

Coffee and tea consumption in relation to estimated glomerular filtration rate: results from the population-based longitudinal Doetinchem Cohort Study¹

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ABSTRACT

Background: Although coffee consumption and tea consumption have been linked to diabetes, the relation with kidney function is less clear and is underresearched.

Objective: We investigated the prospective associations of coffee and tea consumption with estimated glomerular filtration rate (eGFR).

Design: We included 4722 participants aged 26–65 y from the Doetinchem Cohort Study who were examined every 5 y for 15 y. Coffee and tea consumption (in cups/d) were assessed at each round. eGFR was assessed by using the Chronic Kidney Disease Epidemiology Collaboration equation based on both plasma creatinine and cystatin C. We determined the association between categories of coffee and tea intake and 1) eGFR and 2) subsequent annual changes in eGFR by using generalized estimating equation analyses.

Results: Baseline mean \pm SD eGFR was $108.0 \pm 14.7 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$. Tea consumption was not associated with eGFR. Those individuals who drank >6 cups coffee/d had a 1.33 (95% CI: 0.24, 2.43) $\text{mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ higher eGFR than those who drank <1 cup/d (P -trend = 0.02). This association was most apparent among those with a median age of ≥ 46 y at baseline, with eGFR being 2.47 (95% CI: 0.42, 4.51) $\text{mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ higher in participants drinking >6 cups/d compared with <1 cup/d (P -trend = 0.02). Adjustment for biological risk factors and coffee constituents did not attenuate the associations. Neither coffee nor tea consumption was associated with changes in eGFR.

Conclusions: Coffee consumption was associated with a slightly higher eGFR, particularly in those aged ≥ 46 y. The absence of an association with eGFR changes suggests that the higher eGFR among coffee consumers is unlikely to be a result of glomerular hyperfiltration. Therefore, low to moderate coffee consumption is not expected to be a concern for kidney health in the general population. *Am J Clin Nutr* 2016;103:1370–7.

Keywords: coffee and tea, eGFR, epidemiology, longitudinal, population-based

INTRODUCTION

Coffee and tea are among the most widely consumed beverages around the world (1). Hence, an effect of these beverages on chronic disease risk has important public health implications. Although a link between coffee intake and risk of hypertension (2) and cardiovascular disease (3) remains controversial, coffee and tea consumption has been found to be inversely associated with type 2 diabetes (4).

Because diabetes and kidney failure share many risk factors (5), one could speculate that coffee and tea consumption may protect against a decline in kidney function [i.e., decline in estimated glomerular filtration rate (eGFR)⁶], analogous to the documented protective effects of coffee and tea consumption on the development of diabetes. However, this area has been underresearched, and findings have been inconsistent. In a clinical trial in young Japanese adults, 14 d of coffee, but not tea, consumption resulted in a significantly higher eGFR (6). Furthermore, in 2 studies in Japanese adults, a higher eGFR was observed in habitual coffee consumers (7, 8) but not in tea consumers (8) compared with those who did not drink coffee or tea. However, in a study in Korean women, coffee consumption was associated with a decreased risk of kidney function impairment only in women with diabetes (9), and no association between coffee consumption and eGFR was found in another study in Japanese adults (10).

Most of these studies were cross-sectional and therefore do not provide evidence of a temporal relation between exposure and outcome. Furthermore, associations have been studied in Asian study populations only, and tea consumption on this continent mainly reflects green tea (8). Until now, no studies have

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⁶ Abbreviations used: eGFR, estimated glomerular filtration rate; FFQ, food-frequency questionnaire; GFR, glomerular filtration rate.

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prospectively examined the association between coffee and tea consumption and eGFR in Western populations. Furthermore, it remains to be determined whether a dose-response relation, if any, is present. In addition, although it has been suggested that lower blood pressure and several constituents of coffee and tea, such as magnesium, potassium, and caffeine, could explain possible inverse associations with risk of diabetes (11), the role of these mediating factors in relation to eGFR has not been studied. In view of these considerations, we investigated the prospective association of coffee and tea consumption and (changes in) eGFR in a Western general population sample of men and women with the use of repeated measurements over time of coffee and tea consumption and eGFR.

METHODS

Study setting

The Doetinchem Cohort Study is a population-based prospective study of the impact of (changes in) lifestyle factors and biological risk factors on various aspects of health and well-being in Dutch adults. In 1987–1991 (round 1), self-completed questionnaires were collected and a physical examination was performed in a random sample of 12,405 men and women (response rate: 62%), aged 20–59 y, from the town of Doetinchem. Of those, a two-thirds random sample of 7768 participants were reinvited to be examined in 1993–1997 (round 2; $n = 6113$), 1998–2002 (round 3; $n = 4916$), 2003–2007 (round 4; $n = 4520$), and 2008–2012 (round 5; $n = 4017$). The response rate for the second, third, fourth, and fifth rounds was $\geq 75\%$. Informed consent was obtained from all participants, and ethical clearance was obtained from the Medical Ethics Committees of the Netherlands Organization of Applied Scientific Research. Further details of the study design have been described elsewhere (12).

Study population

In this study, eGFR and eGFR declines, defined as changes in eGFR and risk of rapid decline in eGFR, were used as the main outcomes. Because detailed information on coffee and tea intake was not collected at rounds 1 and 5, we followed participants from round 2 through round 4 for the analysis with eGFR as the outcome (Figure 1A) and from round 2 through round 5 for the analyses with annual changes in and risk of rapid decline in eGFR as the outcome (Figure 1B). Pregnant women were censored at the round at which they reported to be pregnant. Of the 6113 participants who responded in round 2, 4722 with complete data on coffee and tea consumption, covariates, and eGFR for at least 2 rounds were included in the eGFR analysis. Similarly, 3786 participants with complete data on exposures and outcome for at least 3 rounds were included in the annual changes in eGFR and risk of rapid decline in eGFR analyses.

eGFR

In all rounds, a 30-mL nonfasting plasma blood sample was drawn. Creatinine was measured by dry chemistry (Eastman Kodak), with intra- and interassay CVs of 0.9% and 2.9%, respectively. Furthermore, cystatin C was based on a particle-enhanced turbidimetric immunoassay by using reagents from

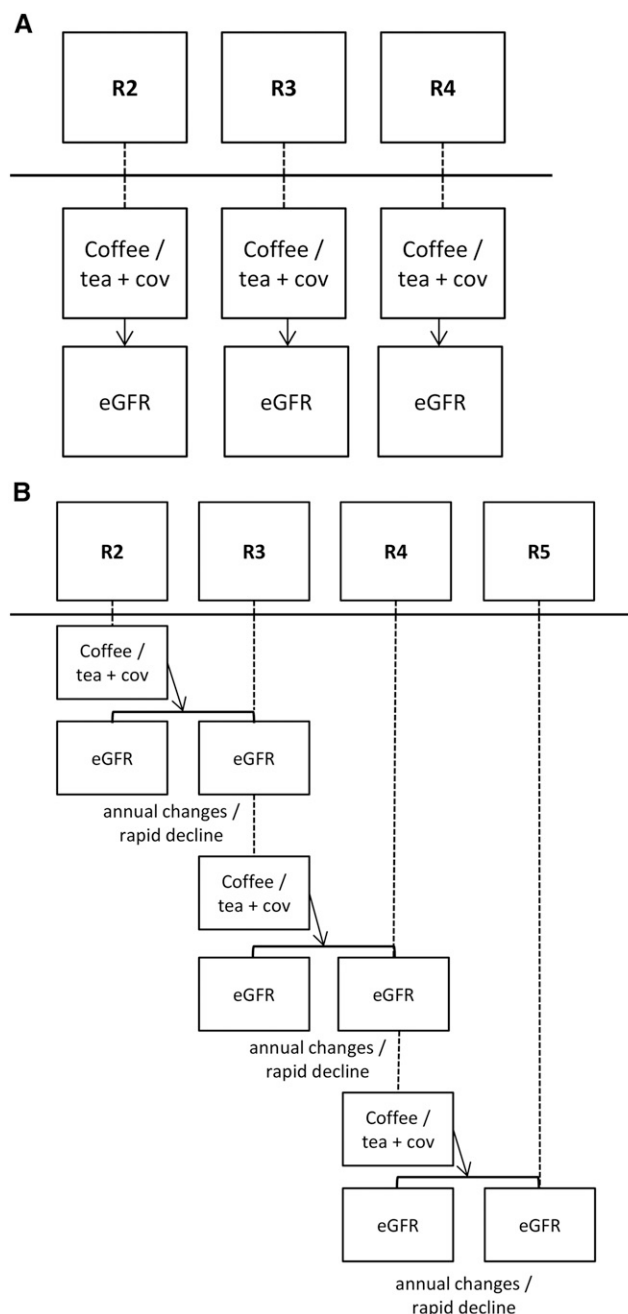


FIGURE 1 Generalized estimating equation regression models to study the associations between coffee and tea consumption (at R2–R4) and eGFR (at R2–R4) (A) and coffee and tea consumption (assessed at R2–R4) and subsequent changes in eGFR (between R3 and R5) (B). cov, covariates; eGFR, estimated glomerular filtration rate; R, round.

Gentian. The intra- and interassay CVs were $<4.1\%$ and 3.3% , respectively. Per participant, all available samples from consecutive rounds were examined in 1 assay run, thereby reducing the variability in measurements to an absolute minimum (13). eGFR is more precise and accurate if derived from both cystatin C and creatinine compared with glomerular filtration rate (GFR) estimation on the basis of cystatin C or creatinine alone (14). Therefore, in the current study, eGFR was estimated with both cystatin C and creatinine according to the Chronic Kidney Disease Epidemiology Collaboration equation (14). Annual

changes in eGFR were then calculated by subtracting eGFR at successive rounds and dividing by 5 (all rounds were 5 y apart). A rapid decline in eGFR was defined by the loss of $>3.0 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ each year in eGFR. This threshold represents a magnitude of change that is 3 times the rate previously described in studies of aging, is beyond the range of measurement error, and has been associated with an increased risk of mortality (15).

Coffee and tea intake

At rounds 2–4, diet over the previous 12 mo was assessed with a food-frequency questionnaire (FFQ), which allows the estimation of the average daily consumption of 178 food and beverage items. Participants were asked to report their usual frequency of consumption of coffee and tea per day, week, month, and year, from which coffee and tea consumption in cups/d (1 cup was defined as 150 mL) was calculated. Caffeinated coffee was the major type of coffee consumed. No specific information on green tea consumption was available. The validity and reproducibility of the FFQ have been described in detail elsewhere (16, 17). In a validation study conducted in a subsample of EPIC-NL (European Prospective Investigation into Cancer and Nutrition–Netherlands cohort) participants [of which the Doetinchem study is part (18)], FFQ assessment of coffee and tea was highly correlated with 24-h recalls (coffee, $r = 0.74$; tea, $r = 0.87$) (11).

Covariates

The following sociodemographic, lifestyle, and chronic disease risk factors were included in the analysis as potentially confounding variables or intermediates and were collected at each round. Education, based on the highest level of education attained, including follow-up, was categorized as follows: low (intermediate secondary education or less), moderate (intermediate vocational or higher secondary education), or high (higher vocational education or university education). A physical activity score (the Cambridge Physical Activity Index) was derived from questions on frequency and total duration of various types of activity at work and leisure time and classified as inactive, moderately inactive, moderately active, or active (19). Smoking was classified as never-smoker, ex-smoker, or current smoker; and alcohol consumption as nondrinker, light drinker (0–4.9 g/d for both women and men), moderate drinker (5.0–14.9 g/d for women, 5.0–29.9 g/d for men), or heavy drinker (≥ 15.0 g/d for women, ≥ 30.0 g/d for men) (20). BMI was calculated from measured weight and height as weight (in kg) divided by height (in m) squared. Systolic and diastolic blood pressures were also measured, and hypertension was defined as systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, and/or the use of antihypertensive medication. Hypercholesterolemia was defined as nonfasting total cholesterol ≥ 6.5 mmol/L and/or self-reported use of cholesterol-lowering medication. Diabetes was defined as self-reported diabetes or a random glucose concentration ≥ 11.1 mmol/L. Finally, total daily intakes of energy, vitamin C, fiber, total fat, saturated fat, magnesium, potassium, and caffeine were calculated by using the Dutch 1996 food-composition database (21).

Statistical analyses

We first described baseline characteristics of the study population by coffee and tea intake. Coffee intake was categorized as <1 , 1–2, 3–4, 5–6, or >6 cups/d; and tea intake was categorized as <1 , 1–2, 3–4, or >4 cups/d, with the lowest category being used as the reference group. Given that we have data at multiple time points available, we adopted the technique of generalized estimating equations, because they enable the use of longitudinal linear and logistic regression by taking into account correlations within each participant. First, β s with 95% CIs were calculated for the association between each of coffee and tea intake (at rounds 2–4) and eGFR assessed at the same round (rounds 2–4) (Figure 1A). This first analysis pools together both cross-sectional and longitudinal associations. However, we also examined the longitudinal associations between each of coffee and tea intake (at rounds 2–4) and subsequent changes in eGFR (between rounds 3 and 5) (Figure 1B). Furthermore, ORs were calculated for the association between coffee and tea intake (at rounds 2–4) and subsequent risk of rapid decline of eGFR (between rounds 3 and 5). All generalized estimating equation models were performed by using an exchangeable correlation structure, implying that all correlations between repeated observations of the outcome variable from each participant were assumed to be equal, irrespective of the time period between measurements (22). We first adjusted for age and sex (model 2) before adjusting for education, physical activity, BMI, smoking, alcohol consumption, daily energy intake, and energy-adjusted intakes of fiber, vitamin C, total protein, fat, and saturated fat (model 3) and coffee (for tea analysis) or tea (for coffee analysis) (model 4). To examine possible mediating pathways through which coffee and tea intake affects eGFR, we additionally adjusted for hypertension, diabetes, and hypercholesterolemia (model 5) and energy-adjusted intakes of magnesium, potassium, and caffeine (model 6). All potential confounders and intermediates were included as time-varying covariates. All nutrients were adjusted for total energy intake by using the residual method (23). Once participants reported a chronic condition, they were considered to have this condition at each subsequent round. Tests for trends across categories were conducted by modeling the median value for each category of exposure as a continuous variable. Smoking is strongly correlated with coffee intake. Given that the never-smoker, ex-smoker, and current smoker categorization in our study is rather crude, we performed a secondary analysis in which we additionally controlled for number of cigarettes smoked daily and found almost identical results. Furthermore, because the numbers of never-smokers in each category of cups of coffee per day were too small to allow for a meaningful analysis, we also analyzed coffee intake as a continuous variable in the never-smokers and again found similar results. Because the impact of caffeinated beverages on health outcomes has earlier been found to be modified by age and sex (24–26), we also evaluated effect modification by age and sex. Finally, we performed a sensitivity analysis, in which we repeated the primary analysis but censored the participants who reported a diagnosis of hypertension from the time of the survey at which they reported to have the diagnosis. Differences with P values <0.05 were considered to be significant. Analyses were performed by using SAS 9.3 (SAS Institute).

RESULTS

Baseline characteristics

At baseline, the mean \pm SD age of our population was 45.5 ± 9.8 y, 48% of whom were men. Mean \pm SD baseline eGFR was 108.1 ± 14.6 mL \cdot min⁻¹ \cdot 1.73 m⁻², and mean annual decline in eGFR over 15 y of follow up was 1.01 ± 0.75 mL \cdot min⁻¹ \cdot 1.73 m⁻². Compared with those drinking <1 cup coffee/d, those who drank ≥ 1 cup/d were significantly more likely to be older, men, heavier, a current smoker, a heavy drinker, and to have hypertension and hypercholesterolemia. Furthermore, compared with those drinking <1 cup tea/d, those who drank ≥ 1 cup/d were significantly more likely to be older, women, and leaner and less likely to be lower educated, a current smoker, a heavy drinker, and to have hypertension (Table 1).

Associations of coffee and tea consumption with eGFR

The interaction between age and coffee consumption (at rounds 2–4) in relation to eGFR (at rounds 2–4) was significant ($P < 0.001$). Because limited studies are available on the overall association between coffee consumption and eGFR, we present both analyses of the total group and age-specific analyses, with results of the total group shown in Table 2. In the age- and sex-adjusted analysis, coffee consumption was associated with a higher eGFR, with significant β s of 1.29, 1.19, and 1.28 mL \cdot min⁻¹ \cdot 1.73 m⁻² for participants drinking 3–4, 5–6, or >6 cups/d, respectively, compared with <1 cup/d (P -trend = 0.04). This association remained after additional adjustment for other potential confounders. Additional adjustment for magnesium, potassium, and caffeine strengthened the association of coffee consumption with eGFR, with significant β s of 1.35, 1.36, and 1.61 mL \cdot min⁻¹ \cdot 1.73 m⁻² for participants drinking 3–4, 5–6, or >6 cups/d, respectively, compared with <1 cup/d (P -trend = 0.01).

The associations between coffee consumption and eGFR stratified by median age at baseline are shown in Table 3. Below the median age, there was no significant association between coffee consumption (at rounds 2–4) and eGFR (at rounds 2–4). In participants aged ≥ 46 y at baseline, the sex-adjusted analysis indicated a higher eGFR in those drinking 3–4, 5–6, or >6 cups coffee/d than in those drinking <1 cup/d (P -trend = 0.04). This association became stronger after adjustment for confounders in model 4, with eGFR being 2.40, 2.35, and 2.47 mL \cdot min⁻¹ \cdot 1.73 m⁻² higher in participants drinking 3–4, 5–6, or >6 cups/d than in those drinking <1 cup/d (P -trend = 0.02). Additional adjustment for biological risk factors and coffee constituents further strengthened the associations, resulting in significant β s of 2.72, 2.83, and 3.19 mL \cdot min⁻¹ \cdot 1.73 m⁻² for those drinking 3–4, 5–6, or >6 cups/d, respectively, compared with <1 cup/d (P -trend = 0.002).

The consumption of tea (at rounds 2–4) was not associated with eGFR (at rounds 2–4) (fully adjusted β : -0.28 ; 95% CI: $-0.90, 0.33$ mL \cdot min⁻¹ \cdot 1.73 m⁻² for >4 cups/d compared with <1 cup/d; Table 2). No interactions between tea intake and sex and age in relation to eGFR were observed (P -interaction > 0.10).

Association of coffee and tea consumption with change in eGFR

Coffee was not associated with subsequent annual changes in eGFR (fully adjusted β : -0.10 ; 95% CI: $-0.25, 0.04$ mL \cdot min⁻¹ \cdot 1.73 m⁻² for >6 cups/d compared with <1 cup/d; Table 4). Similar results were obtained for tea intake. The absence of an association between both coffee and tea consumption and subsequent annual changes in eGFR was also observed when we analyzed rapid decline in eGFR, defined by the loss of >3.0 mL \cdot min⁻¹ \cdot 1.73 m⁻² each year in eGFR. ORs ranged from 0.99 to 1.02 and were not significant (results not shown). Tests for interaction of coffee or tea intake by sex and age in relation to changes in eGFR or risk of rapid decline in eGFR offered no evidence of effect modification (P -interaction > 0.20). Finally, all results were similar when participants who reported a diagnosis of hypertension were censored (data not shown).

DISCUSSION

In this cohort of the general population, coffee, but not tea, consumption was associated with a slightly higher eGFR. When stratifying for age at baseline, this association was only apparent among those aged ≥ 46 y and was not explained by a range of potential confounders and intermediates. No associations were observed, however, between coffee and tea intake and subsequent changes in eGFR or risk of a rapid decline in eGFR.

Our results are consistent with previous findings of 2 observational studies in healthy Japanese adults, which showed that coffee consumption was associated with higher eGFR (7, 8). Of note, one study in Korean women showed that coffee consumption was associated with a decreased risk of renal function impairment in those with diabetes only (9). However, null findings have also been reported (10). In addition to the small scale of most of these studies (7, 8, 10), another limitation is their use of the creatinine-based abbreviated Modification of Diet in Renal Disease formula to estimate GFR, which is known to perform less well in those with normal eGFR (27–29). Furthermore, studies varied with regard to factors adjusted for in the multivariable analysis, and some were unable to adjust for confounding factors at all (10). In addition, due to their cross-sectional design, little light can be shed on causal pathways and hence the biological mechanisms involved.

Until now, only 1 clinical trial to our knowledge had examined the effects of coffee and tea consumption on eGFR. Similar to our findings, this study in 19 young Japanese nonsmokers showed that 14 d of coffee, but not green tea, consumption resulted in a significantly higher cystatin C–based eGFR (6). However, it is unclear whether the associations observed varied according to the dose of coffee. Furthermore, although magnesium concentrations were found to be significantly increased after coffee consumption, its potential mediating effects were not studied. We showed a clear dose-response relation, with a higher eGFR with increasing intake of coffee. Our finding that the association between coffee consumption and eGFR is not accounted for by a range of biological risk factors and coffee components—including caffeine—is novel. Nevertheless, given that blood samples in our study were nonfasting, it is impossible to rule out acute effects of caffeine entirely. Adjustment for time of last drink or meal before blood samples were taken, however, did not alter our findings. This suggests that other mechanisms are at

TABLE 1
Baseline characteristics of 4722 men and women according to coffee and tea intake¹

Characteristics	Coffee intake (cups/d)						Tea intake (cups/d)						P
	<1 (n = 249)	1-2 (n = 468)	3-4 (n = 1378)	5-6 (n = 616)	>6 (n = 1973)	P	<1 (n = 1555)	1-2 (n = 1666)	3-4 (n = 952)	>4 (n = 511)	P		
Age, y	40.9 ± 10.6	45.1 ± 10.9	46.8 ± 10.0	46.3 ± 9.7	45.1 ± 9.1	<0.001	44.3 ± 9.6	45.8 ± 9.6	46.7 ± 9.9	46.3 ± 10.5	<0.001		
BMI, kg/m ²	24.5 ± 4.0	24.8 ± 3.6	25.2 ± 3.6	25.4 ± 3.5	25.7 ± 3.5	<0.001	25.7 ± 3.7	25.4 ± 3.5	25.1 ± 3.6	24.8 ± 3.6	<0.001		
SBP, mm/Hg	120.9 ± 16.1	123.3 ± 16.4	125.0 ± 17.3	125.3 ± 16.3	124.8 ± 15.4	0.001	125.1 ± 15.4	124.9 ± 16.8	124.4 ± 16.7	122.0 ± 16.1	<0.001		
DBP, mm/Hg	78.5 ± 10.9	78.9 ± 10.1	79.9 ± 11.1	79.9 ± 10.8	79.8 ± 10.4	0.12	80.2 ± 10.4	79.7 ± 11.0	79.8 ± 10.5	78.4 ± 10.2	0.01		
TC, mmol/L	5.2 ± 1.0	5.3 ± 1.0	5.5 ± 1.0	5.5 ± 1.0	5.5 ± 1.0	<0.001	5.5 ± 1.0	5.5 ± 1.0	5.5 ± 1.0	5.4 ± 1.0	0.06		
Glucose, mmol/L	5.2 ± 1.6	5.3 ± 1.3	5.3 ± 1.3	5.3 ± 1.1	5.4 ± 1.3	0.22	5.4 ± 1.3	5.3 ± 1.3	5.3 ± 1.3	5.1 ± 0.8	<0.001		
Nutrient intake/d													
Energy, kcal	2110 ± 623	2097 ± 525	2159 ± 580	2286 ± 609	2377 ± 647	<0.001	2322 ± 650	2260 ± 617	2210 ± 591	2157 ± 572	<0.001		
Fat, g	83.5 ± 12.0	84.7 ± 11.1	84.8 ± 11.0	85.5 ± 11.5	86.7 ± 11.3	<0.001	86.7 ± 11.6	85.6 ± 11.0	85.0 ± 10.7	83.3 ± 12.0	<0.001		
Saturated fat, g	34.8 ± 6.1	35.0 ± 5.5	35.5 ± 5.5	35.7 ± 5.5	36.2 ± 5.5	<0.001	36.3 ± 5.7	35.7 ± 5.5	35.6 ± 5.3	34.7 ± 5.8	<0.001		
Total protein, g	81.9 ± 12.8	81.7 ± 11.5	82.3 ± 10.4	82.5 ± 10.1	82.3 ± 10.7	0.71	83.0 ± 11.1	81.9 ± 10.3	82.2 ± 10.6	81.3 ± 11.1	<0.001		
Fiber, g	23.9 ± 5.0	24.4 ± 4.9	24.9 ± 4.6	25.2 ± 4.6	24.6 ± 4.6	0.001	23.8 ± 4.7	24.8 ± 4.5	25.4 ± 4.5	25.9 ± 4.7	<0.001		
Vitamin C, g	117.9 ± 52.6	114.3 ± 45.0	112.9 ± 42.2	108.1 ± 41.3	99.1 ± 39.6	<0.001	99.3 ± 42.2	105.0 ± 37.8	114.7 ± 44.8	121.7 ± 47.2	<0.001		
Magnesium, mg	335 ± 52	344 ± 50	358 ± 44	370 ± 43	377 ± 48	<0.001	368 ± 50	363 ± 47	363 ± 46	363 ± 49	0.04		
Potassium, mg	3286 ± 527	3410 ± 497	3574 ± 448	3653 ± 428	3787 ± 493	<0.001	3741 ± 512	3615 ± 468	3582 ± 483	3545 ± 519	<0.001		
Caffeine, mg	240 ± 147	261 ± 105	362 ± 123	434 ± 121	574 ± 208	<0.001	472 ± 240	414 ± 185	435 ± 172	476 ± 174	<0.001		
eGFR, mL · min ⁻¹ · 1.73 m ⁻²	107.1 ± 13.5	105.3 ± 14.7	103.0 ± 14.4	103.9 ± 14.3	104.4 ± 13.7	<0.001	105.3 ± 14.0	103.7 ± 14.1	103.7 ± 14.2	103.4 ± 14.2	0.01		
Men, n (%)	75 (30.1)	161 (34.4)	510 (37.0)	307 (49.8)	1187 (60.2)	<0.001	922 (59.3)	823 (49.4)	336 (35.3)	159 (31.1)	<0.001		
Low education, n (%)	95 (38.2)	199 (42.5)	629 (45.7)	282 (45.8)	884 (44.8)	0.32	712 (45.8)	752 (45.1)	427 (44.9)	198 (38.8)	<0.001		
Current smoker	38 (15.3)	91 (19.5)	285 (20.7)	166 (27.0)	805 (40.8)	<0.001	646 (41.6)	462 (27.7)	184 (19.3)	93 (18.2)	<0.001		
Inactive, n (%)	10 (4.6)	13 (3.9)	43 (3.7)	11 (2.2)	68 (4.1)	0.06	61 (4.5)	47 (3.4)	26 (3.3)	11 (2.5)	0.64		
Heavy drinker, n (%)	14 (5.6)	46 (9.8)	147 (10.7)	93 (15.1)	338 (17.1)	<0.001	297 (19.1)	206 (12.4)	89 (9.4)	46 (9.0)	<0.001		
Diabetes, n (%)	3 (1.2)	5 (1.1)	22 (1.6)	8 (1.3)	29 (1.5)	0.92	23 (1.5)	22 (1.3)	16 (1.7)	6 (1.2)	0.84		
Hypertension, n (%)	59 (23.7)	127 (27.1)	443 (32.2)	191 (31.0)	584 (29.6)	0.04	484 (31.1)	519 (31.2)	274 (28.8)	127 (24.9)	0.03		
Hypercholesterolemia, n (%)	40 (16.1)	91 (19.5)	311 (22.6)	147 (23.9)	473 (24.0)	0.02	363 (23.4)	392 (23.6)	210 (22.1)	97 (19.0)	0.15		
Rapid eGFR decline, n (%)	17 (7.6)	29 (7.2)	104 (8.7)	46 (8.5)	153 (9.1)	0.76	123 (9.3)	125 (8.7)	64 (7.7)	37 (8.1)	0.58		

¹Values are means ± SDs unless otherwise indicated. P values were determined by using ANOVA or chi-square test. DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure; TC, total cholesterol.

TABLE 2

Regression coefficients (95% CIs) for the associations between coffee and tea intake at rounds 2–4 and estimated glomerular filtration rate at rounds 2–4 in the total study population¹

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Coffee intake, cups/d						
<1	Reference	Reference	Reference	Reference	Reference	Reference
1–2	−0.31 (−1.36, 0.73)	0.70 (−0.29, 1.70)	0.71 (−0.30, 1.73)	0.69 (−0.34, 1.73)	0.71 (−0.33, 1.74)	0.76 (−0.28, 1.81)
3–4	0.28 (−0.79, 1.35)	1.29 (0.27, 2.30)	1.28 (0.25, 2.31)	1.24 (0.18, 2.29)	1.23 (0.17, 2.29)	1.35 (0.25, 2.44)
5–6	0.48 (−0.63, 1.59)	1.19 (0.14, 2.24)	1.24 (0.17, 2.31)	1.20 (0.10, 2.30)	1.20 (0.09, 2.30)	1.36 (0.20, 2.52)
>6	0.82 (−0.28, 1.93)	1.28 (0.24, 2.33)	1.40 (0.34, 2.46)	1.33 (0.24, 2.43)	1.35 (0.25, 2.44)	1.61 (0.41, 2.81)
<i>P</i> -trend	0.004	0.04	0.01	0.02	0.05	0.01
Tea intake, cups/d						
<1	Reference	Reference	Reference	Reference	Reference	Reference
1–2	−0.64 (−1.04, −0.24)	−0.22 (−0.61, 0.16)	−0.43 (−0.82, −0.04)	−0.37 (−0.76, 0.02)	−0.36 (−0.75, 0.03)	−0.36 (−0.76, 0.03)
3–4	−0.57 (−1.08, −0.06)	0.10 (−0.38, 0.59)	−0.17 (−0.66, 0.33)	−0.04 (−0.54, 0.45)	−0.04 (−0.54, 0.46)	−0.02 (−0.53, 0.49)
>4	−0.83 (−1.45, −0.22)	−0.12 (−0.71, 0.47)	−0.56 (−1.15, 0.03)	−0.29 (−0.90, 0.33)	−0.28 (−0.90, 0.33)	−0.22 (−0.87, 0.44)
<i>P</i> -trend	0.005	0.76	0.11	0.43	0.45	0.52

¹*n* = 4722. Generalized estimating equation regression model 1: crude; model 2: adjusted for age and sex; model 3: adjusted as in model 2 and for highest attained level of education and time-dependent physical activity, BMI, smoking, alcohol consumption, daily energy intake (kcal), and energy-adjusted intakes of fiber, vitamin C, total protein, fat, and saturated fat; model 4: adjusted as in model 3 and for intake of tea (for coffee analysis) or coffee (for tea analysis); model 5: adjusted as in model 4 and for hypercholesterolemia, hypertension, and diabetes; model 6: adjusted as in model 5 and for energy-adjusted intakes of magnesium, potassium, and caffeine.

play. Findings from a secondary analysis in our study showed that censoring participants with a reduced eGFR (<60 mL · min^{−1} · 1.73 m^{−2}) during follow-up attenuated but did not remove the associations. Reverse causation therefore appears unlikely. Further research is required to study whether other coffee compounds, including quinides and niacin, may explain the slightly higher eGFR in coffee consumers, possibly through their antioxidant properties (30).

Increased coffee intake in our study was associated with a slightly higher eGFR only from middle age onward, whereas there was no such relation in younger participants. The relatively

wide CIs in the older group may be because fewer participants have the lowest consumption amounts (i.e., the reference group) compared with the number of low coffee consumers in the younger group. The possibility that the association between coffee intake and eGFR is age dependent therefore warrants further investigation. Interestingly, results from our group showed that higher coffee consumption was associated with lower blood pressure in participants >39 y of age but not in younger persons (26). This agrees with the findings of a study in which salt sensitivity was found to be more prevalent in older age groups (31). Perhaps the potential protective effects of

TABLE 3

Regression coefficients (95% CIs) for the associations between coffee intake at rounds 2–4 and estimated glomerular filtration rate at rounds 2–4, stratified by median age at baseline¹

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Age <46 y (<i>n</i> = 2382), cups/d						
<1	Reference	Reference	Reference	Reference	Reference	Reference
1–2	−0.14 (−1.21, 0.92)	0.40 (−0.65, 1.44)	0.40 (−0.66, 1.45)	0.30 (−0.77, 1.37)	0.32 (−0.75, 1.39)	0.29 (−0.80, 1.37)
3–4	−0.32 (−1.35, 0.72)	0.37 (−0.65, 1.39)	0.28 (−0.75, 1.31)	0.13 (−0.93, 1.19)	0.11 (−0.95, 1.17)	0.003 (−1.10, 1.11)
5–6	−0.52 (−1.63, 0.58)	0.13 (−0.97, 1.22)	0.12 (−1.00, 1.23)	−0.04 (−1.19, 1.12)	−0.07 (−1.22, 1.09)	−0.24 (−1.48, 1.00)
>6	−0.42 (−1.49, 0.65)	0.18 (−0.88, 1.25)	0.24 (−0.84, 1.32)	0.08 (−1.05, 1.22)	0.09 (−1.05, 1.22)	−0.14 (−1.42, 1.15)
<i>P</i> -trend	0.35	0.83	0.95	0.86	0.84	0.61
Age ≥46 y (<i>n</i> = 2340), cups/d						
<1	Reference	Reference	Reference	Reference	Reference	Reference
1–2	1.15 (−0.73, 3.02)	1.32 (−0.54, 3.18)	1.34 (−0.58, 3.26)	1.42 (−0.53, 3.36)	1.43 (−0.52, 3.39)	1.57 (−0.41, 3.54)
3–4	2.33 (0.39, 4.28)	2.27 (0.34, 4.20)	2.36 (0.39, 4.33)	2.40 (0.40, 4.40)	2.40 (0.39, 4.42)	2.72 (0.66, 4.78)
5–6	2.60 (0.60, 4.59)	2.16 (0.18, 4.13)	2.31 (0.29, 4.32)	2.35 (0.30, 4.40)	2.37 (0.30, 4.43)	2.83 (0.69, 4.98)
>6	2.98 (0.98, 4.99)	2.28 (0.29, 4.27)	2.49 (0.48, 4.50)	2.47 (0.42, 4.51)	2.50 (0.44, 4.55)	3.19 (0.99, 5.38)
<i>P</i> -trend	<0.001	0.04	0.01	0.02	0.02	0.002

¹Generalized estimating equation regression model 1: crude; model 2: adjusted for sex; model 3: adjusted as in model 2 and for highest attained level of education and time-dependent physical activity, BMI, smoking, alcohol consumption, daily energy intake (kcal), and energy-adjusted intakes of fiber, vitamin C, total protein, fat, and saturated fat; model 4: adjusted as in model 3 and for intake of tea; model 5: adjusted as in model 4 and for hypercholesterolemia, hypertension, and diabetes; model 6: adjusted as in model 5 and for energy-adjusted intakes of magnesium, potassium, and caffeine.

TABLE 4

Regression coefficients (95% CIs) for the associations between coffee and tea intake at rounds 2–4 and subsequent annual changes in estimated glomerular filtration rate between rounds 3 and 5 in the total study population¹

	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Coffee intake, cups/d						
<1	Reference	Reference	Reference	Reference	Reference	Reference
1–2	−0.02 (−0.14, 0.11)	0.05 (−0.08, 0.17)	0.02 (−0.11, 0.14)	0.02 (−0.10, 0.15)	0.02 (−0.10, 0.15)	−0.002 (−0.13, 0.12)
3–4	−0.01 (−0.12, 0.09)	0.05 (−0.06, 0.16)	0.01 (−0.10, 0.11)	0.02 (−0.10, 0.13)	0.01 (−0.10, 0.12)	−0.05 (−0.17, 0.07)
5–6	0.05 (−0.08, 0.17)	0.09 (−0.04, 0.21)	0.03 (−0.09, 0.16)	0.04 (−0.09, 0.17)	0.02 (−0.11, 0.15)	−0.06 (−0.20, 0.08)
>6	0.06 (−0.05, 0.17)	0.08 (−0.03, 0.19)	0.02 (−0.09, 0.13)	0.02 (−0.09, 0.14)	0.01 (−0.11, 0.13)	−0.10 (−0.25, 0.04)
<i>P</i> -trend	0.03	0.11	0.79	0.79	0.89	0.06
Tea intake, cups/d						
<1	Reference	Reference	Reference	Reference	Reference	Reference
1–2	−0.04 (−0.10, 0.02)	−0.01 (−0.07, 0.05)	−0.01 (−0.07, 0.05)	−0.01 (−0.07, 0.06)	−0.004 (−0.07, 0.06)	0.003 (−0.06, 0.07)
3–4	−0.08 (−0.15, −0.01)	−0.03 (−0.10, 0.04)	−0.03 (−0.10, 0.04)	−0.03 (−0.10, 0.04)	−0.03 (−0.10, 0.04)	−0.03 (−0.10, 0.05)
>4	−0.05 (−0.13, 0.03)	−0.01 (−0.09, 0.07)	0.01 (−0.08, 0.09)	0.02 (−0.08, 0.11)	0.006 (−0.09, 0.10)	−0.01 (−0.11, 0.09)
<i>P</i> -trend	0.23	1.00	0.86	0.79	0.86	0.98

¹*n* = 3786. Generalized estimating equation regression model 1: crude; model 2: adjusted for sex; model 3: adjusted as in model 2 and for highest attained level of education and time-dependent physical activity, BMI, smoking, alcohol consumption, daily energy intake (kcal), and energy-adjusted intakes of fiber, vitamin C, total protein, fat, and saturated fat; model 4: adjusted as in model 3 and for intake of tea (for coffee analysis) or coffee (for tea analysis); model 5: adjusted as in model 4 and for hypercholesterolemia, hypertension, and diabetes; model 6: adjusted as in model 5 and for energy-adjusted intakes of magnesium, potassium, and caffeine.

potassium, which is a salt constituent in coffee, may only become apparent once people age (26). However, although coffee is a rich source of potassium (78 mg/100 mL) (21), adjustment for potassium in our analysis strengthened, rather than weakened, our observed associations. This suggests that the effects of potassium are unlikely to fully explain the findings reported here. Alternatively, it has been suggested that the unfavorable detrimental short-term effects of coffee intake on blood pressure attenuate after prolonged use of coffee in older persons (32, 33). Although blood pressure is closely linked to eGFR, we cannot be sure that this would explain our observed association between coffee consumption and a higher eGFR in older participants.

Although the current findings suggest that coffee consumption seems to influence eGFR, the slightly increased eGFR does not necessarily reflect improved kidney function. The participants in this study had normal eGFR at baseline, and an increase in eGFR may reflect glomerular hyperfiltration (i.e., recruitment of renal functional reserve capacity). However, because hyperfiltration is supposed to reflect glomerular hypertension, which is considered a risk factor for hastened decline of eGFR over time (34), our finding of no association with eGFR changes at least does not support the view that the higher eGFR results from compensatory hyperfiltration. Therefore, coffee consumption is likely to be safe for the kidneys in the general population. This is in keeping with results from other studies that showed that coffee consumption was inversely associated with type 2 diabetes (4). Given the high consumption of coffee worldwide, our findings are of importance for public health. Further longitudinal studies, however, are needed to investigate whether coffee consumption reduces the risk of chronic kidney disease.

Until now, only 2 studies to our knowledge had examined the associations of tea consumption with eGFR (6, 8). Similar to our findings, these studies showed no significant association. There are several potential explanations. First, the consumption of tea was much lower than coffee, reducing the power to detect any

association. Second, the ability to detect significant associations may have been restricted because tea, relative to coffee, may have lower amounts of bioactive constituents that might have been responsible for the associations found with coffee. Alternatively, it may be that tea consumption is not associated with eGFR.

Our study has a number of strengths. The study population was large and community-based, which improves the generalizability of findings to the general population of this age group. The use of the equation that combines creatinine and cystatin C is another strength because it provides the most precise and accurate estimate of GFR (14). By measuring all available samples for each participant in one assay run, we obtained the most reliable measurements of biomarkers to estimate GFR (13). Further strengths were that, unlike in previous studies, participants in our study were surveyed periodically to obtain repeated-measures data, which enabled us to more effectively control for changes in exposures.

Limitations include the potential misclassification of the exposures because of self-report; this would probably bias the results toward the null, assuming it is nondifferential in nature. Results from a validation study in a subsample of participants also showed that coffee and tea were among the foods most accurately reported in the FFQ (11). Second, although we adjusted for a range of potential confounders, residual confounding due to unmeasured factors, such as medication use and sodium intake, cannot be excluded.

In this prospective study, we found that a higher coffee, but not tea, consumption was associated with a slightly higher eGFR, particularly in those aged ≥ 46 y. This association was not explained by sex, education, lifestyle, diet, biological risk factors, or coffee constituents. The absence of an association with subsequent annual changes in or risk of a rapid decline in eGFR suggests that the higher eGFR among coffee consumers is unlikely to be a result of glomerular hyperfiltration. Therefore, low to moderate coffee consumption is not expected to be a concern for kidney health in the general population.

The authors' responsibilities were as follows—G-CMH-G and AMWS: designed the research and were responsible for the manuscript's contents; G-CMH-G and HvE: performed the statistical analyses; G-CMH-G: wrote the manuscript; and all authors: were involved in the interpretation of the data, critically reviewed the manuscript, and approved the final version. The supporting agency had no role in the design or conduct of the study; the collection, analysis, or interpretation of the data; or the preparation or approval of the manuscript. None of the authors declared a conflict of interest.

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