Alcohol consumption is inversely associated with the risk of developing chronic kidney disease

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There are few reports of associations between alcohol consumption and risk of chronic kidney disease (CKD). To investigate this further, we studied 5476 participants aged 28–75 years in the Prevention of Renal and Vascular End-Stage Disease (PREVEND) study, a prospective population-based cohort, who were free of CKD at baseline (1997/1998). Alcohol consumption was self-reported on a questionnaire validated against serum high-density lipoprotein cholesterol. The primary outcome was *de novo* CKD defined as a combination of a creatinine–cystatin C–based estimated glomerular filtration rate (eGFR) under 60 ml/min per 1.73 m^2 and/or the mean of two consecutive 24-h urinary albumin excretions over 30 mg. During four serial follow-up examinations (median 10.2 years until February 2012), 903 participants developed CKD. Compared with those abstaining from alcohol, the multivariable-adjusted hazard ratios (95% confidence interval) for CKD risk were 0.85 (0.69–1.04) for occasional (under 10 g/week), 0.82 (0.69–0.98) for light (10–69.9 g/week), 0.71 (0.58–0.88) for moderate (70–210 g/week), and 0.60 (0.42–0.86) for heavier (over 210 g/week) alcohol consumers (significant trend). Similar inverse associations for alcohol consumption were found when CKD was defined as eGFR <60 ml/min per 1.73 m^2 or as 24-h urinary albumin excretion over 30 mg. Thus, in this population-based cohort, alcohol consumption was inversely associated with the risk of developing CKD.

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Although alcohol consumption, particularly in moderation, has consistently been linked to a lower risk of cardiovascular disease[1] and type 2 diabetes,[2] its association with the risk of chronic kidney disease (CKD) has received considerably less attention. So far, longitudinal cohort studies that have examined the effect of alcohol consumption on the development of CKD observed mostly inverse associations,[3–5] although some inconsistency exists.[5,6]

Most previous studies on alcohol and CKD risk relied on serum creatinine–based equations to assess glomerular filtration rate (GFR), such as the Cockgroft–Gault[7] or the Modification of Diet in Renal Disease (MDRD),[8] with uncertain validity in general population cohorts with higher GFR.[9,10] Furthermore, creatinine-based estimates to assess GFR are relatively imprecise owing to variation in nonrenal determinants of serum creatinine, a by-product of muscle breakdown. Such nonrenal influences—for example, meat intake, lean body mass, and muscle metabolism—may be related to alcohol consumption, which may introduce a varying degree of measurement bias in the estimation of GFR. A recently developed and validated equitation that also uses serum cystatin C as complementary filtration marker has been shown to be more accurate for estimating GFR,[11] and may thus be less subjective to the aforementioned shortcomings.

Besides estimated GFR (eGFR), urinary albumin excretion (UAE) can be used to supplement the classification of CKD.[12] So far, only two prospective cohort studies have investigated the relationship between alcohol intake and both components of CKD, albeit separately, and with opposing findings on albuminuria.[4,5]

Hence, we evaluated the association between alcohol consumption and the risk of CKD among participants in a population-based cohort study free of CKD at baseline and with serial measurements of serum creatinine, serum cystatin C, and UAE for a more optimal and integral definition of CKD.

RESULTS

Baseline characteristics of the study population according to alcohol consumption categories are shown in Table 1.

Table 1 | Baseline characteristics according to alcohol consumption among 5476 participants of the PREVEND study

Variables	Overall	Alcohol consumption categories (g of alcohol)					P-value
		No	Occasional (<10 g/wk)	Light (10–69.9 g/wk)	Moderate (70–210 g/wk)	Heavier (>210 g/wk)	
Participants, *N* (%)	5476	1285 (23.5)	860 (15.7)	1949 (35.6)	1121 (20.5)	261 (4.8)	
Age (years)	48.4 ± 11.7	50.2 ± 12.6	47.4 ± 12.5§	47.1 ± 11.4§	48.8 ± 10.7‡	49.2 ± 10.1	<0.001
Female, *n* (%)	2881 (52.6)	889 (69.2)	554 (64.4)*	928 (47.6)§	445 (39.8)§	65 (24.9)§	<0.001
Smoking, n *(%)*							
Never	1729 (31.7)	540 (42.3)	351 (41.0)	589 (30.3)‡	213 (19.1)§	36 (13.8)§	<0.001
Former	1985 (36.4)	372 (29.1)	287 (33.5)	761 (39.1)	477 (42.6)	88 (33.7)	
Current <6 cigarettes/day	298 (5.5)	56 (4.4)	46 (5.4)	114 (5.9)	71 (6.3)	11 (4.2)	
Current 6–20 cigarettes/day	1136 (20.8)	254 (19.9)	150 (17.5)	385 (19.8)	279 (24.9)	68 (26.1)	
Current >20 cigarettes/day	311 (5.7)	56 (4.4)	22 (2.6)	97 (5.0)	78 (7.0)	58 (22.2)	
Educational level, n *(%)*							
Low	2271 (41.5)	774 (60.2)	376 (43.7)§	674 (34.6)§	342 (30.5)§	105 (40.2)§	<0.001
Middle	1431 (26.1)	314 (24.4)	245 (28.5)	536 (27.5)	272 (24.2)	64 (24.5)	
High	1774 (32.4)	197 (15.3)	239 (27.8)	739 (37.9)	507 (45.2)	92 (35.2)	
Parental history of CKD, *n* (%)	82 (1.5)	25 (1.9)	11 (1.3)	24 (1.2)	17 (1.5)	5 (1.9)	0.49
History of CVD, *n* (%)	179 (3.3)	62 (4.8)	20 (2.3)‡	61 (3.1)*	32 (2.9)*	4 (1.5)*	0.003
Height (cm)	173.1 ± 9.4	169.6 ± 9.3	171.3 ± 9.0§	174.4 ± 9.2§	175.4 ± 9.1§	176.6 ± 8.7§	<0.001
Weight (kg)	77.1 ± 13.5	76.4 ± 14.6	76.2 ± 13.8	77.1 ± 12.8	77.9 ± 13.0‡	80.5 ± 13.6§	<0.001
Body mass index (kg/m^2)	25.7 ± 4.0	26.5 ± 4.7	25.9 ± 4.3§	25.3 ± 3.5§	25.3 ± 3.4§	25.8 ± 3.8‡	<0.001
Diastolic BP (mm Hg)	73 ± 9	73 ± 9	72 ± 9*	72 ± 9	74 ± 9‡	77 ± 9§	<0.001
Systolic BP (mm Hg)	126 ± 18	127 ± 20	125 ± 18	124 ± 17	127 ± 17	131 ± 17	<0.001
Use of BP-lowering drugs, (%)	639 (11.7)	222 (17.3)	95 (11.0)§	192 (9.9)§	100 (8.9)§	30 (11.5)*	<0.001
Hypertension, *n* (%)	1446 (26.4)	414 (32.2)	218 (25.3)‡	441 (22.6)§	284 (25.3)§	89 (34.1)	0.004
Total cholesterol (mmol/l)	5.6 ± 1.1	5.6 ± 1.1	5.5 ± 1.2*	5.5 ± 1.1‡	5.6 ± 1.1	5.8 ± 1.2‡	<0.001
HDL-cholesterol (mmol/l)	1.35 ± 0.39	1.30 ± 0.38	1.34 ± 0.4	1.36 ± 0.40§	1.40 ± 0.42§	1.37 ± 0.40*	<0.001
Triglycerides (mmol/l)	1.1 (0.8–1.6)	1.2 (0.9–1.7)	1.1 (0.8–1.6)‡	1.1 (0.8–1.5) §	1.1 (0.8–1.6)	1.2 (0.9–1.8)‡	<0.001
Use of lipid-lowering drugs, *n* (%)	281 (5.1)	91 (7.1)	41 (4.8)	78 (4.0) §	57 (5.1) *	14 (5.4)	0.016
Hypercholesterolemia, *n* (%)	1586 (29.0)	417 (32.5)	246 (28.6)	509 (26.1)§	323 (28.8)	91 (34.9)	0.15
Glucose (mmol/l)	4.7 ± 0.9	4.8 ± 1.1	4.7 ± 0.9‡	4.7 ± 0.7§	4.8 ± 0.9	5.0 ± 0.9	<0.001
HOMA-IR score	1.6 (1.1–2.4)	1.7 (1.2–2.7)	1.7 (1.2–2.5)	1.5 (1.0–2.2)§	1.5 (1.0–2.3)§	1.6 (1.0–2.5)	<0.001
Use of glucose-lowering drugs, *n* (%)	57 (1.0)	28 (2.2)	8 (0.9)*	12 (0.6)§	7 (0.6)‡	2 (0.8)	<0.001
Type 2 diabetes, *n* (%)	108 (2.0)	44 (3.4)	15 (1.7)*	21 (1.1)§	20 (1.8)*	8 (3.1)	0.009
C-reactive protein (mg/l)	1.1 (0.5–2.6)	1.4 (0.6–3.1)	1.1 (0.5–2.8)‡	0.9 (0.4–2.1)§	1.0 (0.4–2.5)§	1.4 (0.7–3.2)	<0.001
Creatinine (mg/dl)	0.80 ± 0.15	0.76 ± 0.15	0.78 ± 0.14	0.81 ± 0.15§	0.82 ± 0.15§	0.82 ± 0.14§	<0.001
Cystatin C (mg/l)	0.86 (0.77–0.95)	0.87 (0.78–0.97)	0.86 (0.77–0.95)	0.85 (0.77–0.94)§	0.86 (0.77–0.94)‡	0.87 (0.79–0.96)	<0.001
eGFR (ml/min per 1.73 m^2)	97.3 ± 14.8	95.1 ± 15.9	97.2 ± 14.8‡	98.3 ± 14.5§	98.0 ± 14.1§	98.2 ± 13.4‡	<0.001
Urine volume (ml per 24 h)	1576 ± 527	1513 ± 540	1568 ± 550*	1572 ± 513‡	1631 ± 502§	1714 ± 548§	<0.001
Urinary albumin excretion (mg per 24 h)	8.0 (5.8–12.3)	8.2 (5.8–12.3)	7.7 (5.7–11.8)	8.2 (6.0–12.0)	8.3 (6.1–12.4)	8.1 (5.9–12.9)	0.221

Abbreviations: BP, blood pressure; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate based on a combined creatinine-cystatin C equation; HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment-insulin resistance; PREVEND, Prevention of Renal and Vascular End-Stage Disease; wk, week.

Data are expressed as mean ± s.d., median (interquartile range) or proportion *n* (%).

P-values were based on analysis of variance (nonskewed continuous variables), Kruskal–Wallis test (skewed continuous variables), or χ^2-test (categorical variables). Superscripts denote whether a categorical level of alcohol consumption category differs significantly from the categorical level of no alcohol consumption in that row; *$P<0.05$, ‡$P<0.01$, §$P<0.001$.

Consistent with prior studies, subjects who consumed more alcohol were more likely to be male, current smokers, and more highly educated. Because of the substantial difference in gender across drinking categories, we additionally stratified baseline characteristics by gender (Supplementary Table S1 online). To validate self-reported alcohol consumption at baseline, we determined the relationship between alcohol consumption categories and high-density lipoprotein (HDL)-cholesterol. Mean serum HDL-cholesterol concentrations increased with increasing alcohol consumption category in both women and men (Table 2).

Alcohol consumption was fairly stable during follow-up. For instance, alcohol consumption at the first (baseline) and second examination (a median of 4.2 years later) was highly correlated ($\rho = 0.82$; $P<0.001$; $N = 5414$). In addition, 3655 (67.5%) subjects who attended the second examination reported the same alcohol category as the first examination, and 5186 (95.8%) subjects were in the same or an adjacent alcohol consumption category.

During a median follow-up of 10.2 years (interquartile range, 6.2–11.4 years), a total of 903 participants developed CKD (defined as a creatinine–cystatin C–based eGFR