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Relationship of coffee consumption with a decline in kidney function among patients with type 2 diabetes: The Fukuoka Diabetes Registry

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ABSTRACT

Aims/Introduction: The evidence regarding the effects of coffee consumption on incident chronic kidney disease is inconclusive, and no studies have investigated the relationship in patients with diabetes. We aimed to prospectively investigate the relationship between coffee consumption and the decline in estimated glomerular function rate (eGFR) in patients with type 2 diabetes.

Materials and Methods: A total of 3,805 patients (2,112 men, 1,693 women) with type 2 diabetes (mean age 64.2 years) and eGFR ≥60 mL/min/1.73 m^2 were followed (completion of follow up, 97.6%; median 5.3 years). Coffee consumption was assessed at baseline. The end-point was a decline in eGFR to <60 mL/min/1.73 m^2 during the follow-up period.

Results: During follow up, 840 participants experienced a decline in eGFR to <60 mL/min/1.73 m^2. Higher coffee consumption reduced the risk of decline in eGFR. Compared with no coffee consumption, the multivariate-adjusted hazard ratios (95% confidence intervals) were 0.77 (0.63–0.93) for less than one cup per day, 0.77 (0.62–0.95) for one cup per day and 0.75 (0.62–0.91) for two or more cups per day (*P* for trend 0.01). This trend was unaffected by further adjustment for baseline eGFR and albuminuria. The mean eGFR change per year was −2.16 mL/min/1.73 m^2 with no coffee consumption, −1.89 mL/min/1.73 m^2 with less than one cup per day, −1.80 mL/min/1.73 m^2 with one cup per day and −1.78 mL/min/1.73 m^2 with two or more cups per day (*P* for trend 0.03).

Conclusions: Coffee consumption is significantly associated with a lower risk of decline in eGFR in patients with type 2 diabetes.

INTRODUCTION

With the aging of the population, the number of patients with a chronic disease, such as diabetes or chronic kidney disease (CKD), is increasing rapidly around the world[1,2]. Diabetic kidney disease is a serious microvascular complication that results in lower life expectancy, poorer quality of life and higher medical costs[3,4]. Although new treatments have been reported to reduce the deterioration in kidney function[5–7], lifestyle improvements are still regarded as fundamental for the prevention of diabetic complications[8]. Lifestyle management for patients with diabetes consists of the cessation of smoking, physical activity and dietary therapy, including the management not only of food intake, but also that of beverages[9].

Coffee is one of the most commonly consumed beverages around the world and contains numerous bioactive chemicals, such as caffeine and phenolic components. Coffee was once considered to be potentially harmful to health, through several mechanisms, such as increases in the risks of hypertension and myocardial infarction, which are principally caused by caffeine[10,11]. However, a recent umbrella review found that coffee consumption has beneficial effects on cardiovascular disease

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and its risk factors, such as diabetes and hypertension[12], through mechanisms including anti-inflammatory, anti-oxidant and anti-obesity effects[13,14]. We also previously reported that high coffee consumption is related to lower all-cause mortality in patients with diabetes[15]. Despite these findings, whether coffee consumption is beneficial for kidney function is unclear. Four cross-sectional studies have shown non-significant relationships between coffee consumption and the prevalence of CKD, defined as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 in the general population[16]. Three recent prospective studies have shown that high coffee consumption is associated with a lower risk of subsequent eGFR decline and end-stage renal disease (ESRD) in the general population[17–19], although another did not show a relationship[20]. The reduction in the risk of kidney impairment that is associated with substantial coffee consumption is speculated to be mediated through a lower risk of diabetes mellitus[17,21], although the mechanism remains to be elucidated. If this hypothesis is correct, the beneficial effects of coffee consumption on kidney function might not be present in patients with diabetes. However, to date, there have been no studies of this relationship in patients with pre-existing diabetes. Therefore, we aimed to prospectively investigate the relationship between the consumption of coffee and the decline in eGFR in patients with type 2 diabetes.

MATERIALS AND METHODS

Study sample

The Fukuoka Diabetes Registry is a multicenter prospective study (UMIN Clinical Trial Registry 000002627) of patients aged ≥20 years who attend teaching hospitals or clinics certified by the Japan Diabetes Society in Fukuoka Prefecture, Japan[22]. Overall, 5,131 patients with diabetes were registered between April 2008 and October 2010. The exclusion criteria were as follows: (i) ESRD requiring dialysis; (ii) steroid-induced diabetes; and (iii) serious diseases other than diabetes, including advanced malignant tumors. A study flow chart is shown as Figure S1. After excluding 1,071 patients with eGFR <60 mL/min/1.73 m^2 at baseline, 178 with type 1 diabetes mellitus and 77 for whom no follow-up data regarding kidney function were available, 3,805 patients remained and were enrolled in the present study. The study was approved by the Kyushu University Institutional Review Board and conformed to the principles of the Declaration of Helsinki. Written informed consent was provided by all the participants.

Clinical evaluation and laboratory measurements

We obtained information regarding the amount of alcohol consumed; current smoking habits; the duration of diabetes; symptoms of depression; the intensity of daily activity; the amount of leisure time physical activity; and any history of photocoagulation for diabetic retinopathy, cardiovascular disease, defined as stroke or ischemic heart disease, or liver disease, using a self-administered questionnaire at baseline. Leisure time physical activity was calculated as metabolic equivalent hours per week[23]. The presence of symptoms of depression was recorded on the basis of the Center for Epidemiologic Studies Depression Scale[24]: participants who scored ≥16 were defined as having such symptoms. Blood pressure was measured in a sitting position. The use of all medications, including oral hypoglycemic agents, insulin and renin–angiotensin system (RAS) inhibitors, were assessed by reviewing medical records.

We carried out the dietary survey, which included coffee consumption, and total energy and protein intake, using a brief diet history questionnaire (BDHQ; Gender Medical Research Inc., Tokyo, Japan) that itemized the frequency of consumption of 58 food items. Information regarding the addition of sugar to coffee or tea was also obtained. This approach has previously been validated in adult Japanese people[25]. The consumption of coffee was assessed using a question regarding the frequency of consumption, and the participants were placed into the following four groups on the basis of their responses: none, less than one cup per day, one cup per day, or two or more cups per day of coffee consumed. Questions regarding the consumption of decaffeinated or caffeinated beverages were not included, because the consumption of the former is uncommon in Japan.

We calculated the urinary albumin/creatinine ratio (UACR) by dividing the urinary albumin concentration by the urinary creatinine concentration. The albuminuria of the participants was categorized as normoalbuminuria (UACR <30 mg/g Cr), microalbuminuria (30 ≤ UACR <300 mg/g Cr) or macroalbuminuria (UACR ≥300 mg/g Cr). We calculated eGFR using the equation proposed by the Japanese Society of Nephrology, based on the serum creatinine concentration[26]. During the follow-up period, participants visited a hospital or clinic several times a year. Their annual serum creatinine, hemoglobin A_{1c} (HbA_{1c}) and blood pressure data were obtained from medical records, and the mean HbA_{1c} and blood pressure values were calculated for the follow-up period.

Outcome

The primary end-point was a decline in eGFR to <60 mL/min/1.73 m^2, based on two consecutive measures of eGFR during the follow-up period. We also evaluated the eGFR trend using least squares linear regression analysis of all the eGFR values calculated during the follow-up period. A rapid decline was defined as an eGFR slope of <−5.0 mL/min/1.73 m^2/year[27].

Statistical analysis

Trends in proportions or mean values across categories were analyzed using the Cochran–Armitage test or Jonckheere–Terpstra test, as appropriate. We used a direct method to calculate the incidence of the kidney outcome. The hazard ratios (HRs) and 95% confidence intervals (CIs) for the decline in eGFR were calculated using Cox proportional hazards models. We adjusted for potential risk factors or protective factors for a decline in eGFR in the multivariate-adjusted model: age, sex, body mass index (BMI), current smoking, current alcohol

consumption, duration of diabetes, protein consumption, leisure time physical activity, mean HbA_{1c} during follow up, low-density lipoprotein cholesterol, eGFR, category of albuminuria, mean systolic blood pressure; SBP during follow up, a history of cardiovascular disease, a history of liver disease and the use of an RAS inhibitor. We also carried out sensitivity analyses in which participants who had eGFRs <70 mL/min/1.73 m^2 at baseline, and in which participants who tended to add sugar to their coffee, were excluded.

We evaluated the relationship between coffee consumption and a rapid decline in eGFR using logistic regression analysis and generated odds ratios (ORs) and 95% CIs. The multivariate-adjusted model included age, sex, BMI, duration of diabetes, current smoking habit, current alcohol consumption, protein consumption, leisure time physical activity, mean HbA_{1c} during follow up, low-density lipoprotein cholesterol, eGFR, category of albuminuria, mean SBP during follow up, a history of cardiovascular disease, a history of liver disease and the use of an RAS inhibitor. We determined the modification of the association between coffee consumption and other confounding factors on incident CKD by adding an interaction term to the statistical model: age (≥70 or <70 years), sex, duration of diabetes (≥15 or <15 years), BMI (≥25 or <25 kg/m^2), current smoking (yes or no), regular exercise (yes or no), baseline HbA_{1c} (≥8 or <8%), UACR (≥30 or <30 mg/g Cr), eGFR (≥90 or <90 mL/min/1.73 m^2) or baseline blood pressure (SBP ≥140 and/or DBP ≥90 mmHg or SBP <140 and DBP <90 mmHg). Statistical analyses were carried out using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA), and $P < 0.05$ was regarded as showing statistical significance.

RESULTS

Table 1 presents the baseline clinical characteristics of the participants, categorized according to coffee consumption. Male sex; current smoking, current alcohol consumption, and the mean total energy intake, total protein intake, HbA_{1c}, eGFR and frequency of insulin use were significantly positively associated with high coffee consumption. In contrast, the mean age, prevalence of the addition of sugar to coffee or tea, albuminuria, SBP, the prevalence of a history of cardiovascular disease and the prevalence of RAS inhibitor use were significantly negatively associated with high coffee consumption.

During the follow-up period, 840 participants experienced a decline in eGFR of <60 mL/min/1.73 m^2. Table 2 shows the crude incidences of a decline in eGFR and the multivariate-adjusted relative risks, according to the level of coffee consumption. The crude incidence was lower in the groups with higher coffee consumption: 71.8/1,000 person-years with no coffee consumption, 52.1/1,000 person-years with less than one cup/day, 47.0/1,000 person-years with one cup/day and 41.4/1,000 person-years with two or more cups/day (P for trend <0.001). Compared with no coffee consumption, the multivariate-adjusted HRs (95% CIs) for a decline in eGFR were 0.77 (0.63–0.93) for less than one cup per day, 0.77 (0.62–0.95) for one cup per day and 0.75 (0.62–0.91) for two or more cups per day (P for trend 0.01). This statistically significant trend remained after adjustment for eGFR and albuminuria.

We carried out sensitivity analyses by excluding participants with eGFR <70 mL/min/1.73 m^2. The results were near identical in the categorial model, although the P-value was higher in the continuous model (P for trend 0.12; Figure S2). In addition, the results were almost identical in the sensitivity analyses in which we excluded participants who tended to add sugar to their coffee (Figure S3).

Figure 1 shows the decline in eGFR according to the level of coffee consumption during the follow-up period. The mean change in eGFR per year was −2.16 mL/min/1.73 m^2 with no coffee, −1.89 mL/min/1.73 m^2 with less than one cup per day, −1.80 mL/min/1.73 m^2 with one cup per day and −1.78 mL/min/1.73 m^2 with two or more cups per day (P for trend 0.03). The relationship between coffee consumption and a rapid decline in eGFR is shown in Table S1. The multivariate-adjusted ORs (95% CIs) for a rapid decline in eGFR were 0.74 (0.53–1.02) for less than one cup per day, 0.67 (0.47–0.95) for one cup per day and 0.69 (0.50–0.94) for two or more cups per day (P for trend 0.03).

Finally, we carried out interaction analyses for the relationship between coffee consumption and a decline in eGFR, accounting for potential confounding factors (Figure 2). Overall, the risk of decline in eGFR was significantly lower in participants who consumed any coffee than in those who did not consume coffee; the multivariate-adjusted HR (95% CI) was 0.76 (0.65–0.90). The reduction in risk of a decline in eGFR associated with coffee consumption narrowly missed statistical significance in participants with a long duration of diabetes (≥15 years) versus those with a shorter duration, but was significantly larger in participants with poor glycemic control (baseline HbA_{1c} ≥8%) than in those with better glycemic control. There were no significant interactions between coffee consumption and age (≥70 or <70 years), sex, BMI (≥25 or <25 kg/m^2), smoking status, regular exercise versus no exercise, UACR (≥30 or <30 mg/g Cr), eGFR (≥90 or <90 mL/min/1.73 m^2) or baseline blood pressure (SBP ≥140 and/or DBP ≥90 mmHg or SBP <140 and DBP <90 mmHg).

DISCUSSION

In the present study, we have shown that coffee consumption is associated with a significantly lower risk of a decline in eGFR in patients with type 2 diabetes. This association remained significant after adjustment for potential confounders, including smoking, the use of an RAS inhibitor, eGFR and albuminuria at baseline. To our knowledge, this is the first prospective study to show a significant inverse association between coffee consumption and a decline in eGFR in patients with type 2 diabetes. Patients with diabetes are at higher risk of renal dysfunction than individuals without diabetes; therefore, these findings might be important for their clinical care.

Table 1 | Baseline clinical characteristics of the participants, classified according to the amount of coffee consumed

	Coffee consumption				*P* for trend
	None	<1 cup/day	1 cup/day	≥2 cups/day	
n	684	970	754	1397	
Age (years)	67.7 ± 10.4	65.0 ± 10.2	64.4 ± 10.1	61.7 ± 9.6	<0.001
Male sex (%)	49.6	52.8	52.3	62.1	<0.001
Duration of diabetes (years)	14.8 ± 10.3	14.6 ± 10.1	14.6 ± 10.1	14.8 ± 10.1	0.80
BMI (kg/m^2)	23.7 ± 3.7	23.9 ± 3.9	23.8 ± 4.0	23.5 ± 3.7	0.09
Current smoker (%)	14.2	12.7	15.7	29.4	<0.001
Current alcohol intake (%)	31.3	40.8	42.7	44.2	<0.001
Depressive symptom (%)	9.4	9.9	7.0	9.0	0.44
Intensity of daily activity					
No work (%)	6.6	5.9	4.1	4.2	0.08
Light work (%)	74.6	72.4	72.3	72.4	
Moderate work (%)	16.8	20.5	22.0	22.1	
Hard work (%)	2.1	1.2	1.6	1.4	
Total energy intake (kcal/day)	1646 ± 462	1699 ± 509	1705 ± 478	1758 ± 504	<0.001
Total protein intake (g/day)	67.5 ± 25.1	67.1 ± 23.9	68.2 ± 23.3	69.9 ± 24.9	<0.001
Adding sugar to coffee or tea (%)	4.2	12.0	8.1	3.5	<0.001
LTPA (MET h/week)	11.6 ± 14.6	11.4 ± 14.9	13.0 ± 15.9	11.8 ± 14.9	0.34
HbA_{1c} (%)	7.4 ± 1.1	7.4 ± 1.0	7.4 ± 1.0	7.5 ± 1.1	<0.001
HbA_{1c} (mmol/mol)	57.8 ± 12.0	57.5 ± 11.4	57.8 ± 11.0	58.8 ± 11.6	<0.001
eGFR (mL/min/1.73 m^2)	80.7 ± 16.6	81.6 ± 15.2	83.3 ± 17.7	83.6 ± 16.5	<0.001
Albuminuria category					
Normoalbuminuria	64.5	66.9	67.2	70.0	0.01
Microalbuminuria	29.1	26.5	27.1	24.4	
Macroalbuminuria	6.4	6.6	5.7	5.6	
LDL cholesterol (mmol/L)	2.87 ± 0.72	2.87 ± 0.69	2.84 ± 0.67	2.90 ± 0.68	0.22
HDL cholesterol (mmol/L)	1.50 ± 0.40	1.47 ± 0.37	1.50 ± 0.40	1.51 ± 0.40	0.08
Systolic blood pressure (mmHg)	131 ± 17	131 ± 16	131 ± 17	128 ± 16	<0.001
Diastolic blood pressure (mmHg)	74 ± 11	75 ± 10	75 ± 10	75 ± 10	0.09
History of PC for retinopathy (%)	19.2	18.7	15.3	18.2	0.44
History of CVD (%)	23.4	19.4	17.5	15.6	<0.001
History of liver disease (%)	26.8	28.9	28.1	25.3	0.23
Insulin therapy (%)	25.0	21.0	24.7	29.3	<0.001
Oral hypoglycemic agent (%)	64.5	68.3	66.3	64.9	0.60
RAS inhibitors (%)	42.4	40.2	39.5	33.9	<0.001

Values are expressed as mean ± standard deviation or percentage. CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HbA_{1c}, hemoglobin A_{1c}; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LTPA, leisure time physical activity; MET, metabolic equivalent; PC, photocoagulation; RAS, renin–angiotensin system.

There have been several recent prospective studies of the relationship between coffee consumption and kidney outcomes in the general population[17–19]. In the Atherosclerosis Risk in Communities study of 14,209 individuals in the USA aged 45–64 years, with eGFR ≥60 mL/min/1.73 m^2 at baseline, and 3,845 patients with incident CKD, defined as eGFR <60 mL/min/1.73 m^2 accompanied by a ≥25% decline in eGFR, CKD-related hospitalization or death, or ESRD, the HR (95% CI) for incident CKD was 0.84 (0.75–0.94) for three or more cups/day of coffee versus no consumption[17]. Although, in that study, a subgroup analysis of patients with diabetes was carried out, no significant relationship was found, probably because of a lack of statistical power: <10% of the participants had diabetes. The Singapore Chinese Health Study of 63,257 men and women aged 45–74 years showed that greater coffee consumption was inversely associated with incident ESRD, defined as eGFR <15 mL/min/1.73 m^2 or the requirement for renal replacement therapy[18]. However, as the baseline data were collected during interviews at the participants' homes in that study, the medical history data might not be accurate. Another study of 8,717 Korean individuals with normal kidney function (mean age 62 years) showed that high coffee consumption was associated with a lower risk of incident CKD, defined as eGFR <60 mL/min/1.73 m^2[19]. Only one study failed to show a significant relationship between coffee consumption and incident CKD: the multivariate-adjusted HR (95% CI) for each additional cup per

Table 2 | Unadjusted and adjusted hazard ratios and 95% confidence intervals for estimated glomerular filtration rate <60 mL/min/1.73 m^2 in patients with type 2 diabetes and estimated glomerular filtration rate ≥60 mL/min/1.73 m^2, according to coffee consumption

	Coffee consumption				*P* for trend
	None	<1 cup/day	1 cup/day	≥2 cups/day	
No. at risk	684	970	754	1397	
No. events	202	222	156	260	
Incidence (/1,000 PYs)	71.8	52.1	47.0	41.4	
HR (95% CI)					
Unadjusted	1.0 (Ref.)	0.65 (0.53–0.80)	0.57 (0.47–0.68)	0.53 (0.41–0.70)	<0.001
Age- and sex-adjusted	1.0 (Ref.)	0.82 (0.67–0.99)	0.77 (0.62–0.95)	0.74 (0.61–0.90)	0.004
Multivariate-adjusted	1.0 (Ref.)	0.77 (0.63–0.93)	0.77 (0.62–0.95)	0.75 (0.62–0.91)	0.01

Adjustment was carried out for age, sex, body mass index, duration of diabetes, current smoking, current alcohol consumption, total energy consumption, total protein consumption, leisure time physical activity, mean hemoglobin A_{1c} during follow up, low-density lipoprotein cholesterol, estimated glomerular filtration rate (eGFR), albuminuria category, mean systolic blood pressure during follow up, a history of cardiovascular disease, a history of liver disease and the use of a renin–angiotensin system inhibitor. CI, confidence interval; HR, hazard ratio; PY, person-year, Ref, reference.

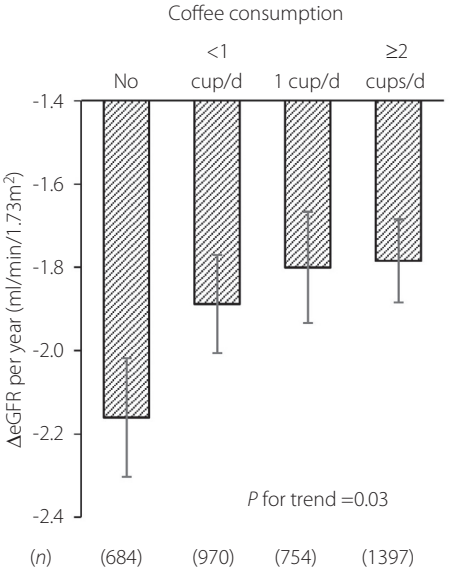

Figure 1 | Change in estimated glomerular filtration rate (eGFR) per year in the participants, according to coffee consumption. Vertical error bars represent 95% confidence intervals.

week for incident CKD was 0.97 (0.91–1.04) in the Tehran Lipid and Glucose Study of 1,780 individuals[20]. In the present study, we showed a significant inverse association between coffee consumption and kidney dysfunction in patients with diabetes. Furthermore, unlike in the aforementioned three studies, we adjusted for albuminuria and the use of an RAS inhibitor, which were both closely related to an impairment in kidney function in the multivariate-adjusted model.

In previous studies, the reduction in the relative risk for CKD associated with coffee consumption was hypothesized to be mediated through a lower risk of developing diabetes mellitus[17,21]. However, in the present study, coffee consumption was significantly associated with a lower risk of a decline in eGFR in patients with type 2 diabetes, and the finding remained statistically significant after adjustment for the level of glycemic control (Table 2). Furthermore, participants with poor glycemic control (baseline HbA_{1c} ≥8%) gained more benefit from coffee consumption than those with better glycemic control (baseline HbA_{1c} <8%; Figure 2). Albuminuria is another potential mediator of the relationship between coffee and kidney disease. An analysis of UK Biobank data recently showed that an extra cup of coffee per day confers a protective effect against albuminuria (OR 0.81)[28]. However, the point estimates were not changed after adjusted for albuminuria in the present study. Thus, mechanisms other than lower risks of diabetes, poor glycemic control or substantial albuminuria might be presumed to exist.

The biological mechanisms underlying the lower risk of impaired kidney function related in coffee consumers are not fully understood, partly because coffee is a complex mixture of substances. There is speculation regarding the specific components of coffee that affect kidney function. Some bioactive chemicals, such as caffeine and phenolic components, have been proposed to have favorable effects[29]. Chlorogenic acid is a phenolic component that has been shown to affect health through various mechanisms, including through effects on antioxidant capacity and chronic inflammation[13,14,29]. Chlorogenic acid attenuates ischemic injury in the kidney by reducing inflammation and renal tubular injury in a mouse model[30]. In the present study, the renal protective effect of coffee was greater in the participants with longer durations of diabetes and in those with poor glycemic control (Figure 2), who were likely to have been exposed to chronic inflammation. Caffeine is another component of coffee that might contribute to its favorable effects. Umemura *et al.*[31] reported that the acute administration of caffeine augments endothelium-dependent vasodilation in humans through an increase in nitric oxide production. In the present study, the baseline systolic blood pressure of the participants with higher coffee consumption was

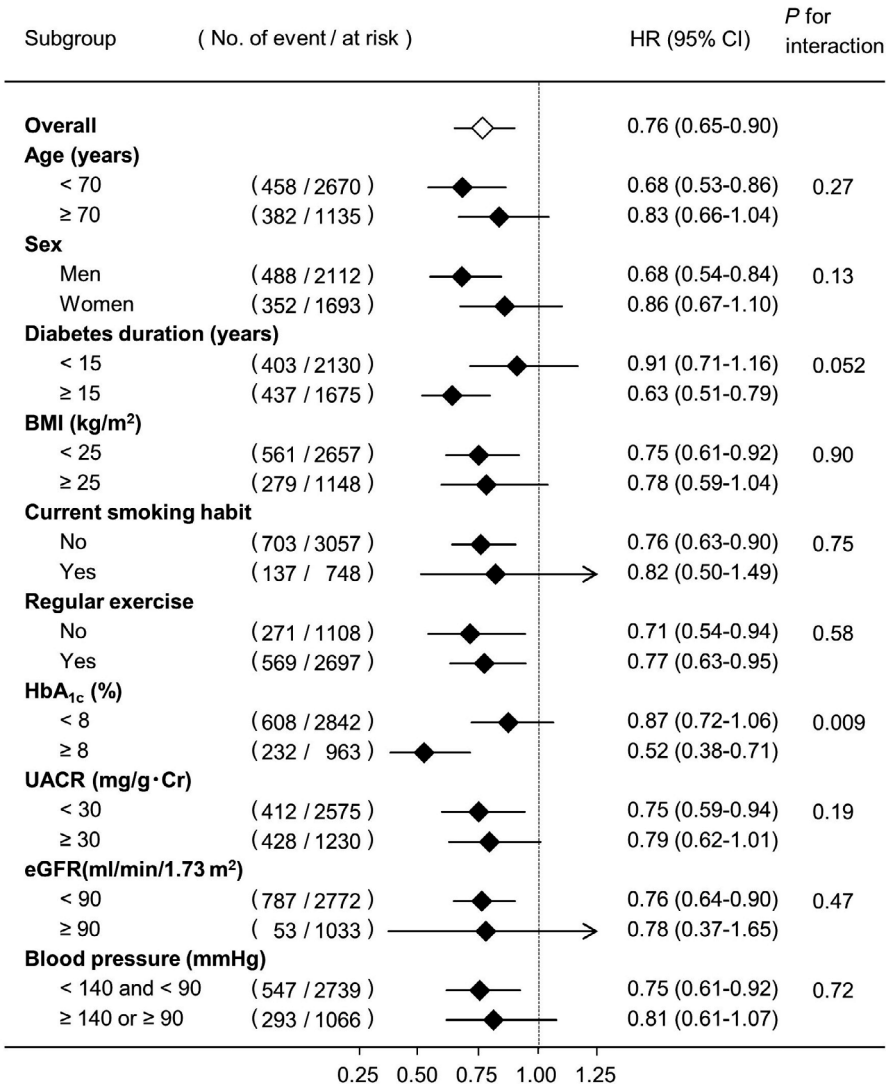

Figure 2 | Subgroup analyses of the relationship between coffee consumption and a decline in estimated glomerular filtration rate (eGFR). The reference group was no coffee consumption. The results are stratified according to age (≥70 or <70 years), sex, duration of diabetes (≥15 or <15 years), body mass index (BMI; ≥25 or <25 kg/m^2), current smoking, regular exercise, baseline hemoglobin A_{1c} (HbA_{1c}; ≥8% or <8%), UACR (≥30 or <30 mg/g Cr), eGFR (≥90 or <90 mL/min/1.73 m^2) and baseline blood pressure (systolic blood pressure ≥140 and/or diastolic blood pressure ≥90 mmHg or systolic blood pressure <140 and diastolic blood pressure <90 mmHg). Estimates were adjusted for age, sex, BMI, duration of diabetes, current smoking, current alcohol consumption, total energy consumption, total protein consumption, leisure time physical activity, mean HbA_{1c} during follow up, low-density lipoprotein cholesterol, eGFR, albuminuria category, mean systolic blood pressure during follow -up, a history of cardiovascular disease, a history of liver disease and the use of a renin–angiotensin system inhibitor. CI, confidence interval; HR, hazard ratio; UACR, urinary albumin/creatinine ratio.

significantly lower (Table 1), which might have been associated with lower glomerular pressure. In addition, coffee might protect against other CKD risk factors, such as obesity[12]. Consistent with this, a recent meta-analysis showed that substantial coffee intake is associated with lower adiposity[32].

In the present study, the relative reduction in risk of a decline in eGFR was almost the same among participants that were consuming of less than one, one or two or more cups per day, whereas a previous study showed a dose-dependent effect of coffee consumption to reduce the incidence of CKD[17]. This discrepancy might be explained by differences in the participants. In the general population, there is a dose-dependent relationship between coffee consumption and the reduction in type 2 diabetes incidence[21], and, therefore, the reduction in the incidence of diabetic kidney disease. Because all the participants in the present study already had type 2 diabetes at baseline, this

dose-dependent reduction might not have been so marked. However, further studies will be required to confirm this.

One strength of the present study was the high follow-up completion rate (97.6%) and the relatively large number of participants, which improved its statistical power. In addition, we adjusted for potential confounders, including lifestyle factors, physical activity, the presence of diabetic complications and laboratory data, which enabled us to more accurately investigate the relationship between coffee consumption and kidney function.

Some limitations of the study should also be discussed. First, because it was observational in nature, we cannot definitively ascribe a causal effect to the additional coffee intake on the change in kidney function. There might be other confounding factors in the relationship between coffee consumption and kidney function, such as educational factors, socioeconomic level and living environment. A high level of education has been reported to be associated with greater coffee consumption[33] and a lower risk of kidney dysfunction[34], in comparison with a lower level. To minimize the possibility of confounding of the present analysis, we accounted for lifestyle factors, including smoking status, BMI and physical activity, as potential confounders. Second, coffee consumption was assessed using a single self-reported questionnaire, which might have led to misclassification. However, the coffee consumption recorded in this questionnaire closely correlated with that in 16 non-consecutive dietary records kept by 184 Japanese men and women in a previous study[25]. Third, we did not obtain data regarding albuminuria during the follow-up period. Because CKD was defined on the basis of a low eGFR and albuminuria[35], we did not include every instance of incident CKD. However, patients with diabetes might experience a decline in eGFR without albuminuria, because of hypertension, obesity or vascular disease[36]. Fourth, we did not have data regarding the frequency of clinic visits. However, because all the hospitals and clinics participating in the current study had been certified by the Japan Diabetes Society, the level of treatment and care was unlikely to have substantially differed. Finally, because only Japanese participants were included in the study, it remains unclear whether its conclusions can be generalized to other ethnic groups. A global atlas of diabetes-related ESRD showed that its incidence in East Asia is two-to-threefold higher than in European countries, and the investigators suggested that the difference between these regions might be at least in part the result of differing diets[37]. People in European countries consume more coffee than those in East Asia, where green tea is more frequently consumed. The findings of the present study suggest that the difference in coffee consumption might contribute to the difference in the incidence of ESRD between East Asia and Europe.

In conclusion, we have shown that coffee consumption is significantly associated with a lower risk of a decline in eGFR, implying progressive impairment in renal function, in patients with type 2 diabetes. However, coffee is one of the most frequently consumed beverages worldwide and cannot be considered separately from the nutritional therapy of diabetes. A randomized clinical trial is required to confirm the renoprotective effect of this beverage.

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DISCLOSURE

The authors declare no conflict of interest.

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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 | Unadjusted and adjusted odds ratios and 95% confidence intervals (CIs) for rapid estimated glomerular filtration rate decline (ΔeGFR <–5 mL/min/1.73 m^2/year) in the participants, according to coffee consumption.

Figure S1 | Study flow diagram.

Figure S2 | Sensitivity analyses of the relationship between coffee consumption and a decline in estimated glomerular filtration rate in participants with or without estimated glomerular filtration rate <70 mL/min/1.73 m^2.

Figure S3 | Sensitivity analyses of the relationship between coffee consumption and a decline in estimated glomerular filtration rate in participants who did not add sugar.