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CLINICAL TRIAL

Prevalence of albuminuria and renal dysfunction, and related clinical factors in Japanese patients with diabetes: The Japan Diabetes Complication and its Prevention prospective study 5

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ABSTRACT

Aims/Introduction: To clarify the prevalence of albuminuria and renal dysfunction, and related factors in Japanese patients with diabetes, we analyzed the baseline data of the Japan Diabetes Complication and its Prevention prospective study.

Materials and Methods: We used the data of 355 patients with type 1 diabetes and 5,194 patients with type 2 diabetes to evaluate the prevalence of albuminuria and renal dysfunction, and related factors. A binomial logistic regression analysis was used to investigate independent contributing factors for estimated glomerular filtration rate <60 mL/min/1.73 m^2 or albuminuria.

Results: The prevalence of microalbuminuria and macroalbuminuria was 15.2% (54/355) and 3.1% (11/355) in type 1 diabetes patients, and 25.0% (1,298/5,194) and 5.1% (265/5,194) in type 2 diabetes patients, respectively. The proportion of renal dysfunction (estimated glomerular filtration rate <60 mL/min/1.73 m^2) was 9.9% (35/355) in type 1 diabetes patients, and 15.3% (797/5,194) in type 2 diabetes patients. The proportion of patients with renal dysfunction with normoalbuminuria was 7.3% (26/355) for type 1 diabetes patients, and 9.0% (467/5,194) for type 2 diabetes patients. The factors related to albuminuria in type 2 diabetes patients were glycated hemoglobin, hypertension, age, duration of diabetes, body mass index and estimated glomerular filtration rate. In contrast, factors to related renal dysfunction were age, duration of diabetes, dyslipidemia, hypertension, body mass index, male sex and albuminuria.

Conclusions: We showed the recent prevalence of albuminuria and renal dysfunction, and related factors in Japanese type 1 and type 2 diabetes patients using the baseline data of the Japan Diabetes Complication and its Prevention prospective study. The current results suggest that renal disease in patients with type 2 diabetes is heterogeneous, and different mechanisms might be involved in albuminuria and deterioration of renal function.

INTRODUCTION

Diabetic kidney disease is a major cause of end-stage renal failure in many countries[1,2], and approximately 16,000 patients with diabetic kidney disease undergo dialysis in Japan each year[3]. Microalbuminuria is an important clinical indicator to diagnose the early stage of diabetic nephropathy. Furthermore, albuminuria is well known to be a risk for cardiovascular diseases. Estimated glomerular filtration rate (eGFR) is widely used

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to estimate the renal function of diabetes patients. A variety of data have been reported on the incident rate of albuminuria and renal dysfunction in diabetes patients. The difference of the data might be caused by ethnicity, study protocol, sample size and method for measurement of albuminuria. It is well known that low eGFR is found in some normoalbuminuric diabetes patients, suggesting that different factors might contribute to albuminuria or deterioration of renal function.

The aim of the present study was to analyze the recent prevalence of albuminuria and renal dysfunction, and risk factors in Japanese patients with type 1 and type 2 diabetes using baseline data of the Japan Diabetes Complication and its Prevention prospective (JDCP) study, which is a large-scale, prospective observational study of Japanese diabetes patients[4–7] carried out by the Japan Diabetes Society.

METHODS

Participants

We used the baseline data of the JDCP study. The details of the JDCP study were previously described[4–7]. In brief, the JDCP study is a multicenter prospective observational cohort study with a 5-year follow-up period. Participants in the JDCP study are men and women aged 40–75 years with type 1 and type 2 diabetes who are treated as outpatients at participating institutions. The JDCP study is designed to assess the prevalence of diabetic complications, the status of treatment and management of diabetes, and the risk factors related to the onset and/or progression of diabetic complications, and thus obtaining results from the JDCP study are expected to provide important therapeutic insights into the management of type 1 and type 2 diabetes, particularly for the prevention and treatment of diabetic complications. A total of 7,700 participants were enrolled between June 2007 and November 2009 from university hospitals, secondary or tertiary hospitals, and clinics where diabetologists reside (total 464 clinics).

The inclusion criteria were as follows: (i) patients with type 1 and type 2 diabetes; and (ii) patients aged ≥40 to <75 years. The exclusion criteria were: (i) cannot attend the hospital or clinic regularly; (ii) have proliferative diabetic retinopathy, (iii) undergoing dialysis; (iv) diagnosed with a malignant disease 5 years before registration; and (v) judged to be ineligible for this study by an attending physician.

The 6,338 patients with type 1 or type 2 diabetes who met the study eligibility criteria were registered between July 2007 and September 2011. In the current study, we used the baseline data of 355 patients with type 1 diabetes and 5,194 patients with type 2 diabetes. The JDCP study was approved by the Japan Diabetes Society Ethics Review Committee for Scientific Surveys and Studies, and by the ethics committee and institutional review board of each site.

Data collection

Data were collected as previously described[4–6]. The urinary albumin-to-creatinine ratio (UACR) was measured twice yearly in spot urine samples, and mean values were categorized as follows: normoalbuminuria (UACR <30 mg/gCr), microalbuminuria (UACR ≥30 mg/gCr and <300 mg/gCr) or macroalbuminuria (UACR ≥300 mg/gCr). The eGFR was calculated using the modified Modification of Diet in Renal Disease formula[8].

Statistical analysis

Continuous variables were expressed as the mean ± standard deviation, and categorical variables were shown as the number or percentages. The variable urinary albumin excretion rate was converted into a natural logarithm. The Shapiro–Wilk test was used for Gaussian distribution of continuous variables. A comparison between the two groups was analyzed by a Student's *t*-test for continuous variables, and a χ^2-test was used for frequency. A binomial logistic regression analysis was used to investigate independent contributing factors for eGFR <60 mL/min/1.73 m^2 or albuminuria. We used the IBM SPSS Statistics 22 software program (IBM, Armonk, NY, USA) and the StatFlex version 6.0 software program (Artech Co., Osaka, Japan) for statistical analyses.

RESULTS

Data of albuminuria and eGFR of patients with type 1 and type 2 diabetes are shown in Table 1. The prevalence of microalbuminuria (30–299 mg/gCr) and macroalbuminuria (≥300 mg/gCr) was 15.2% (54/355) and 3.1% (11/355) in type 1 diabetes patients, and 25.0% (1,298/5,194) and 5.1% (265/5,194) in type 2 diabetes patients. The proportion of renal dysfunction (eGFR <60 mL/min/1.73 m^2) was 9.9% (35/355) in type 1 diabetes patients, and 15.3% (797/5,194) in type 2 diabetes patients. The proportion of patients with renal dysfunction (eGFR <60 mL/min/1.73 m^2) without albuminuria (normoalbuminuria) was 7.3% (26/355) in type 1 diabetes patients, and 9.0% (467/5,194) in type 2 diabetes patients.

Clinical data of the patients with type 1 and type 2 diabetes are shown in Tables 2 and 3. Duration of diabetes, past history or presence of hypertension, systolic blood pressure and the rate of prescription of angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) were higher in type 1 diabetes patients with micro- or macroalbuminuria as compared with normoalbuminuria (Table 2). The parameters that were increased in type 2 diabetes patients with micro- or macroalbuminuria were age, proportion of insulin therapy, duration of diabetes, past history or presence of hypertension and dyslipidemia, bodyweight, body mass index (BMI), waist circumference, glycated hemoglobin (HbA1c), blood glucose level, fasting immunoreactive insulin level, blood pressure, the level of total cholesterol, non-high-density lipoprotein cholesterol and triglycerides, serum creatinine level, and the rate of prescription of ACE inhibitors or ARBs. High-density lipoprotein cholesterol and eGFR were lower in type 2 diabetes patients with albuminuria (Table 3).

Table 1 | Number of type 1 and type 2 diabetes patients classified by estimated glomerular filtration rate and albuminuria

CKD stage	Total, *n* = 355 (100%)	Normoalbuminuria, *n* = 290 (81.7%)	Microalbuminuria, *n* = 54 (15.2%)	Macroalbuminuria, *n* = 11 (3.1%)
Type 1 diabetes				
Stage 1 (eGFR ≥90)	104 (29.3%)	82 (23.1%)	21 (5.9%)	1 (0.3%)
Stage 2 (60 ≤ eGFR < 90)	216 (60.8%)	182 (51.3%)	27 (7.6%)	7 (2.0%)
Stage 3 (30 ≤ eGFR < 60)	34 (9.6%)	26 (7.3%)	6 (1.7%)	2 (0.6%)
Stage 4 (15 ≤ eGFR < 30)	1 (0.3%)	0 (0.0%)	0 (0.0%)	1 (0.3%)
Stage 5 (eGFR <15)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CKD stage	Total, *n* = 5,194 (100%)	Normoalbuminuria, *n* = 3,631 (69.9%)	Microalbuminuria, *n* = 1,298 (25.0%)	Macroalbuminuria, *n* = 265 (5.1%)
Type 2 diabetes				
Stage 1 (eGFR ≥90)	1,159 (22.3%)	788 (15.2%)	327 (6.3%)	44 (0.8%)
Stage 2 (60 ≤ eGFR < 90)	3,238 (62.3%)	2,376 (45.7%)	759 (14.6%)	103 (2.0%)
Stage 3 (30 ≤ eGFR < 60)	763 (14.7%)	460 (8.9%)	209 (4.0%)	94 (1.8%)
Stage 4 (15 ≤ eGFR < 30)	27 (0.5%)	6 (0.1%)	3 (0.1%)	18 (0.3%)
Stage 5 (eGFR <15)	7 (0.1%)	1 (0.0%)	0 (0.0%)	6 (0.1%)

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

In contrast, the parameters that were increased in type 2 diabetes patients with renal dysfunction (eGFR <60 mL/min/1.73 m^2) were age, proportion of insulin therapy, duration of diabetes, past history or presence of hypertension and dyslipidemia, bodyweight, BMI, waist circumference, fasting immunoreactive insulin level, triglycerides level, urinary albumin-to-creatinine ratio, and the rate of prescription of ACE inhibitors or ARBs (Table 4). The proportion of regular alcohol intake, HbA1c and blood glucose level, the level of total cholesterol, and high-density lipoprotein cholesterol were lower in type 2 diabetes patients with renal dysfunction. Age was higher in type 1 diabetes patients with renal dysfunction (Table S1).

Factors related to albuminuria and renal dysfunction in patients with type 1 and type 2 diabetes by logistic regression model are shown in Tables 5 and S2. The duration of diabetes (95% confidence interval (CI) 1.010–1.071, $P = 0.009$) and past history or presence of hypertension (95% CI 1.324–4.846, $P = 0.005$) were positively related to micro- and macroalbuminuria, and age (95% CI 1.062–1.182, $P < 0.001$), and duration of diabetes (95% CI 1.006–1.088, $P = 0.023$) was positively related to low eGFR in patients with type 1 diabetes (Table S2). Factors positively related to albuminuria in type 2 diabetes were age (95% CI 1.002–1.020, $P = 0.017$), duration of diabetes (95% CI 1.011–1.027, $P < 0.001$), past history or presence of hypertension (95% CI 1.455–1.892, $P < 0.001$), BMI (95% CI 1.033–1.069, $P < 0.001$), HbA1c (95% CI 1.175–1.295, $P < 0.001$) and eGFR (95% CI 1.301–1.819, $P < 0.001$). In contrast, positively related factors to renal dysfunction were male sex (95% CI 1.260–1.828, $P < 0.001$), age (95% CI 1.062–1.089, $P < 0.001$), duration of diabetes (95% CI 1.006–1.026, $P = 0.002$), past history or presence of dyslipidemia (95% CI 1.075–1.495, $P = 0.005$) and hypertension (95% CI 1.340–1.884, $P < 0.001$), BMI (95% CI 1.029–1.074, $P < 0.001$), and albuminuria (95% CI 1.313–1.839, $P < 0.001$). HbA1c (95% CI 0.825–0.963, $P = 0.003$) and regular alcohol intake (95% CI 0.526–0.767, $P < 0.001$) were negatively related to renal dysfunction (Table 5).

The factors related to renal dysfunction in normoalbuminuric patients with type 1 and type 2 diabetes by logistic regression model are shown in Tables S3 and S4. Only age (95% CI 1.069–1.218, $P < 0.001$) was positively related to low eGFR in normoalbuminuric patients with type 1 diabetes (Table S3). Factors positively related to renal dysfunction in normoalbuminuric patients with type 2 diabetes were male sex (95% CI 1.046–1.672, $P = 0.020$), age (95% CI 1.067–1.101, $P < 0.001$), past history or presence of hypertension (95% CI 1.152–1.765, $P = 0.001$) and BMI (95% CI 1.036–1.095, $P < 0.001$). Regular alcohol intake (95% CI 0.514–0.835, $P = 0.001$) was negatively related to low eGFR (Table S4).

We further assessed if the incidence rate of low eGFR with normoalbuminuria is related to increased prescription of ACE inhibitor or ARB. As shown in Table S5, age (95% CI 1.058–1.197, $P < 0.001$) was positively related to renal dysfunction in normoalbuminuric patients with type 1 diabetes; however, there was no significant relationship between the use of ACE inhibitor or ARB and renal dysfunction. Factors positively related to renal dysfunction in normoalbuminuric patients with type 2 diabetes were male sex (95% CI 1.021–1.629, $P = 0.033$), age (95% CI 1.070–1.104, $P < 0.001$) and BMI (95% CI 1.042–1.101, $P < 0.001$), but not the use of ACE inhibitor or ARB. Regular alcohol intake (95% CI 0.525–0.851, $P = 0.001$) was negatively related to low eGFR (Table S6).

DISCUSSION

We analyzed the incidence rate of albuminuria and renal dysfunction, and related factors in patients with diabetes using

Table 2 | Albuminuria and clinical data in patients with type 1 diabetes

Characteristics	*n*	Normoalbuminuria (*n* = 290)	Micro- or macroalbuminuria (*n* = 65)	*P*-value
Age (years)	355	56 ± 9	58 ± 8	0.117
Male (%)	355	43.4	46.2	0.691
Duration of diabetes (years)	353	11 ± 8	15 ± 11	0.009
Past history or presence of				
Hypertension (%)	355	19.3	41.5	<0.001
Dyslipidemia (%)	355	25.2	29.2	0.500
None (%)	355	48.3	35.4	0.059
Regular alcohol intake (%)	354	25.6	26.2	0.927
Smoker, past/current (%)	354	37.0	36.9	0.988
Bodyweight (kg)	355	57.0 ± 9.6	55.8 ± 10.8	0.483
BMI (kg/m^2)	354	22.1 ± 2.9	21.9 ± 3.1	0.581
Waist circumference (cm)	329	78.2 ± 9.2	77.5 ± 9.2	0.547
HbA1c (%)	353	7.7 ± 1.4	8.0 ± 1.6	0.215
FPG (mg/dL)	88	134.7 ± 62.2	129.6 ± 59.6	0.724
PPPG (mg/dL)	310	173.9 ± 88.3	162.4 ± 82.6	0.332
Systolic blood pressure (mmHg)	352	124 ± 15	131 ± 18	0.002
Diastolic blood pressure (mmHg)	352	72 ± 10	74 ± 11	0.106
Lipid profiles (mg/dL)				
Total cholesterol	331	198.1 ± 27.4	201.0 ± 38.2	0.707
LDL cholesterol	333	108.1 ± 22.8	106.8 ± 30.3	0.503
HDL cholesterol	350	72.3 ± 16.9	74.2 ± 22.5	0.819
Non-HDL cholesterol	326	125.5 ± 23.8	127.2 ± 33.2	0.869
Triglycerides	157	83.1 ± 46.0	86.6 ± 49.6	0.860
Serum creatinine (mg/dL)	355	0.7 ± 0.1	0.7 ± 0.2	0.674
eGFR (mL/min/1.73 m^2)	355	81.1 ± 16.5	81.1 ± 19.9	0.666
ACEIs or ARBs (%)	355	17.6	40.0	<0.001

Data are the mean ± standard deviation, or percentages. ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin-receptor blockers; BMI, body mass index; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PPPG, postprandial plasma glucose.

baseline data of the JDCP study. The incidence rate of microalbuminuria in type 2 diabetes patients was 25.0%, and that of macroalbuminuria was 5.1%. Previously, Mogensen reported that approximately 30% of patients with diabetes progress to microalbuminuria at 15 years from the onset[9]. The incidence of microalbuminuria was approximately 2% per year, and the prevalence was 25% at 10 years and 38% at 15 years after diagnosis of type 2 diabetes in the United Kingdom Prospective Disease Study[10]. Parving *et al.*[11] reported that the incidence rate of normoalbuminuria, microalbuminuria and macroalbuminuria was 51%, 39% and 10%, respectively, in the cohort of type 2 diabetes patients in 33 countries worldwide. The prevalence in Asian diabetes patients was reported to be 40% in the MicroAlbuminuria Prevalence study[12]. The incidence rate of microalbuminuria in the current study is much lower as compared with these previous studies, suggesting that the prognosis of type 2 diabetes has recently been improving[13]. As for Japanese diabetes patients, the Japan Diabetes Clinical Data Management (JDDM) study reported that the incidence rate of microalbuminuria was 32% in 8,897 Japanese patients with type 2 diabetes[14]. The patients were registered from 2004 to 2005, the average age and duration of diabetes were 63 and 12 years, respectively, in the JDDM study. In contrast, the patients were registered from 2007 to 2011, and the average age and duration were 61 and 11 years, respectively, in the JDCP study. The average HbA1c was higher in the JDCP study (7.4%) as compared with the JDDM study (7.1%). The difference between these two studies suggests that the rate of development of nephropathy has been decreasing in Japanese patients with type 2 diabetes; however, it might be caused by the difference of age or disease duration.

The proportion of renal dysfunction (eGFR <60 mL/min/1.73 mm^2) was 15.3% in type 2 diabetes patients in the present study. The United Kingdom Prospective Disease Study reported that deterioration of GFR (eGFR <60 mL/min/1.73 mm^2) occurred in 29% of the participants after 15 years from the diagnosis[10]. In the JDDM study, the prevalence of low eGFR (<60 mL/min/1.73 mm^2) was 11% (in JDDM10)[14] and 15.3% (in JDDM15)[15], which is similar to the present result. The proportion of patients with low eGFR (eGFR <60 mL/min/1.73 m^2) with normoalbuminuria was 9.0% in total patients, and 12.9% in type 2 diabetes patients with normoalbuminuria.

Table 3 | Albuminuria and clinical data in patients with type 2 diabetes

	n	All (*n* = 5,194)	Normoalbuminuria (*n* = 3,631)	Micro- or macroalbuminuria (*n* = 1,563)	*P*-value
Age (years)	5,194	61 ± 8	61 ± 8	62 ± 8	<0.001
Male (%)	5,194	59.1	59.0	59.4	0.798
Diet/tablet/insulin (%)	5,187	10/62/27	12/64/25	7/60/33	<0.001
Duration of diabetes (years)	5,122	11 ± 8	10 ± 8	12 ± 9	<0.001
Past history or presence of					
Hypertension (%)	5,194	46.9	42.4	57.5	<0.001
Dyslipidemia (%)	5,194	48.5	47.3	51.4	0.006
None (%)	5,194	23.0	24.8	18.7	<0.001
Regular alcohol intake (%)	5,180	38.4	38.4	38.2	0.839
Smoker, past or current (%)	5,177	38.1	38.2	37.9	0.818
Bodyweight (kg)	5,134	63.8 ± 12.1	63.2 ± 11.9	65.2 ± 12.4	<0.001
BMI (kg/m^2)	5,131	24.5 ± 3.9	24.2 ± 3.8	25.2 ± 4.0	<0.001
Waist circumference (cm)	4,941	86.3 ± 10.4	85.6 ± 10.2	88.1 ± 10.5	<0.001
HbA1c (%)	5,185	7.4 ± 1.3	7.3 ± 1.2	7.6 ± 1.4	<0.001
FPG (mg/dL)	2,096	135.3 ± 37.5	133.6 ± 35.2	139.3 ± 42.3	0.017
PPPG (mg/dL)	4,304	160.7 ± 58.6	156.4 ± 55.7	170.5 ± 63.6	<0.001
Fasting IRI (μU/mL)	1,061	7.9 ± 14.2	7.6 ± 12.4	8.8 ± 17.8	<0.001
Systolic blood pressure (mmHg)	5,156	130 ± 15	128 ± 15	134 ± 15	<0.001
Diastolic blood pressure (mmHg)	5,156	75 ± 10	74 ± 10	76 ± 11	<0.001
Lipid profiles (mg/dL)					
Total cholesterol	4,993	194.7 ± 33.1	193.9 ± 31.9	196.8 ± 35.8	0.047
LDL cholesterol	5,036	112.7 ± 28.1	112.2 ± 27.2	113.9 ± 30.0	0.164
HDL cholesterol	5,142	57.4 ± 15.8	58.0 ± 15.9	56.0 ± 15.3	<0.001
Non-HDL cholesterol	4,946	137.5 ± 33.1	136.0 ± 31.9	140.9 ± 35.6	<0.001
Triglycerides	2,507	125.9 ± 83.6	120.5 ± 76.0	137.8 ± 97.4	<0.001
Serum creatinine (mg/dL)	5,194	0.8 ± 0.3	0.7 ± 0.2	0.8 ± 0.4	<0.001
eGFR (mL/min/1.73 m^2)	5,194	77.3 ± 18.7	78.0 ± 17.1	75.7 ± 22.0	<0.001
ACEIs or ARBs (%)	5,188	39.2	34.4	50.4	<0.001

Data are the mean ± standard deviation, or percentages. ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin-receptor blockers; BMI, body mass index; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; IRI, immunoreactive insulin; LDL, low-density lipoprotein; PPPG, postprandial plasma glucose.

These values are also similar to the results from the JDDM study (7.9% and 11.4%, respectively; JDDM15).

Recently, it has been reported that the incidence rate of low eGFR with normoalbuminuria has been increasing. The rate of progression to end-stage renal disease is lower in diabetes patients with low eGFR without proteinuria than in patients with proteinuria, although low eGFR is an important risk indicator of cardiovascular diseases[16,17]. Previous papers reported that 30–50% of patients with type 2 diabetes associated with low GFR were non-proteinuric[10,18]. The differences of race and ethnicity were reported in the incidence rate of renal disease in diabetes patients[19,20]. Recently, Bhalla *et al.*[21] reported that there are significant differences in the incidence rate of proteinuric diabetic renal injury among different ethnic groups using electronic health data in northern California in the USA.

The common related factors to albuminuria and renal dysfunction in patients with type 2 diabetes were age, duration of diabetes, past history or presence of hypertension and BMI. HbA1c was positively related to albuminuria and negatively related to low eGFR. Fasting and postprandial blood glucose levels were higher in albuminuric patients and lower in patients with low eGFR. The current results suggest that hyperglycemia affects glomerular and/or tubular functions through various mechanisms, including hemodynamic change resulting in albuminuria. In contrast, renal dysfunction might lower the blood glucose level through a change of insulin turn over and a decrease in gluconeogenesis in the kidney. Male sex and dyslipidemia were related to low eGFR, but not to albuminuria, suggesting that the factors associated with atherosclerosis contribute to renal dysfunction in addition to the common risk factors. Interestingly, regular alcohol intake was negatively related to renal dysfunction, although the reason remains unclear. The United Kingdom Prospective Disease Study reported that female sex, older age and insulin resistance were risk factors for low GFR, but not for albuminuria, whereas male sex, hyperglycemia, hyperlipidemia and obesity were risk factors for microalbuminuria, but not for low GFR[10]. Some these data are different from the results of the JDCP and the JDDM,

Table 4 | Estimated glomerular filtration rate and clinical data in patients with type 2 diabetes

	n	eGFR ≥60 mL/min/1.73 m^2 (*n* = 4,397)	eGFR <60 mL/min/1.73 m^2 (*n* = 797)	*P*-value
Age (years)	5,194	61 ± 8	65 ± 7	<0.001
Male (%)	5,194	58.9	60.2	0.485
Diet/tablet/insulin (%)	5,187	11/63/26	8/61/31	0.005
Duration of diabetes (years)	5,122	10 ± 8	12 ± 9	<0.001
Past history or presence of				
Hypertension (%)	5,194	44.1	62.5	<0.001
Dyslipidemia (%)	5,194	47.3	55.6	<0.001
None (%)	5,194	24.8	13.0	<0.001
Regular alcohol intake (%)	5,180	39.4	32.7	<0.001
Smoker, past or current (%)	5,177	38.0	38.8	0.691
Bodyweight (kg)	5,134	63.7 ± 12.1	64.7 ± 11.9	0.020
BMI (kg/m^2)	5,131	24.4 ± 3.9	25.0 ± 3.9	<0.001
Waist circumference (cm)	4,941	86.0 ± 10.3	88.1 ± 10.4	<0.001
HbA1c (%)	5,185	7.4 ± 1.3	7.3 ± 1.2	<0.001
FPG (mg/dL)	2,096	136.1 ± 37.9	130.5 ± 35.0	0.008
PPPG (mg/dL)	4,304	161.8 ± 59.2	154.9 ± 54.5	0.006
Fasting IRI (μU/mL)	1,061	7.8 ± 14.5	8.8 ± 12.1	0.004
Systolic blood pressure (mmHg)	5,156	130 ± 15	131 ± 16	0.154
Diastolic blood pressure (mmHg)	5,156	75 ± 10	74 ± 10	<0.001
Lipid profiles (mg/dL)				
Total cholesterol	4,993	195.2 ± 32.8	192.0 ± 34.8	0.009
LDL cholesterol	5,036	113.1 ± 28.0	110.6 ± 28.2	0.052
HDL cholesterol	5,142	57.9 ± 15.7	54.4 ± 15.9	<0.001
Non-HDL cholesterol	4,946	137.5 ± 32.7	137.2 ± 35.3	0.656
Triglycerides (mg/dL)	2,507	124.2 ± 85.7	135.3 ± 70.3	<0.001
UACR (mg/gCr)	4,968	45.2 ± 202.8	103.9 ± 463.8	<0.001
Log UACR		1.21 ± 0.55	1.35 ± 0.66	
ACEIs or ARBs (%)	5,188	58.9	60.2	<0.001

Data are the mean ± standard deviation, or percentages. ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin-receptor blockers; BMI, body mass index; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; IRI, immunoreactive insulin; LDL, low-density lipoprotein; PPPG, postprandial plasma glucose; UACR, urinary albumin-to-creatinine ratio.

Table 5 | Factors related to micro- and macroalbuminuria and low estimated glomerular filtration rate in patients with type 2 diabetes

Variable	Micro/microalbuminuria†			eGFR <60 mL/min/1.73 m^2‡		
	Wald χ^2	Odds ratio (95% CI)	*P*-value	Wald χ^2	Odds ratio (95% CI)	*P*-value
Sex (men)	3.117	1.138 (0.986–1.315)	0.077	19.268	1.517 (1.260–1.828)	<0.001
Age (years)	5.734	1.011 (1.002–1.020)	0.017	128.112	1.075 (1.062–1.089)	<0.001
Duration of diabetes (years)	22.315	1.019 (1.011–1.027)	<0.001	9.856	1.016 (1.006–1.026)	0.002
Past history or presence of dyslipidemia	0.377	1.041 (0.916–1.182)	0.539	7.978	1.268 (1.075–1.495)	0.005
Past history or presence of hypertension	57.371	1.659 (1.455–1.892)	<0.001	28.346	1.589 (1.340–1.884)	<0.001
Regular alcohol intake (%)	0.086	1.022 (0.886–1.179)	0.769	22.171	0.635 (0.526–0.767)	<0.001
Smoker, past or current (%)	0.284	0.966 (0.850–1.098)	0.594	0.007	1.007 (0.854–1.187)	0.935
BMI (kg/m^2)	33.314	1.051 (1.033–1.069)	<0.001	20.146	1.051 (1.029–1.074)	<0.001
HbA1c (%)	71.584	1.234 (1.175–1.295)	<0.001	8.605	0.891 (0.825–0.963)	0.003
eGFR <60 mL/min/1.73 m^2	25.440	1.539 (1.301–1.819)	<0.001	ND	ND	ND
Micro- or macroalbuminuria	ND	ND	ND	26.324	1.554 (1.313–1.839)	<0.001

†Versus normoalbuminuria. ‡Versus estimated glomerular filtration rate (eGFR) ≥60 mL/min/1.73 m^2. BMI, body mass index; HbA1c, glycated hemoglobin; ND, not done.

although the reason is unknown. In the present study, we could not determine the causal relationship between each clinical parameter and renal disease in diabetes patients, because the current results were obtained from the cross-sectional data of the baseline in the JDCP study. The follow-up data from the JDCP study will clarify the contributing clinical factors to albuminuria and renal dysfunction.

Factors positively related to renal dysfunction in normoalbuminuric patients with type 2 diabetes were male sex, hypertension and BMI, although use of ACE inhibitor or ARB was not related to low eGFR without albuminuria. These findings suggest that hypertension and obesity might contribute to renal dysfunction in normoalbuminuric patients with type 2 diabetes.

In patients with type 1 diabetes, the prevalence of microalbuminuria and renal dysfunction were 15.2% and 9.9%, respectively. It was reported that incidence rate of microalbuminuria in patients with type 1 diabetes was 27.2% and 25.4% in the two studies carried out in Europe[22–24]. Common risk factors for microalbuminuria and macroalbuminuria were disease duration, HbA1c and dyslipidemia. Blood pressure was a risk factor for microalbuminuria, and male sex was positively related to macroalbuminuria. The prevalence of microalbuminuria in the present study was much lower as compared with the previous studies. It might be possible that the disease duration of the present participants was much shorter than in the other previous studies, although recent epidemiological studies have shown that the prevalence of nephropathy and end-stage renal disease are decreasing[20]. The current results suggest that disease duration, hypertension and hyperglycemia contribute to the development of nephropathy in patients with type 1 diabetes. We could not determine whether there is any difference in the associated factors of nephropathy between type 1 and type 2 diabetes, because the present study is cross-sectional and the sample size of patients with type 1 diabetes is relatively small.

In the present study, we showed the recent prevalence of albuminuria and renal dysfunction, and related factors in Japanese patients with diabetes using the baseline data of the JDCP study. The current results suggest that renal disease in patients with type 2 diabetes is heterogeneous, and there might be different factors contributing to albuminuria and the deterioration of renal function. The prospective follow-up data of the JDCP study will clarify the causal relationships between the clinical factors and progression or regression of diabetic kidney disease.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1 | Estimated glomerular filtration rate and clinical data in patients with type 1 diabetes.
Table S2 | Factors related to micro- and macroalbuminuria and low estimated glomerular filtration rate in patients with type 1 diabetes.
Table S3 | Factors related to low estimated glomerular filtration rate in normoalbuminuric patients with type 1 diabetes.
Table S4 | Factors related to low estimated glomerular filtration rate in normoalbuminuric patients with type 2 diabetes.
Table S5 | Binomial logistic regression including the use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers as variables in normoalbuminuric patients with type 1 diabetes.
Table S6 | Binomial logistic regression including the use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers as variables in normoalbuminuric patients with type 2 diabetes.