Predictors of Estimated GFR Decline in Patients with Type 2 Diabetes and Preserved Kidney Function

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Summary

Background and objectives This study examined predictors of the annual decline in estimated GFR (eGFR) in patients with type 2 diabetes and preserved kidney function.

Design, setting, participants, & measurements In a prospective, observational cohort study, 1682 individuals with type 2 diabetes and baseline eGFR ≥60 ml/min per 1.73 m^2 (as estimated by the Chronic Kidney Disease Epidemiology Collaboration equation) were followed for 10 years. Linear regression was used to estimate participants' changes in eGFR over time.

Results During follow-up, 263 (15.6%) individuals had a rapid eGFR decline defined as >4.0% per year. Average eGFR decline was −5.8±3 and −0.6±2 ml/min per 1.73 m^2 per year in rapid decliners and nondecliners, respectively. Compared with normotensive, normoalbuminuric patients (−0.2±0.2 ml/min per 1.73 m^2 per year), those with hypertension (−1.0±0.1 ml/min per 1.73 m^2 per year), hemoglobin A_{1c}≥7% (−1.0±0.1 ml/min per 1.73 m^2 per year), longer diabetes duration (−1.0±0.1 ml/min per 1.73 m^2 per year), obesity (−1.2±0.1 ml/min per 1.73 m^2 per year), insulin treatment (−1.5±0.1 ml/min per 1.73 m^2 per year), microalbuminuria (−1.3±0.2 ml/min per 1.73 m^2 per year), or macroalbuminuria (−2.7±0.4 ml/min per 1.73 m^2 per year) had significantly faster age-adjusted annual eGFR declines. Multivariable linear regression analyses revealed that albuminuria ($P<0.001$) was the strongest predictor of annual eGFR decline. Other independent predictors of annual eGFR decline were older age, hypertension, insulin treatment, and lower baseline eGFR.

Conclusions Annual eGFR decline is predicted by multiple modifiable risk factors in patients with type 2 diabetes and preserved kidney function.

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Introduction

Several renal functions, particularly renal hemodynamic parameters, decline in elderly individuals even in the absence of renal disease. However, aging *per se* seems to exert only a modest adverse effect on renal hemodynamics (1–3). Age-related loss of kidney function is mainly due to other important comorbidities, such as diabetes, hypertension, and obesity (4–6).

Diabetic nephropathy develops in 40%–60% of individuals with type 2 diabetes and is characterized by a progressive and persistent decline in kidney function that with time can lead to ESRD (7,8). The estimated GFR (eGFR) is the most widely used parameter for the evaluation of changes in kidney function in clinical practice. However, the course of GFR is very complex and heterogeneous in type 2 diabetes, mainly depending on individual, ethnic, and disease-specific conditions (8–14). For instance, it was recently reported that albuminuria is the strongest risk factor of faster annual eGFR decline in 153 Caucasian patients with type 2 diabetes with a baseline eGFR <50 ml/min per 1.73 m^2 during a 2.5-year follow-up (15). Conversely, chronic hyperglycemia has been found to play a key role in decreasing eGFR and accelerating the annual eGFR decline during a 3-year follow-up period in 729 Japanese patients with type 2 diabetes and preserved kidney function (16).

To our knowledge, most published studies aimed at examining the predictors of annual eGFR decline among patients with type 2 diabetes are limited by a relatively small sample size, short length of follow-up, and lack of sequential measurements in kidney function. In addition, data on predictors of eGFR decline in patients with type 2 diabetes and preserved kidney function are scarce.

The aim of this observational study was to examine the predictors of annual eGFR decline during a 10-year follow-up in a cohort of individuals with type 2 diabetes and a baseline eGFR ≥60 ml/min per 1.73 m^2. Knowledge of the rate of annual eGFR decline and its main risk factors is of clinical importance to improve the therapeutic strategies for the primary prevention of kidney disease in patients with type 2 diabetes and preserved kidney function.

Materials and Methods

Patients

The study was performed within the frame of the Verona Diabetes Study, an observational longitudinal study on chronic complications in patients with type 2 diabetes attending the diabetes clinic at the University Hospital of Verona (17). Data included in this analysis are based on the cohort of 1682 Caucasian outpatients with type 2 diabetes, who were recruited between January 2000 and January 2002 and then followed-up until January 2011. These participants represent approximately 45% of the whole cohort of outpatients with type 2 diabetes (n=3924), who regularly attended the clinic during 2000–2002, after excluding the following: patients with an eGFR <60 ml/min per 1.73 m^2 (n=1229), those who had <3 GFR estimates during the follow-up (n=320), and those who had incomplete laboratory data for analysis (n=693).

Notably, baseline demographics and laboratory data, including eGFR and albuminuria, were not significantly different between the 1682 participants in the study and those who had <3 GFR estimates during the follow-up (data not shown).

The study participants were periodically seen at the diabetes clinic (every 8–12 months) for routine medical examinations of glycemic control, kidney function parameters, and chronic complications of diabetes. The local ethics committee approved the study protocol. All participants gave their informed consent.

Clinical and Laboratory Data

Body mass index (BMI) was calculated by dividing weight in kilograms by the square of height in meters. BP was measured by a physician with a mercury sphygmomanometer (at the right upper arm using an appropriate cuff size) after the patient sat quietly for at least 5 minutes. Participants were considered to have hypertension if their BP was ≥140/90 mmHg or if they were taking any antihypertensive drugs.

Information on medical history and smoking status was obtained from all patients by interviews during medical examinations. Detailed information regarding specific classes of antihypertensive drugs (*e.g.*, angiotensin-converting enzyme [ACE] inhibitors, angiotensin receptor blockers [ARBs]) was not currently available in our information database. Diagnosis of diabetic retinopathy was based on funduscopy after pupillary dilation (18).

Venous blood was drawn the morning after an overnight fast. Serum creatinine (measured using a Jaffé rate-blanked and compensated assay), lipids, and other biochemical blood measurements were determined by standard laboratory procedures (DAX 96; Bayer Diagnostics, Milan, Italy). LDL cholesterol was calculated using Friedewald's equation. Hemoglobin A_{1c} was measured by an automated high-performance liquid chromatography analyzer (Bio-Rad Diamat, Milan, Italy); the upper limit of normal for our laboratory was 5.6%.

GFR was estimated from the Chronic Kidney Disease Epidemiology Collaboration creatinine equation (19). eGFR was also estimated from the four-variable Modification of Diet in Renal Disease (MDRD) equation (20). The urinary albumin excretion rate was measured from a 24-hour urine sample by an immuno-nephelometric method. Presence of abnormal albuminuria (≥30 mg/d) was confirmed in a least two of three consecutive samples (8).

Statistical Analyses

Data are presented as means ± SD or SEM and frequencies. Skewed variables were logarithmically transformed to improve normality before analysis (diabetes duration, triglycerides, and eGFR). The unpaired t test and the chi-squared test with Yates's correction for continuity (for categorical variables) were used to analyze the differences among the baseline characteristics of participants stratified by presence or absence of a rapid eGFR decline (Table 1). For each patient, a linear regression model of time on eGFR (least-squares method) was created, and the slope of the regression line was used to estimate the patient's changes in eGFR over time. The eGFR slope was expressed as percentage per year by dividing the slope by the baseline eGFR value (*i.e.*, annual eGFR decline). Because no definite criteria for eGFR decliner exist, individuals with a rapid decline in eGFR were defined as those who had an eGFR decline >4.0% per year, in accord with previous studies (3,16); this threshold corresponds approximately to an eGFR loss ≥3 ml/min per 1.73 m^2 per year, which has been previously used as a cut-off that reflects three times more rapid decline than expected by normal aging (21). Annual eGFR decline according to different clinical features was compared among patients' groups by analysis of covariance after adjustment for age (Table 2 and Figures 1 and 2). Multivariable linear regression analysis was also performed to test the independent associations of annual eGFR decline (*i.e.*, the dependent variable) with baseline covariates. We formally checked that the change in eGFR over time was linear, allowing us to use a linear regression model. In the fully adjusted regression model, sex, age, BMI, hypertension (or systolic BP included as continuous variable), diabetes duration, insulin treatment, history of previous cardiovascular disease (defined as angina, myocardial infarction, or stroke), HbA_{1c}, eGFR (or serum creatinine), and albuminuria were included as covariates (Table 3). We also tested for a formal interaction between hypertension and albuminuria in the multivariable regression model. The hypertension × albuminuria interaction term (P=0.41) was not statistically significant.

These covariates were chosen as potential confounding factors on the basis of their significance in univariate analysis or on the basis of their biologic plausibility. A multivariable logistic regression analysis was also performed with the status of rapid eGFR decliners (yes/no) as the dependent variable. The same set of covariates was included in this logistic regression model. Statistical analysis was performed with SPSS 19.0 statistical package software. P values <0.05 were considered statistically significant.

Results

The 1682 patients with type 2 diabetes (mean age 65.1±9 years; 61.7% men) included in this study had a mean baseline eGFR of 79.6±12 ml/min per 1.73 m^2; 79% (n=1328) had normal albuminuria, 17.1% (n=288) had microalbuminuria, and 3.9% (n=66) had macroalbuminuria. Approximately 85% (n=1439) of patients had hypertension (BP ≥140/90 mmHg or drug treatment). Mean HbA_{1c} was 7.5%±1.5%.

Table 1. Baseline clinical and biochemical characteristics of patients with type 2 diabetes and preserved kidney function stratified by eGFR decline during a 10-year follow-up period

Parameter	Rapid Decliners (n=263)	Nondecliners (n=1419)	P Value
Sex (M/F)	168/95	869/550	0.19
Age (yr)	67±9	64±9	<0.001
Diabetes duration (yr)	16.7±9	14±9	<0.001
Body mass index (kg/m^2)	28.5±5	28.2±4.4	0.29
Systolic BP (mmHg)	142±19	137±18	<0.001
Diastolic BP (mmHg)	81±10	81±9	0.83
Hypertension (%)	93.9	84.0	<0.001
Current smokers (%)	28.9	20.5	<0.05
Hemoglobin A_{1c} (%)	7.6±1.5	7.5±1.5	0.42
LDL cholesterol (mmol/L)	3.33±0.9	3.39±0.9	0.36
HDL cholesterol (mmol/L)	1.40±0.4	1.36±0.3	0.15
Triglycerides (mmol/L)	1.62±1.1	1.56±1.0	0.40
Any grade of retinopathy (%)	36.8	28.8	<0.05
Microalbuminuria (%)	23.4	15.9	<0.001
Macroalbuminuria (%)	9.6	2.9	<0.001
eGFR at baseline (ml/min per 1.73 m^2)	78.3±12	79.9±12	0.56
eGFR at follow-up (ml/min per 1.73 m^2)	50.6±16	74.3±16	<0.001
eGFR decline (ml/min/1.73 m^2 per year)	−5.8±3	−0.6±2	<0.001
eGFR decline (% per yr)	−7.5±4	−0.9±2	<0.001
Diabetes treatment			<0.001
diet only (%)	3.4	10.1	
oral hypoglycemic agents (%)	54.0	60.7	
insulin only (%)	42.6	29.2	

The cohort size totaled 1682 participants. Data are expressed as means ± SD or percentages. P values refer to the unpaired t test or the chi-squared test (for categorical variables). Hypertension was defined as BP ≥140/90 mmHg or any antihypertensive drug treatment. eGFR, estimated GFR.

Table 2. Age-adjusted annual eGFR decline in patients with type 2 diabetes and preserved kidney function stratified by different clinical categories

Parameter	Clinical Category	n	Annual eGFR Decline (ml/min 1.73 m^2 per year)	P Value	Annual eGFR Decline (% per year)	P Value
Diabetes duration	<15 yr	722	−0.7±0.1	<0.05	−0.8±0.1	<0.01
	≥15 yr	960	−1.0±0.1		−1.4±0.1	
Hemoglobin A_{1c}	<7%	659	−0.6±0.1	<0.01	−0.8±0.1	<0.01
	≥7%	1023	−1.0±0.1		−1.4±0.1	
Diabetes treatment	Diet	153	−0.4±0.2	<0.001	−0.4±0.3	<0.001
	Oral agents	1004	−0.6±0.1		−0.8±0.1	
	Insulin	525	−1.5±0.1		−2.0±0.2	
Obesity	No	1180	−0.7±0.1	<0.01	−0.9±0.1	<0.01
	Yes	502	−1.2±0.1		−1.6±0.2	
Hypertension	No	243	−0.1±0.2	<0.001	−0.2±0.2	<0.001
	Yes	1439	−1.0±0.1		−1.3±0.1	
Prior CVD	No	1512	−0.8±0.1	<0.05	−1.1±0.1	<0.05
	Yes	170	−1.3±0.2		−1.5±0.3	
Albuminuria	Normoalbuminuria	1328	−0.6±0.1	<0.001	−0.8±0.1	<0.001
	Microalbuminuria	288	−1.3±0.2		−1.6±0.2	
	Macroalbuminuria	66	−2.7±0.4		−3.4±0.5	

The cohort size totaled 1682 participants. Data on the age-adjusted annual eGFR decline are expressed as absolute and percentage changes per year (mean ± SEM). Obesity was defined as body mass index ≥30 kg/m^2. Hypertension was defined as BP ≥140/90 mmHg or any antihypertensive drug treatment. Normoalbuminuria was defined if urinary albumin excretion rate was <30 mg/d, microalbuminuria if ≥30–299 mg/d, and macroalbuminuria if ≥300 mg/d. CVD, cardiovascular disease; eGFR, estimated GFR.

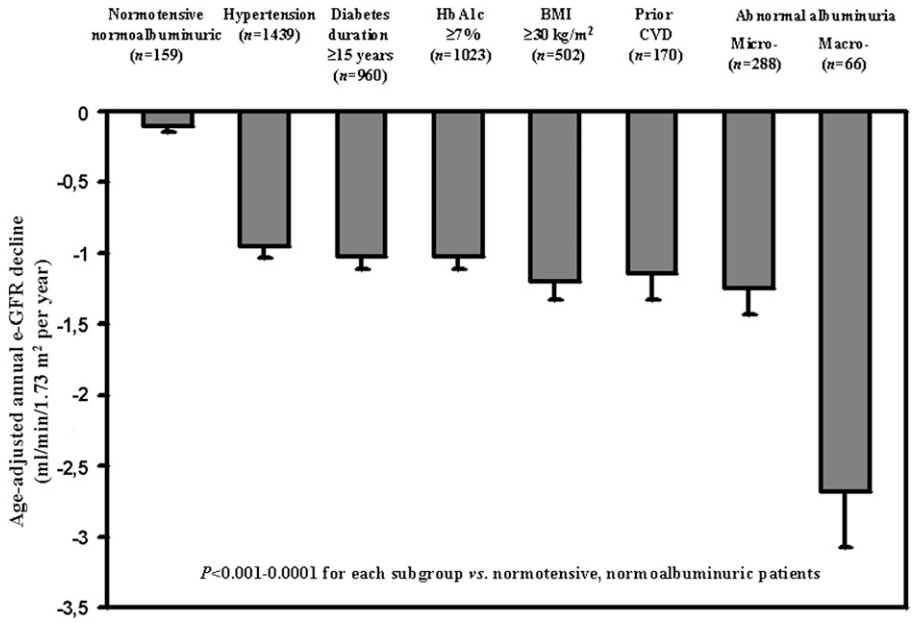

Figure 1. | Age-adjusted annual eGFR decline in 1682 patients with type 2 diabetes and preserved kidney function stratified by different clinical categories. Data are expressed as mean ± SEM. CVD, cardiovascular disease; eGFR, estimated GFR.

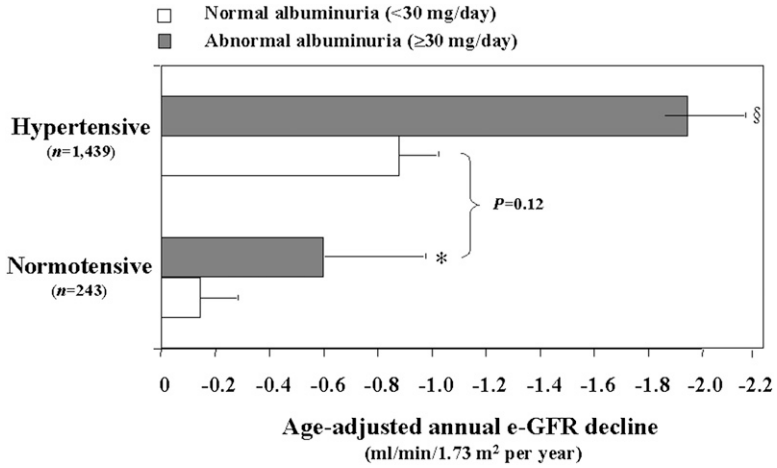

Figure 2. | Age-adjusted annual eGFR decline in 1682 patients with type 2 diabetes and preserved kidney function stratified by hypertension and albuminuria. Data are expressed as mean ± SEM. *$P<0.05$ versus normotensive patients with normoalbuminuria. §$P<0.01$ versus hypertensive patients with normoalbuminuria. eGFR, estimated GFR.

During a mean follow-up of 10 years, all patients had ≥5 measurements of serum creatinine (median 13; range, 5–25) to accurately calculate the change in eGFR over time. Annual eGFR decline of the whole cohort was −0.9±2.9 ml/min per 1.73 m^2 per year without differences between sexes (−0.9±3 and −0.8±2.6 ml/min per 1.73 m^2 per year in men and women, respectively; P=0.58).

During follow-up, there were 263 (15.6%) rapid decliners, defined as those with an eGFR decline >4.0% per year. Thirty-four (2% of total) patients died, 9 (3.4%) in the group of rapid decliners and 25 (1.7%) in the group of nondecliners (P=0.06 by chi-squared test). No other patients were lost to follow-up. The follow-up rate for the cohort was 98%.

Baseline characteristics of patients grouped according to presence or absence of rapid annual eGFR decline are summarized in Table 1. Rapid decliners were significantly older, had a longer duration of diabetes, and were more likely to have hypertension, diabetic retinopathy, and abnormal albuminuria, and were more likely to be smokers and treated with insulin therapy compared with nondecliners. They also had higher systolic BP and lower eGFR at the end of follow-up. Sex, BMI, diastolic BP, HbA_{1c}, plasma lipids, and baseline eGFR did not differ between the groups.

Table 2 shows the age-adjusted annual eGFR decline among patients at different risk categories. Patients with hypertension, diabetes duration ≥15 years, HbA_{1c} ≥7%, obesity, insulin treatment, history of cardiovascular

Table 3. Multivariable linear regression analysis: Independent predictors of annual eGFR decline in patients with type 2 diabetes and preserved kidney function

Parameter	Standardized Coefficient	*P* Value
Sex (male versus female)	0.01	0.73
Age (yr)	−0.07	<0.05
Diabetes duration (yr)	−0.05	0.10
Body mass index (kg/m^2)	−0.05	0.10
Hemoglobin A_{1c} (%)	−0.04	0.25
Prior cardiovascular disease (yes/no)	−0.01	0.65
Hypertension (yes/no)	−0.10	<0.001
Insulin therapy (yes/no)	−0.10	<0.001
Baseline eGFR (ml/min per 1.73 m^2)	−0.07	<0.05
Albuminuria (mg/d)	−0.16	<0.001

The cohort size totaled 1682 participants. Hypertension was defined as BP ≥140/90 mmHg or any antihypertensive drug treatment. In this multivariable linear regression model the dependent variable was the annual eGFR decline, which was included as a continuous measure. Standardized coefficients or β coefficients are the estimates resulting from an analysis carried out on variables that have been standardized so that their variances are 1. Therefore, standardized coefficients refer to how many SDs a dependent variable will change, per SD increase (or decrease) in the predictor variable. eGFR, estimated GFR.

disease, microalbuminuria, and macroalbuminuria showed significantly faster age-adjusted annual eGFR declines than their counterparts without those risks. In contrast, annual eGFR decline was not significantly different in current smokers versus ex-smokers and nonsmokers (−0.9±0.2 versus −0.7±0.1 versus −0.7±0.1 ml/min per 1.73 m^2 per year, respectively; *P*=0.12), in those with LDL cholesterol ≥100 versus <100 mg/dl (−0.8±0.1 versus–1.0±0.2; *P*=0.16), in those with HDL-cholesterol ≥50 mg/dl versus <50 mg/dl (-0.8±0.1 versus −0.9±0.2; *P*=0.39), or in those with triglycerides ≥150 versus <150 mg/dl (−1.0±0.1 versus −0.8±0.1; *P*=0.21).

Figure 1 shows the age-adjusted annual eGFR decline among participants belonging at the above-mentioned risk categories compared with that observed in normotensive, normoalbuminuric patients. The fastest annual eGFR decline was observed in those with macroalbuminuria.

Figure 2 shows the age-adjusted annual eGFR decline in patients stratified by hypertension and albuminuria. Patients with abnormal albuminuria showed a faster annual eGFR decline than their counterparts with normal albuminuria, irrespective of hypertension status. Notably, the combined presence of hypertension and abnormal albuminuria was associated with the fastest eGFR decline, whereas eGFR decline did not significantly differ in normotensive patients with microalbuminuria versus normoalbuminuric patients with hypertension.

In multivariable linear regression analysis (Table 3), albuminuria strongly predicted annual eGFR decline after adjustment for potential confounders. Other significant predictors of eGFR decline were hypertension, older age, insulin treatment, and lower eGFR at baseline. The results remained essentially unchanged when baseline serum creatinine replaced eGFR as a covariate in this regression model. In fact, the annual eGFR decline was independently (*P*<0.05–0.001) related to age (standardized coefficient: –0.07), hypertension (standardized coefficient: –0.10), insulin treatment (standardized coefficient: –0.11), serum creatinine (standardized coefficient: –0.07), and albuminuria (standardized coefficient: –0.15).

Almost identical results were also found when we included systolic BP as a continuous variable (standardized coefficient: –0.11; *P*<0.01) instead of hypertension status in the multivariable linear regression model or when we performed a multivariable logistic regression model in which eGFR decliner status was included as the dependent variable (not shown). Albuminuria was also the strongest predictor (*P*<0.001) of annual eGFR decline in these patients.

Similar results were observed when all of the above-mentioned statistical analyses were repeated using the four-variable MDRD study equation (data not shown).

Discussion

Most published studies aimed at assessing the predictors of eGFR decline in patients with type 2 diabetes are limited by a small sample size, short length of follow-up, and lack of sequential measurements in kidney function (*i.e.*, most studies had only two or three serum creatinine determinations to calculate the annualized changes in eGFR). In addition, epidemiologic data on the predictors of eGFR decline in patients with type 2 diabetes and preserved kidney function are limited.

In a large cohort of individuals with type 2 diabetes and a baseline eGFR ≥60 ml/min per 1.73 m^2 (approximately 80% normoalbuminuric) who were followed for 10 years, we found that the rate of annual eGFR decline was −0.9±2.9 ml/min per 1.73 m^2 per year without any significant difference between sexes. Notably, we found that the most powerful risk factor of faster age-adjusted annual eGFR decline was abnormal albuminuria: −1.3±0.2 ml/min per 1.73 m^2 per year for microalbuminuria and −2.7±0.4 ml/min per 1.73 m^2 per year for macroalbuminuria, respectively. After adjustment for established risk factors and confounders, albuminuria remained the strongest predictor of annual eGFR decline. Other independent predictors of eGFR decline were hypertension, older age, insulin treatment, and lower baseline eGFR.

Previous studies show that albuminuria, even within the normal range, predicts adverse renal outcomes in both individuals without diabetes and patients with type 2 diabetes (22–24). A small prospective study reported that microalbuminuric, but not normoalbuminuric, participants with type diabetes (*n*=65, follow-up 10 years) showed a faster annual decline in GFR (as measured by the ^{51}Cr-EDTA technique) compared with participants without diabetes (25). Nelson *et al.* (26) reported significant annual GFR changes (as measured by urinary clearance of iothalamate) in proteinuric, but not in microalbuminuric, Pima Indians with diabetes (*n*=194; 4-year follow-up). Velussi *et al.* (27) reported a GFR decline of −2.2 ml/min per year (as measured by the ^{51}Cr-EDTA technique) in 18

microalbuminuric patients with type 2 diabetes and hypertension, who were treated for 3 years with either cilazapril or amlodipine. Parving (28) reviewed the published studies of proteinuric patients with type 2 diabetes during any antihypertensive treatment, and reported a GFR decline of −4.8 ml/min per year. In a study involving 729 Japanese patients with type 2 diabetes and preserved kidney function and normoalbuminuria, Yokoyama *et al.* (16) found that the degree of chronic hyperglycemia plays a crucial role in accelerating the annual eGFR decline during a 3-year follow-up period. In a study of 227 Caucasian patients with type 2 diabetes who were followed early after the onset of diabetic nephropathy, Rossing *et al.* (29) identified several modifiable risk factors (including abnormal albuminuria, hypertension, higher HbA_{1c}, and smoking) that were independently associated with a faster progression of kidney disease (as measured by the ^{51}Cr-EDTA technique). In our study, current smokers also tended to have a faster annual eGFR decline than ex-smokers and those who never smoked; however, this difference did not reach independent statistical significance.

Albuminuria has long been regarded as a marker of the extent of glomerular damage; however, experimental and clinical studies suggest that albuminuria might also contribute to the development and progression of glomerular and tubulointerstitial lesions (8,28,30). Accordingly, in a *post hoc* analysis of the Reduction of End-Points in NIDDM with the Angiotensin II Receptor Antagonist Losartan (RENAAL) study, abnormal albuminuria strongly predicted the development of ESRD in patients with type 2 diabetes and nephropathy (13). Recently, Yokoyama *et al.* (31) confirmed that in 1002 Japanese patients with type 2 diabetes with relatively well preserved kidney function (approximately 70% normoalbuminuric) who were followed for 4 years, urinary albumin excretion was among the most important risk factors for both albuminuria progression and annual eGFR decline.

In this study, we also found that hypertension was closely associated with a faster annual eGFR decline. Studies of albuminuric patients with type 2 diabetes not receiving early antihypertensive treatment demonstrated that annual GFR decline (as measured by the ^{51}Cr-EDTA technique) ranged from 10 to 14 ml/min per year (25). Conversely, early antihypertensive treatment significantly reduced albuminuria and improved the rate of annual GFR decline (approximately 5 ml/min per year) in albuminuric patients with type 2 diabetes (29), as was also confirmed by several other studies (28,32–34) in which GFR was directly measured by isotopic methods. Similarly, the rate of annual eGFR decline that was observed in the ARB groups of both the RENAAL and the Irbesartan Diabetic Nephropathy trials was approximately −5 ml/min per 1.73 m^2 per year (35,36).

Collectively, hypertension has been demonstrated to be a strong risk factor for the development and progression of diabetic nephropathy, and several interventional trials have shown that antihypertensive treatment may reduce the incidence of nephropathy and slow the progression of kidney disease in patients with type 2 diabetes (35–40). Accordingly, several guidelines recommend an early, aggressive treatment of hypertension in patients with type 2 diabetes regardless of whether albuminuria is present (8,28,40–42). Randomized clinical trials of patients with type 2 diabetes with early or advanced nephropathy also suggest a specific renoprotective effect by ACE inhibitors or ARBs compared with other antihypertensive agents not blocking the renin-angiotensin system (13,35–40).

This study provides further strong evidence that albuminuria is the most important risk factor of faster annual eGFR decline in patients with type 2 diabetes and preserved kidney function, and that its screening may help identify individuals at increased renal risk. Thus, albuminuria represents a target for renoprotective therapy independent from BP in patients with type 2 diabetes (43,44).

Some limitations of our study merit comment. First, because our cohort comprises Caucasian individuals with type 2 diabetes who were followed at an outpatient diabetes clinic, our results may not necessarily be generalizable to other diabetic populations. Other important limitations of our study include the following: a possible selection bias of excluding the patients who either had <3 GFR estimates during the follow-up or who had incomplete laboratory data at baseline; an inability to adjust for certain specific antihypertensive agents (*i.e.*, ACE inhibitors and ARBs that are associated with reduced eGFR and lower albuminuria); and the use of an estimated GFR instead of a directly measured GFR to define kidney function (*e.g.*, isotopic GFR measurements). Nonetheless, current GFR estimates facilitate the detection, evaluation, and management of CKD, and many organizations recommend the use of prediction equations for the evaluation of kidney function in large epidemiologic studies and in clinical practice (8,39–41).

Strengths of our observational study include its prospective design, the large number of participants from both sexes, the long duration of follow-up, the complete nature of the dataset, the sequential determinations of serum creatinine during the follow-up within the same laboratory (all patients had ≥5 measurements of serum creatinine), the measurements of albuminuria on 24-hour urine samples, and the ability to adjust for multiple important risk factors.

In conclusion, our study demonstrates that in a large cohort of patients with type 2 diabetes and preserved kidney function who were followed for 10 years, the annual eGFR decline is predicted by multiple modifiable risk factors. The most important risk factors seem to be the presence of abnormal albuminuria and hypertension.

Disclosures

None.

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