C (mg/l)	0.97 ± 0.23	1.10 ± 0.35	<0.001‡	1.24 ± 0.41	1.43 ± 0.55	<0.001‡
Serum Cr (μmol/l)	90.2 ± 14.6	96.4 ± 19.2	<0.001‡	95.5 ± 22.3	102.1 ± 30.5	0.026‡
Diabetes	59	88	—	24	16	—
Serum Cys C (mg/l)	1.01 ± 0.24	1.09 ± 0.31	0.050‡	1.62 ± 0.71	1.47 ± 0.55	NS‡
Serum Cr (μmol/l)	90.6 ± 13.2	98.6 ± 23.1	0.035‡	115.0 ± 45.0	109.4 ± 26.2	NS‡
Duration of diabetes (years)	4.5 ± 5.1	7.0 ± 6.2	0.009	9.6 ± 7.9	3.9 ± 4.1	0.022

Data are means ± SD. *Five (age <80 years) and two (age ≥80 years) subjects with missing values were excluded; †adjusted for age, sex, use of glucocorticoids, coronary heart disease, and diabetes; ‡adjusted for age, sex, use of glucocorticoids, and coronary heart disease.

whereas in the older group significance was not reached.

Elevated levels of Cys C and Cr according to reference limits

When the adult reference limit for Cys C was applied, 64.7% of diabetic subjects (age <80 years, 57.1%, and age ≥80 years, 92.5%) turned out to have elevated Cys C levels. According to age-adjusted reference limits, 21.4% (age <80 years, 15.7%, and age ≥80 years, 42.5%) had pathological Cys C levels. The difference between the proportions of pathological Cys C levels in diabetic and nondiabetic subjects (21.4 vs. 12.7%) was significant (P = 0.002). According to sex-specific reference limits, the prevalence of pathological Cr levels in the diabetic group was 15% (age <80 years, 8.8%, and age ≥80 years, 37.5%), which was not significantly different from that in the nondiabetic group (11.3%). In 24 diabetic subjects, decreased renal function was similarly identified by Cys C and Cr. The number identified by Cr in the presence of normal Cys C levels, according to age-adjusted reference limits, was small (n = 4), whereas 16 individuals had elevated Cys C levels despite normal Cr levels. Eleven (68.8%) of these individuals had functional limitations (functional index ≤25), whereas the corresponding proportions of all diabetic and nondiabetic subjects were 51.1 and 36.2%, respectively.

In 64.1% of the diabetic subjects, classified to have elevated Cys C levels based on the age-adjusted reference limits, microalbuminuria was absent. (For Cr the corresponding proportion was 48.2%.) The proportions were greater in the younger group (73.9% for Cys C and 53.9% for Cr) than in the older group (50.0% for Cys C and 42.9% for Cr).

CONCLUSIONS — Some limitations of the present study should be acknowledged. Elevated serum glucose and urinary ACR values were not confirmed by repeated sampling. Glycated hemoglobin was not measured, and 2-h glucose tolerance tests were not performed. Especially in older people, fasting and postload glycemia may not identify the same people (18). Furthermore, the cross-sectional design of the study should be acknowledged when interpreting results.

Hyperglycemia and hypertension have, in earlier research, been established as the main risk factors for micro- and macrovascular complications in diabetic subjects (19,20). In the present study, the impacts of diabetes and hypertension on serum levels of Cys C and Cr were found to be markedly different in subjects <80 and ≥80 years of age. Diabetes, compared to hypertension, was a more powerful determinant of decreased renal function in

Table 3—*Serum Cys C and serum Cr concentrations in normo- and microalbuminuric diabetic subjects according to age*

	All diabetic subjects (n = 176)*		Diabetic subjects age <80 years (n = 139)		Diabetic subjects age ≥80 years (n = 37)	
	Microalbuminuria		Microalbuminuria		Microalbuminuria	
	No	Yes	No	Yes	No	Yes
n	121	55	97	42	24	13
Duration of diabetes (years)	5.1 ± 5.2	8.2 ± 7.2†	4.8 ± 5.2	7.6 ± 6.3‡	6.2 ± 5.5	10.0 ± 9.7
Serum Cys C (mg/l)	1.10 ± 0.36	1.25 ± 0.52	1.04 ± 0.26	1.10 ± 0.35	1.37 ± 0.56	1.73 ± 0.70§
Serum Cr (μmol/l)	96.7 ± 25.1	103.3 ± 28.0	94.3 ± 19.1	98.2 ± 23.0	106.6 ± 40.6	119.7 ± 36.4

Data are means ± SD. *Nine subjects with macroalbuminuria and two with missing samples were excluded; †P = 0.010, ‡P = 0.017, and §P = 0.071, adjusted for age, sex, urinary infection, and use of oral glucocorticoids.

the older age-group, whereas the impact of hypertension was more pronounced in the younger group. In the older age-group, surprisingly, hypertensive diabetic subjects had lower mean levels of Cys C and Cr than those without hypertension. These results probably reflect the combined impact of selective survival and age-related changes in the pathophysiology of diabetic target organ damage.

Type 2 diabetes is a heterogeneous disease involving both impaired β-cell function and insulin resistance, which is closely linked to many features of the metabolic syndrome (21). Defects in insulin secretion have been associated (22) with the aging process, and it was recently suggested (23) that age-associated mitochondrial dysfunction could explain the increase of type 2 diabetes in the elderly. Hence, lifestyle and environmental factors may be less important risk factors for diabetes in older people. Furthermore, increased cardiovascular mortality may reduce the number of very old diabetic patients with features of the metabolic syndrome (24). For these reasons, target organ damage in elderly type 2 diabetic subjects, especially in the very old, might show similarities to target organ damage in type 1 diabetes, with a microvascular rather than macrovascular profile. In the present study, the differences regarding BMI and the prevalence of hypertension observed between age-groups and between newly diagnosed diabetic subjects and those diagnosed at an earlier age probably indicate variation between groups regarding the prevalence of the metabolic syndrome as well.

The close coexistence of diabetes and hypertension in the younger age-group and the exacerbation of diabetic nephropathy in hypertensive subjects with a longer history of diabetes (mean 7 vs. 4.5 years in those without hypertension) may explain the more powerful influence of hypertension, relative to diabetes, in this age-group.

In the older age-group, diabetic subjects without hypertension surviving beyond 80 years of age were probably less prone to serious macrovascular complications and hence had a longer history of diabetes (mean 9.6 years) compared with those with both diabetes and hypertension (mean 3.9 years). The more long-term susceptibility to chronic hyperglycemia, the main predictor of microvascular complications, possibly explains the elevated Cys and Cr levels in the nonhypertensive group. The shorter duration of the disease in the hypertensive group possibly reflects increased cardiovascular mortality before the manifestation of microvascular complications.

Duration of disease was not associated with elevated Cys C or Cr levels in the diabetic population, probably reflecting the heterogeneous etiology of nephropathy, the difficulty in estimating the exact onset of type 2 diabetes, and the impact of selective survival. Longer duration of diabetes was, however, a significant predictor of microalbuminuria, suggesting microalbuminuria to be a more specific marker of diabetic nephropathy.

The mean levels of Cys C and Cr were higher in microalbuminuric diabetic subjects compared with normoalbuminuric ones. In the study population, microalbuminuria was significantly associated with elevated Cys C levels only, indicating that Cys C is a more sensitive marker of incipient nephropathy.

The prevalence of microalbuminuria in diabetic subjects did not increase significantly with age (28.8 vs.33.3%) and was slightly lower than the prevalence reported for the corresponding age-groups in the Third National Health and Nutrition Examination Survey (NHANES III) (32.2–36.1%) (25). However, in the NHANES III, previously undetected diabetes was not diagnosed by means of laboratory testing. Serum markers of GFR and microalbuminuria identified kidney damage in different segments of the diabetic population since approximately one-half of the subjects with elevated levels of serum markers did not have micro- or macroalbuminuria. This could reflect the heterogeneous etiology of nephropathy in elderly type 2 diabetic subjects and suggests that testing for microalbuminuria as well as serum markers of GFR should be used in screening elderly diabetic populations for kidney damage. The proportion of nonmicroalbuminuric subjects with elevated serum markers of GFR was more pronounced in the younger age-group. Similarly in the NHANES III, nonalbuminuric renal insufficiency was more evident in subjects 60–79 years of age than in those ≥80 years of age (25). The prevalence of microalbuminuria in nondiabetic subjects ≥80 years of age was high and probably reflects the polymorbidity in this aged population (12).

The superiority of Cys C over Cr with respect to GFR measures has been confirmed by both superior correlation coefficients and greater receiver operating characteristic–plot area under the curve values in a recent meta-analysis (6). In the present large study, there was no gold standard for comparing the diagnostic accuracies of Cys C and Cr. In multivariate analysis, the impacts of diabetes and hypertension on renal function were similar regardless of whether Cys C or Cr was used as the dependent variable. However, when Cys C rather than Cr was applied, a considerably greater proportion of diabetic subjects were classified as having decreased renal function. A majority of diabetic subjects classified as having pathological Cys C levels despite normal Cr levels had functional limitations, probably indicative of smaller muscle mass. Cr levels are dependent on muscle mass, and Cr may hence be less sensitive to detect decreased renal function in disabled older adults. The discrepancy between the proportions of diabetic subjects with elevated levels of Cys C depending on whether adult or age-adjusted reference limits were used was pronounced in both age-groups and indicates a need for further research concerning the most appropriate reference limits for Cys C and the possibilities to discriminate between involutional and pathological renal impairment.

This study has characterized renal impairment associated with diabetes in an elderly population. Diabetes, compared to hypertension, was found to be a more powerful determinant of renal dysfunction in the very old, whereas the impact of hypertension was more pronounced in the younger age-group. Serum markers of GFR and microalbuminuria identified renal impairment in different segments of the diabetic population, suggesting that serum markers as well as microalbuminuria tests should be used in screening for kidney damage in older diabetic subjects. A larger number of diabetic subjects were found to have decreased renal function based on Cys C rather than Cr. However, further research is needed to clarify whether adult or age-adjusted reference limits for Cys C should be used in geriatric practice.

Acknowledgments— The study was supported in part by grants from The Red Feather Campaign of the Nordic Lions Clubs and the

February 19th Foundation of the Finnish Heart Association.

The authors thank Dade Behring (Marburg, Germany) for providing kits for the measurement of Cys C.

This study was presented in abstract form at the 40th annual meeting of the European Association for the Study of Diabetes, Munich, Germany, 5–9 September 2004.

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