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Short Communication

Association between habitual coffee consumption and normal or increased estimated glomerular filtration rate in apparently healthy adults

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Habitual coffee consumption is associated with the prevention of type 2 diabetes, which often accompanies diabetic nephropathy. However, the relationship between coffee consumption and kidney function is unclear. Therefore, we investigated the associations between habitual coffee consumption and kidney function and damage assessed by the estimated glomerular filtration rate (eGFR) and proteinuria using dipstick urinalysis, respectively, in a cross-sectional study of 342 apparently healthy adults. Habitual coffee consumption was defined as drinking one or more cups of coffee per d. eGFR in coffee consumers (*n* 182; 80·1 (SD 15·0) ml/min per 1·73 m^2) was significantly higher than that in non-coffee consumers (*n* 160; 76·9 (SD 12·6) ml/min per 1·73 m^2) ($P<0·05$). Multivariate logistic analysis showed that, compared with non-coffee consumption, coffee consumption was significantly associated with normal or increased eGFR (NIGFR) ($\geq$90 ml/min per 1·73 m^2), but not proteinuria, which was not attenuated, even after adjustment for age, sex, smoking, tea consumption and other cardiovascular risks (OR 2·91; 95 % CI 1·51, 5·61; $P=0·001$). When we took into account eGFR measured 1 year before in a subgroup of the subjects (*n* 262), coffee consumption (*n* 142) had a significant relationship with eGFR, which was consistently higher with a difference of 4·0 ml/min per 1·73 m^2 compared with non-coffee consumption ($P=0·01$; two-way repeated ANOVA). Similar associations were observed in both sexes when data were reanalysed according to sex. In conclusion, our findings suggest that habitual coffee consumption is associated with NIGFR independently of clinical confounders. Further studies are needed to confirm this association and to explore whether the effect of coffee consumption on eGFR is beneficial for the kidney.

Coffee consumption: Kidney function: Glomerular filtration rate

Coffee is one of the most frequently consumed beverages worldwide and the consumption of coffee is now relatively common in Japan. About 50–70 % of the population drinks coffee daily[1]. As such, habitual coffee consumption may contribute favourably or harmfully to general health, systemic metabolism and prevention or development of critical diseases such as CVD and cancers[2–4]. Such effects would be of great scientific interest and it is important to address the potential public health implications. Many large studies have shown that coffee consumption can improve insulin resistance and abnormal glucose metabolism, and thus may help in the prevention of type 2 diabetes[2–4]. Of the diabetic complications, kidney dysfunction and damage, i.e. diabetic nephropathy, is often evident, even during the early stage of the pathogenesis[5,6]. In this context, we hypothesised that habitual coffee consumption might have beneficial effects on the kidney.

The prevalence of chronic kidney disease, which is commonly defined as a reduced glomerular filtration rate (GFR) and/or other renal damage, is also increasing worldwide[7]. To date, however, there have been no studies reporting the association between coffee consumption and kidney function, particularly in a healthy population. Therefore, we investigated the association between self-reported coffee consumption and kidney function and damage, as assessed by estimated GFR (eGFR) and proteinuria, respectively, in a cross-sectional study of apparently healthy adults. To confirm the validation, we also took into consideration eGFR values obtained 1 year before in a subgroup of the subjects.

Methods

The present report represents a series of studies performed in collaboration with Josai University, Sakado, Japan and Social Insurance Omiya General Hospital, Saitama, Japan, that have been conducted to better understand lifestyle-related diseases.

Abbreviations: Cr, creatinine; DGFR, decreased estimated glomerular filtration rate; eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; NIGFR, normal or increased estimated glomerular filtration rate.

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The protocol was approved by the Ethics Committee of Josai University and the Ethics Committee of the Hospital. We randomly recruited 342 apparently healthy subjects aged 30–80 years who had undergone a medical check-up and who responded to a questionnaire about their lifestyle characteristics. They had no self-reported medical history of CVD, cancer or kidney diseases such as glomerulonephritis. The recruited subjects gave informed consent. Laboratory tests were carried out after an overnight fast. Clinical and biochemical variables were measured with standard methods. Serum creatinine (Cr) concentrations were measured enzymically using an autoanalyser. HbA1c was only measured in subjects with a relatively high fasting plasma glucose (*n* 226) of about 1100 mg/l.

Subjects were dichotomised into coffee consumers who drink one or more cups of coffee per d, and non-coffee consumers who seldom drink coffee. The coffee consumption per d, such as the number of cups per d, and the way of drinking were not asked. Consumption of tea, which mostly reflects green tea in Japanese populations, was similarly defined. Alcohol consumption was defined as drinking alcohol one or more times per week and smokers were defined as current smokers. eGFR was calculated using the equation of the Modification Diet in Renal Disease study for Japanese subjects[8], as follows:

$$\text{eGFR}\,(\text{ml/min per } 1{\cdot}73\,\text{m}^2) = 194 \times \text{serum Cr}^{-1{\cdot}094} \times \text{age}^{-0{\cdot}287}\,(\text{if female}) \times 0{\cdot}739,$$

serum Cr concentration being measured in mg/dl.

Table 1. Characteristics and clinical variables of subjects
(Mean values and standard deviations or percentages)

	Coffee consumers		Non-coffee consumers	
	Mean	SD	Mean	SD
Subjects (*n*)				
All subjects	182		160	
Men	129		117	
Women	53		43	
Age (years)				
All subjects	47·2	10·9	49·3	13·2
Men	46·0	10·9	47·9	13·1
Women	50·2*	10·6	53·2*	12·8
BMI (kg/m^2)	23·7	3·2	23·5	3·4
Systolic blood pressure (mmHg)	119	18·2	123	20·7
Diastolic blood pressure (mmHg)	74·5	13·3	76·1	13·0
Aspartate transaminase (IU/l)	21·8	8·1	23·0	7·3
Alanine aminotransaminase (IU/l)	23·5	15·7	26·5	18·9
LDL-cholesterol (mg/l)	1190	282	1200	291
TAG (mg/l)	1180	942	1190	783
HDL-cholesterol (mg/l)	614	161	610	165
Fasting blood glucose (mg/l)	984	142	1000	192
Uric acid (mg/l)	56	15	55	15
Blood urea N (mg/l)	137	33	140	32
Serum creatinine (mg/dl)	0·79	0·16	0·81	0·15
HbA1c (%) (*n* 226)	5·3	0·5	5·4	0·8
Proteinuria (%)	4·4		5·6	
Normal or increased GFR (%)	29·7		15·0††	
Estimated GFR (ml/min per 1·73 m^2)				
All subjects	80·1	15·0	76·9‡	12·6
Range	39·7–121		53·4–123	
Men	79·2	13·5	76·1	11·7
Range	47·0–121		53·7–113	
Women	82·2	18·1	79·3	15·0
Range	39·7–121		53·4–123	
Tea consumption (%)	54·4		81·3††††	
Alcohol consumption (%)	48·6		44·4	
Smoking (%)	37·4		35·0	
Medications for:				
Dyslipidaemia (*n*)	4		3	
Hypertension (*n*)	18		22	
Repeated estimated GFR measurements (*n* 262)§§				
Number of subjects	142		120	
1 year before (ml/min per 1·73 m^2)	81·8	14·0	77·7	14·4
Current (ml/min per 1·73 m^2)	79·8	14·4	75·8	11·9

GFR, glomerular filtration rate.
* Mean value was significantly different from that of the men ($P<0{\cdot}05$; *t* test).
Percentage was significantly different from that of the coffee consumers: †† $P<0{\cdot}01$, †††† $P<0{\cdot}0001$ (χ^2 test).
‡ Mean value was significantly different from that of the coffee consumers ($P<0{\cdot}05$; *t* test).
§§ $P=0{\cdot}01$ (two-way repeated ANOVA).

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Normal or increased GFR (NIGFR) and decreased GFR (DGFR) were defined as eGFR $\geq$ 90 ml/min per 1·73 m^2 and $<$ 60 ml/min per 1·73 m^2, respectively, according to the National Kidney Foundation classification[7]. Proteinuria was assessed using dipstick urinalysis with fresh urine. Negative (−) and borderline samples (±) were defined as normal, and the others were defined as having overt proteinuria. We also checked serum Cr values obtained 1 year before the cross-sectional study and examined the effect of coffee consumption on repeated measurement of eGFR using two-way repeated-measures ANOVA (available sample size, *n* 262).

Statistical differences in variables and prevalence of variables between coffee consumers and non-consumers were examined by *t* tests and χ^2 tests, respectively. Multivariate logistic regression models were used to examine the associations between coffee consumption and NIGFR, DGFR and proteinuria. Statistical analysis was performed with the statistical software package SPSS (version 16.0; SPSS, Inc., Chicago, IL, USA).

Results

As shown in Table 1, overall, there was no significant difference in clinical variables and categories between coffee consumers and non-coffee consumers, including serum Cr, fasting plasma glucose, and HbA1c, except for tea consumption and eGFR. The prevalence of subjects with NIGFR in coffee consumers was two-fold higher compared with that in non-coffee consumers. Two-way repeated-measures ANOVA revealed that coffee consumption had a significant relationship with eGFR, i.e. persisted higher eGFR with a difference of 4·0 ml/min per 1·73 m^2, compared with non-coffee consumption, and was independent of the annual change in eGFR (P=0·01; Table 1). Multivariate logistic analysis showed that, compared with non-coffee consumption, coffee consumption was significantly associated with NIGFR, even after adjustment for age, sex, smoking, tea consumption, alcohol intake, proteinuria, medications and other cardiovascular risks including BMI and fasting plasma glucose (OR 2·91; 95 % CI 1·51, 5·61; P=0·001; Table 2). Meanwhile, coffee consumption was not significantly associated with either DGFR or proteinuria. Similar associations were observed in both sexes when the results were reanalysed according to sex. The mean eGFR was significantly higher in women than in men (81·1 (SD 16·5) *v.* 77·7 (SD 12·3) ml/min per 1·73 m^2, respectively; $P<0·05$) despite the significantly higher mean age of the women ($P<0·01$, data not shown). Therefore, we used a different cutoff value of 95 ml/min per 1·73 m^2 for NIGFR in women. Tea consumption was not significantly associated with NIGFR, DGFR or proteinuria, even without adjustment for confounders (OR 1·19 (95 % CI 0·71, 1·99); OR 1·14 (95 % CI 0·51, 2·54); OR 0·34 (95 % CI 0·10, 1·19), respectively; data not shown).

Discussion

To the best of our knowledge, this is the first report to show a positive association between coffee consumption and NIGFR, as assessed by eGFR using an ethnic-specific equation, in apparently healthy adults. Overall, the results were similar in both sexes, although the statistical power in women was weak and unstable because of the small sample size.

Considering that coffee consumers in the present study did not appear to have abnormal glucose metabolism or, conversely, a more favourable profile in terms of glucose metabolism compared with non-coffee consumers, we are unable to

Table 2. Association between coffee consumption and normal or increased estimated glomerular filtration rate (NIGFR), decreased estimated glomerular filtration rate (DGFR) and proteinuria

(Odds ratios and 95 % confidence intervals)

	NIGFR*			DGFR†			Proteinuria		
	OR	95 % CI	*P*	OR	95 % CI	*P*	OR	95 % CI	*P*
				All subjects					
Model 1‡	2·39	1·40, 4·09	0·002	0·68	0·31, 1·51	0·34	0·77	0·29, 2·05	0·60
Model 2§	2·33	1·32, 4·11	0·003	0·86	0·38, 1·97	0·72	0·76	0·28, 2·04	0·58
Model 3‖	2·58	1·38, 4·82	0·003	0·78	0·32, 1·92	0·59	0·98	0·34, 2·78	0·96
Model 4¶	2·91	1·51, 5·61	0·001	0·74	0·30, 1·85	0·52	0·99	0·32, 3·03	0·98
Men									
Model 1‡	2·64	1·31, 5·32	0·007	0·64	0·25, 1·64	0·35	0·55	0·18, 1·73	0·31
Model 2§	2·63	1·27, 5·42	0·009	0·80	0·30, 2·17	0·66	0·53	0·17, 1·68	0·28
Model 3‖	3·12	1·39, 6·99	0·006	0·81	0·29, 2·29	0·69	0·70	0·21, 2·36	0·56
Model 4¶	3·72	1·54, 8·98	0·003	0·74	0·25, 2·17	0·58	0·60	0·15, 2·34	0·46
Women									
Model 1‡	3·90	1·02, 14·9	0·04	0·80	0·31, 3·39	0·75	2·52	0·25, 25·1	0·43
Model 2§	4·03	0·99, 16·3	0·05	1·00	0·22, 4·53	0·99	3·04	0·29, 32·3	0·36
Model 3‖	4·68	1·03, 21·3	0·04	0·57	0·08, 4·10	0·57	2·42	0·22, 26·4	0·46
Model 4¶	19·6	2·14, 179	0·01	1·41	0·06, 33·2	0·83	3·33	0·15, 74·8	0·45

* NIGFR for all subjects and men is defined as estimated GFR $\geq$ 90 ml/min per 1·73 m^2; NIGFR for women is defined as estimated GFR $\geq$ 95 ml/min per 1·73 m^2.

† DGFR is defined as estimated GFR $<$ 60 ml/min per 1·73 m^2.

‡ Model 1: unadjusted.

§ Model 2: model 1 plus adjustment for age, smoking, and sex (all subjects).

‖ Model 3: model 2 plus adjustment for tea consumption, alcohol drinking and medications.

¶ Model 4: model 3 plus adjustment for BMI, blood pressures, LDL-cholesterol, TAG, HDL-cholesterol, fasting glucose, and proteinuria (NIGFR, DGFR) or estimated GFR (proteinuria).

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conclude whether the association is due to hyperfiltration in the early stage of diabetic nephropathy[9,10] or is mediated through improved glucose metabolism. Meanwhile, coffee consumption was not inversely associated with either DGFR or proteinuria. In this context, we hypothesise that the potential effects of coffee on kidney function, if any, may focus on mild rather than moderate or severe kidney dysfunction.

Although the mean age of coffee consumers was apparently lower than that of non-coffee consumers (Table 1), the differences of approximately 2 to 3 years corresponds with differences in eGFR of about 0·88 to 1·32 ml/min per 1·73 m^2, as determined by linear regression analysis between age and eGFR ($y = 100 - 0{\cdot}44x$, where y is eGFR and x is age; R^2 0·16; $P<0{\cdot}0001$). Therefore, differences in mean age are unlikely to substantially influence the associations between coffee consumption and NIGFR. Furthermore, although adjustment for age slightly attenuated the association, the statistical significance remained in all analyses, except for the separate analysis in women.

Coffee contains substantial quantities of caffeine, a member of the methylxanthine family as well as a strong bioavailable constituent[3,4]. Acute effects of caffeine, for example, an increase in diuresis/natriuresis and blood pressure, are commonly observed in human subjects several hours after caffeine ingestion[2,3,11]. Nevertheless, in the present study, before the laboratory test in the morning, the subjects did not consume any beverages. Thus, the acute effects of caffeine are not considered to be involved in the mechanism. It is well known that adenosine receptors and phosphodiesterases play key roles in the regulation of kidney function[12,13]. Because caffeine intake antagonises adenosine receptors and inhibits phosphodiesterases[2,13,14], the mechanism in the observed associations might be mediated through the continuous actions of these agents. Some antioxidant constituents of coffee such as chlorogenic acid, a dietary antioxidant phenol, and micronutrients, including Mg, K and niacin[3,15], could also contribute to the observed associations. Cafestol and kahweol, diterpenes contained in coffee, are unlikely to be associated with the present findings because most coffee consumers in Japan drink filtered coffee, which contains low levels of these diterpenes[15].

Several limitations of the present study should be discussed. First, the sample size is relatively small, especially in women. However, most of the confounding factors assessed were objective continuous variables in blood tests and anthropometric measurements, rather than self-reported clinical categories, which may yield bias. Furthermore, validation of the observed association was confirmed even after considering the annual changes in eGFR. Second, the daily dose of coffee consumption, such as the number of cups per d, was not examined because the present study was not conducted specifically to examine the relationship between coffee consumption and kidney function. Thus, whether the observed association varies according to the dose of coffee consumed remains to be determined. Finally, other measurements for the estimation of GFR, such as serum cystatin C levels, should also be considered to better understand the observed association because the current equation using serum Cr is adjusted for age, sex and ethnic differences but not properly for muscle mass[16].

In conclusion, we observed that habitual coffee consumption is consistently associated with NIGFR independently of clinical confounding. Further detailed studies are needed to confirm the current association and to explore causal constituents, and whether this effect of coffee consumption on GFR is beneficial for the kidney. A prospective study is also needed to examine the causality of this association.

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The contribution of each author to the present paper was as follows: K. N. and H. M. designed the study and analysed the data; K. H., M. E., and K. M. collected the data; K. N. wrote the draft of the manuscript.

There are no conflicts of interest in the present study.

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