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

Kenichi Shikata1,2, Ryo Kodera1,3, Kazunori Utsunomiya1,4, Daisuke Koya1,5, Rimei Nishimura1,6, Satoshi Miyamoto1,2, Naoko Tajima1,4 for the JDCP study group

1The Japan Diabetes Society, Tokyo, 2Center for Innovative Clinical Medicine, Okayama University Hospital, 3Osafune Clinic, Okayama, 4Jikei University School of Medicine, Tokyo, 5Department of Diabetology & Endocrinology, Kanazawa Medical University, Ishikawa, and 6Division of Diabetes, Metabolism & Endocrinology, Department of Internal Medicine, Jikei University School of Medicine, Tokyo, Japan

Keywords
Diabetic nephropathy, Diabetic kidney disease, Japan Diabetes Complication and its Prevention study

Correspondence
Kenichi Shikata
Tel.: +81-86-235-6508
Fax: +81-86-235-6510
E-mail address: shikata@md.okayama-u.ac.jp

J Diabetes Investig 2020; 11: 325–332
doi: 10.1111/jdi.13116

Clinical Trial Registry
University Hospital Medical Information Network Center (UMIN)
UMIN000016519

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 m² 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 m²) 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 related to renal dysfunction were age, duration of diabetes, dyslipidemia, hypertension, body mass index, and 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 countries1,2, and approximately 16,000 patients with diabetic kidney disease undergo dialysis in Japan each year3. 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
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 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. 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. 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.

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–Wilks 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 χ²-test was used for frequency. A binomial logistic regression analysis was used to investigate independent contributing factors for eGFR <60 mL/min/1.73 m² or albuminuria. We used the IBM SPSS Statistics 22 software program (IBM, Armonk, NY, USA) and the Stat-Flex 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 m²) 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 m²) 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, 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).
In contrast, the parameters that were increased in type 2 diabetes patients with renal dysfunction (eGFR <60 mL/min/1.73 m²) 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| 193                       | 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/m²)                      | 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 m²)            | 355| 81.1 ± 16.5               | 81.3 ± 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.

The proportion of renal dysfunction (eGFR <60 mL/min/1.73 m²) 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 m²) occurred in 29% of the participants after 15 years from the diagnosis. In the JDDM study, the prevalence of low eGFR (<60 mL/min/1.73 m²) was 11% (in JDDM10) and 15.3% (in JDDM15), which is similar to the present result. The proportion of patients with low eGFR (eGFR <60 mL/min/1.73 m²) with normoalbuminuria was 9.0% in total patients, and 12.9% in type 2 diabetes patients with normoalbuminuria.
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 diseases16,17. Previous papers reported that 30–50% of patients with type 2 diabetes associated with low GFR were non-proteinuric10,18. The differences of race and ethnicity were reported 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 GFR10. Some of 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

| Variable                                      | n   | eGFR ≥60 mL/min/1.73 m² (n = 4,397) | eGFR <60 mL/min/1.73 m² (n = 797) | P-value |
|-----------------------------------------------|-----|------------------------------------|-----------------------------------|---------|
| Age (years)                                   | 5,194 | 61 ± 8                            | 65 ± 7                            | <0.001  |
| Male (%)                                      | 5,194 | 589                               | 602                               | 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                              | 55.5                              | <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/m²)                                   | 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 | 78.6 ± 14.5                       | 88.8 ± 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)                        | 4,993 | 195.2 ± 32.8                      | 192.0 ± 34.8                      | 0.009   |
| Total cholesterol                             | 5,036 | 113.1 ± 28.0                      | 110.6 ± 28.2                      | 0.052   |
| LDL cholesterol                               | 5,142 | 579.5 ± 15.7                      | 544.4 ± 15.9                      | <0.001  |
| 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 ± 20.8                       | 103.9 ± 463.8                     | <0.001  |
| Log UACR                                       | 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                                      | Wald χ² | Odds ratio (95% CI) | P-value |
|-----------------------------------------------|---------|---------------------|---------|
| Sex (men)                                     | 3.117   | 1.138 (0.986–1.315) | 0.077   |
| Age (years)                                   | 5.734   | 1.011 (1.002–1.020) | 0.017   |
| Duration of diabetes (years)                  | 22.315  | 1.019 (1.011–1.027) | <0.001  |
| Past history or presence of dyslipidemia      | 0.377   | 1.041 (0.916–1.182) | 0.539   |
| Past history or presence of hypertension      | 57.371  | 1.659 (1.455–1.892) | <0.001  |
| Regular alcohol intake (%)                    | 0.086   | 1.022 (0.886–1.179) | 0.769   |
| Smoker, past or current (%)                   | 0.284   | 0.966 (0.850–1.098) | 0.594   |
| BMI (kg/m²)                                   | 33.314  | 1.051 (1.033–1.069) | <0.001  |
| HbA1c (%)                                     | 71.584  | 1.234 (1.175–1.295) | <0.001  |
| eGFR <60 mL/min/1.73 m²                       | 25.440  | 1.539 (1.301–1.819) | <0.001  |
| Micro- or macroalbuminuria                   | ND      | ND                  | ND      |

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.

Note: "Versus normoalbuminuria." Versus estimated glomerular filtration rate (eGFR) ≥60 mL/min/1.73 m². 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. 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. 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.

ACKNOWLEDGMENTS
The JDCP study was supported by a grant-in-aid from the Ministry of Health, Labor and Welfare, Japan Diabetes Society, and the Manpei Suzuki Diabetes Foundation. The JDCP study investigators thank all diabetes patients who participated in this study, and to all physicians and medical staff at the 464 institutions.

DISCLOSURE
KS has received speaker fees from MSD, Eli Lilly Japan, Nippon Boehringer Ingelheim, Novo Nordisk Pharma, Mitsubishi Tanabe and Kyowa Hakko Kirin, and research support from Takeda, MSD, Kyowa Hakko Kirin and Mitsubishi Tanabe. KU has received speaker fees from Eli Lilly Japan, Nippon Boehringer Ingelheim, Mitsubishi Tanabe and research supports from Terumo, Eli Lilly Japan, Nippon Boehringer Ingelheim, Novo Nordisk Pharma, Kyowa Hakko Kirin, Ono, Taisyo Toyama and Dainihon Sumitomo. DK has received speaker fees from Mitsubishi Tanabe, Nippon Boehringer Ingelheim, Daiichi Sankyo, MSD, Astellas, Taisyo Toyama and Kyowa Hakko Kirin, and research support from Mitsubishi Tanabe, Nippon Boehringer Ingelheim, Daiichi Sankyo, MSD, Astellas, Japan Tobacco, Kyowa Hakko Kirin, Kyowa Hakko Kirin, Ono, Takeda, AstraZeneca, Pfizer and Sanofi-Aventis. DD has received donated fund laboratories from Mitsubishi Tanabe, Nippon Boehringer Ingelheim, Ono, Taisho Toyama and Kyowa Hakko Kirin. SM has received research support from Tanabe Mitsubishi. RN has received speaker fees from Astellas, Takeda, Eli Lilly Japan, Nippon Boehringer Ingelheim, Novartis Pharma and Novo Nordisk Pharma. TN has received speaker fees from Astellas, Abbott Japan, MSD, Takeda, Eli Lilly Japan, Nippon Boehringer Ingelheim and Novo Nordisk Pharma. RK declares no conflict of interest.

REFERENCES
1. Umanath K, Lewis JB. Update on diabetic nephropathy: core curriculum 2018. Am J Kidney Dis 2018; 71: 884–895.
2. Anders HJ, Huber TB, Isermann B, et al. CKD in diabetes: diabetic kidney disease versus nondiabetic kidney disease. Nat Rev Nephrol 2018; 14: 361–377.
3. Masakane I, Taniguchi M, Nakai S, et al. An overview of regular dialysis treatment in Japan (As of 31 December 2016) [in Japanese]. Available from: http://docs.jsdt.or.jp/overview/index.html Accessed March 15, 2019.
4. Tajima N, Nishimura R, Izumi K, et al. A large-scale, observational study to investigate the current status of diabetes complications and their prevention in Japan: research outline and baseline data for type 2 diabetes-JDCP study1. J Jpn Diab Soc 2015; 58: 346–357.
5. Nishimura R, Izumi K, Hayashino Y, et al. A large-scale observational study to investigate the current status of diabetes complications and their prevention in Japan: research outline and baseline data for type 1 diabetes—JDCP study 2. Diabetol Int 2016; 7: 4–11.
6. Hayashino Y, Izumi K, Okamura S, et al. Duration of diabetes and types of diabetes therapy in Japanese patients with type 2 diabetes: The Japan Diabetes Complication and its Prevention prospective study 3 (JDCP study 3). J Diabetes Invest 2017; 8: 243–249.
7. Kawasaki R, Kitano S, Sato Y, et al. Factors associated with non-proliferative diabetic retinopathy in patients with type 1 and type 2 diabetes: the Japan Diabetes Complication and its Prevention prospective study (JDCP study 4). Diabetol Int 2018; 26: 3–11.
8. Matsuo S, Imai E, Horio M, et al. Revised equations for estimated GFR from serum creatinine in Japan. Am J Kidney Dis 2009; 53: 982–992.
9. Mogensen CE. Microalbuminuria predicts clinical proteinuria and early mortality in maturity-onset diabetes. N Engl J Med 1984; 310: 356–360.
10. Retnakaran R, Cull CA, Thorne KL, et al. Risk factors for renal dysfunction in type 2 diabetes: a prospective diabetes study 74. Diabetes 2006; 55: 1832–1839.
11. Parving HH, Lewis JB, Ravid M, et al. Prevalence and risk factors for microalbuminuria in a referred cohort of type II diabetic patients: a global perspective. Kidney Int 2006; 69: 2057–2063.
12. Wu AY, Kong NC, de Leon FA, et al. An alarmingly high prevalence of diabetic nephropathy in Asian type 2 diabetic patients: the MicroAlbuminuria Prevalence (MAP) Study. Diabetologia 2005; 48: 17–26.
13. Gheith O, Farouk N, Nampoory N, et al. Diabetic kidney disease: world wide difference of prevalence and risk factors. J Nephropharmacol 2016; 5: 49–56.
14. Yokoyama H, Kawai K, Kobayashi M, et al. Microalbuminuria is common in Japanese. Type 2 diabetic patients. A nationwide survey from the Japan Diabetes Clinical Data Management Study Group (JDDM 10). Diabetes Care 2007; 30: 989–992.
15. Yokoyama H, Sone H, Oishi M, et al. Prevalence of albuminuria and renal insufficiency and associated clinical factors in type 2 diabetes: the Japan Diabetes Clinical Data. Management study (JDDM15). Nephrol Dial Transplant 2009; 24: 1212–1216.
16. Go AS, Chertow GM, Fan D, et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med 2004; 351: 1296–1305.
17. Macisaac RJ, Jerums G. Diabetic kidney disease with and without albuminuria. Curr Opin Nephrol Hypertens 2011; 20: 246–257.
18. Thomas MC, Macisaac RJ, Jerums G, et al. Nonalbuminuric renal impairment in type 2 diabetic patients and in the general population (national evaluation of the frequency of renal impairment co-existing with NIDDM [NEFRON] 11). Diabetes Care 2009; 32: 1497–1502.
19. Mather HM, Chaturvedi N, Kehely AM. Comparison of prevalence and risk factors for microalbuminuria in South Asians and Europeans with type 2 diabetes mellitus. Diabet Med 1998; 15: 672–677.
20. Gall MA, Rossing P, Skott P, et al. Prevalence of micro- and macroalbuminuria, arterial hypertension, retinopathy and large vessel disease in European type 2 (non-insulin dependent) diabetic patients. Diabetologia 1991; 34: 655–661.
21. Bhalla V, Zhao B, Azar KMJ, et al. Racial/ethnic differences in the prevalence of proteinuric and nonproteinuric diabetic kidney disease. Diabetes Care 2013; 36: 1215–1221.
22. Harvey J, Rizvi K, Craney L, et al. Population-based survey and analysis of trends in the prevalence of diabetic nephropathy in type 1 diabetes. Diabet Med 2001; 18: 998–1002.
23. Raile K, Galler A, Hofer S, et al. Diabetic nephropathy in 27,805 children, adolescents, and adults with type 1 diabetes: effect of diabetes duration, A1C, hypertension, dyslipidemia, diabetes onset, and sex. Diabetes Care 2007; 30: 2523–2528.
24. Reutens AT. Epidemiology of diabetic kidney disease. Med Clin N Am 2013; 97: 1–18.

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.