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[Original article]

Effects of daily alcohol intake on glomerular filtration rate over three years

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Abstract

Background : The association between daily alcohol intake and changes in renal function in the Japanese general population is not well established.

Methods : We analyzed data from 150 residents who underwent specific health checkups held in Mishima Town in 2016 and 2019. We divided participants on the basis of alcohol consumption : residents with daily alcohol intake of < 20 g/day (the none-to-low group, $n = 104$, 69.3%) ; those with daily alcohol intake of ≥ 20 but < 40 g/day (the intermediate group, $n = 30$, 20.0%) ; and those with daily alcohol intake of ≥ 40 g/day (the high group, $n = 16$, 10.7%). We compared baseline characteristics. The primary endpoint was a decrease in estimated glomerular filtration rate (eGFR), defined as the decrease in eGFR greater than the median decrease over three years.

Results : The three-year changes in eGFR were +0.3 (−4.8, +3.0), −2.3 (−5.1, +1.2), and −4.9 (−8.2, −2.9) mL/min/1.73 m^2 in the none-to-low, intermediate, and high groups, respectively ($P = 0.007$). In the multivariate logistic regression analysis, a high amount of alcohol intake was independently associated with a decrease in eGFR, with adjusted odds ratio of 11.418 (95% confidence interval 1.554-83.879, $P = 0.017$).

Conclusion : A high average daily alcohol intake is associated with a decrease in eGFR.

Key words : glomerular filtration rate, renal function, specific health checkup, general population, alcohol

Introduction

Renal function is a strong predictor of high mortality not only in patients with heart failure[1)], but also in the general population[2)]. All-cause and cardiovascular mortality increase with a reduction of estimated glomerular filtration rate (eGFR) below 75 mL/min/1.73 m^2 in the general population[2)]. However, baseline renal function is unmodifiable, and it is crucial to predict and prevent deterioration in renal function[3)].

Specific health checkups are useful to detect residents who are at a high risk of cardiovascular disease, and are a good opportunity to provide lifestyle interventions[4)]. However, the usefulness of specific health checkups for predicting deterioration in renal function has not been fully examined, especially in the general population with normal renal function. Regarding modifiability, alcohol consumption is a target for lifestyle intervention[5-8)]. However, the association between daily alcohol intake and change in renal function has not been fully examined, particularly among Japanese. Thus, to clarify these issues in a general population with normal renal function, we carried out a cross-sequential and longitudinal observational study of specific health checkup results in collaboration with local government authorities involved in the administration of Japan's universal healthcare system.

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Methods

Subjects and protocol

This was a cross-sequential and longitudinal observational study of specific health checkups held in Mishima Town in Onuma County, Fukushima Prefecture, Japan. Residents aged 40–74 years old were eligible for the checkups. A study flowchart is shown in the Figure. We collected all the results of National Health Insurance beneficiaries who underwent specific health checkups both in 2016 and 2019 (n = 187). Residents who lacked data on eGFR (n = 3) and those with eGFR of < 60 mL/min/1.73 m^2 in 2016 (n = 34) were excluded. Finally, a total of 150 residents (70 male, 46.7% ; median age 67.0 years old) were included in the study. We divided participants on the basis of alcohol consumption : residents with daily alcohol intake of < 20 g/day (the none-to-low group, n = 104, 69.3%) ; those with daily alcohol intake of ≥ 20 but < 40 g/day (the intermediate group, n = 30, 20.0%) ; and those with daily alcohol intake of ≥ 40 g/day (the high group, n = 16, 10.7%). This study complied with the Declaration of Helsinki and the statement of STROBE (Strengthening the Reporting of Observational studies in Epidemiology)[9,10]. In addition, since the participants' information was anonymized and de-identified at the Mishima Town Office prior to analysis, written informed consent was not required or obtained from each resident, but opt-out methods were explained in public reports of the current study[11]. The study was publicized by posting a summary of the protocol on the website of Fukushima Prefectural Miyashita Hospital, at Mishima Town Office, and in Mishima Town's public relations magazine, where a notice clearly informed all residents of their right to refuse enrollment. The study protocol was approved by the research ethics committee of Fukushima Prefectural Miyashita Hospital (No. 20190001) and registered under the Japanese UMIN Clinical Trials Registration (UMIN 000036620).

We compared baseline (2016) demographic data, social history, past medical history, and the results of blood and urine tests among the three groups. Information about social history and past medical history was obtained from a standardized questionnaire. Regarding alcohol intake, participants were asked "How much do you drink per day, when converted to volume of sake?" with four response options (1, < 180 mL ; 2, ≥ 180 but < 360 mL ; 3, ≥ 360 but < 540 mL ; 4, ≥ 540 mL) and a conversion table "180 mL of sake is equivalent to 500 mL of beer, 110 mL of shochu, 60 mL of whiskey (a double), and 240 mL of wine." In the present study, 180 mL of sake was defined as containing 20 g of alcohol. Blood and urine tests were performed in a fasting state. The modified Modification of Diet in Renal Disease equation was used to calculate eGFR : eGFR (mL/min/1.73 m^2) = 194 * serum creatinine $^{(-1.094)}$ * age $^{(-0.287)}$ * 0.739 (if female)[12]. The rate of annual eGFR decline in the general Japanese population has been reported to be 0.36 mL/min/1.73 m^2, but this rate is affected by the coexisting diseases and baseline eGFR[13]. In this study, we set the primary outcome as a decrease in eGFR greater than the median decrease in this study population. The median three-year change in eGFR of the whole study population was −1.4 mL/min/1.73 m^2. Thus, change in eGFR over three years below −1.4 mL/min/1.73 m^2 was defined as a decrease in eGFR.

Statistical analysis

Continuous variables were presented as median (25th percentile, 75th percentile) and categorical variables were expressed as counts and percentages. The Jonckheere-Terpstra trend test and the Cochran-Armitage trend test were used for the comparisons of continuous and categorical variables, respectively. To avoid the problem of multiple comparisons, P values of the pairwise comparisons of groups after the Jonckheere-Terpstra trend test were adjusted by the Bonferroni correction. The impact of alcohol intake on a decrease in eGFR was assessed using logistic regression analysis. Odds ratios were then adjusted for age and sex, and further adjusted for established factors associated with deterioration in eGFR, namely age, sex, body mass index, current smoking, hypertension, diabetes mellitus, dyslipidemia, estimated glomerular filtration rate, and urine albumin-to-creatinine ratio[13–15]. P values of < 0.05 were considered statistically significant for all analyses. The Cochran-Armitage trend test was performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan) which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria)[16] and all other analyses were performed using SPSS ver. 26 (IBM, Armonk, NY, USA).

Results

In the current study, 16 of the 150 residents (10.7%) belonged to the high group (Figure). Baseline characteristics are shown in Table 1. The

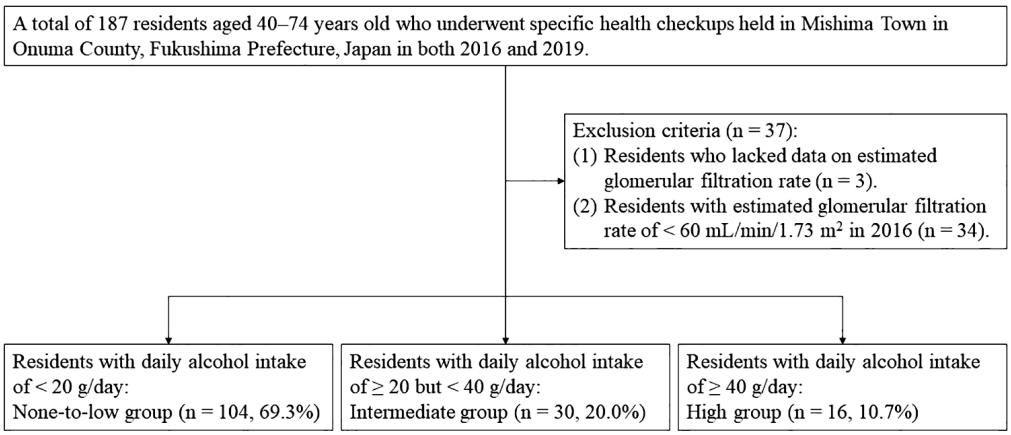

Figure. Study subject flowchart

three-year changes in eGFR were +0.3 (−4.8, +3.0), −2.3 (−5.1, +1.2), and −4.9 (−8.2, −2.9) mL/min/1.73 m^2 in the none-to-low, intermediate, and high groups, respectively (P = 0.007). There was no trend in age among groups, but the percentage of males increased with alcohol consumption (none-to-low, 67.0 years, 30.8% male ; intermediate 68.0 years, 73.3% male ; high, 63.5 years, 100.0% male, P < 0.001). Regarding social history and past medical history, there were significant trends in current smoking, diabetes mellitus, and hyperuricemia. Blood tests revealed that there was no trend in levels of baseline eGFR among the groups (P = 0.728) while there were significant trends from the none-to-low group to the high group in levels of liver enzymes. As to urine tests, there was no statistical trend in urine albumin-to-creatinine ratio.

The results of logistic regression analysis are summarized in Table 2. In the unadjusted model, a high amount of alcohol intake was associated with a decrease in eGFR compared to a low none-to-low amount as reference (odds ratio 9.545, 95% confidence interval 2.063-44.163, P = 0.004). After adjustment for pre-specified confounding factors, a high amount of alcohol intake was independently associated with a decrease in eGFR with adjusted odds ratio of 11.418 (95% confidence interval 1.554-83.879, P = 0.017).

Discussion

In this cross-sequential and longitudinal observational study, we found that a high amount of alcohol intake was significantly associated with a decrease in eGFR. The strength of this study was that we obtained data from specific health checkups available through a system of universal healthcare, so our results can be extrapolated to the general population with normal renal function. This study is of importance not only for daily clinical practice, but also for public policy, because we found that potential deterioration in eGFR can be estimated by specific health checkups.

The association between alcohol intake and prognosis remains controversial. Historically, a small amount of alcohol intake was considered to contribute to the reduction of all-cause mortality in the general population[17,18]. However, this J-curve phenomenon disappears after adjustment for bias and study characteristics[19]. A recent systematic analysis revealed that zero alcohol intake minimizes the overall risk to health[20]. Alcohol intake increases the risk of chronic diseases including cancer, depression, alcohol use disorders, hypertension, and cirrhosis[5,21-23]. On the other hand, the impact of alcohol consumption on renal function is still controversial. A large cohort study of female nurses reported that the amount of alcohol intake was not associated with later renal dysfunction[24], while a retrospective case-control study reported an association between alcohol consumption and end-stage renal disease[25]. According to a recent meta-analysis, alcohol consumption was inversely associated with risk for developing CKD[26]. However, there have been some studies that showed competing results[27,28]. A large community-based observational study in Japan, in which intermediate and high amounts of alcohol consumption were not distinguished, reported that an alcohol intake of more than 20 g/day had a neutral impact on later development of CKD[29]. The present study also focused on a Japanese general population, namely, participants with normal renal function who were eligible for specific health checkups. Our results suggest that a high amount of alcohol consumption (40 g/day or more) is associated with a decrease in eGFR. The

Table 1. Baseline characteristics (n = 150).

	None-to-low (n = 104)	Intermediate (n = 30)	High (n = 16)	P value
Change in eGFR (mL/min/1.73 m^2)	+0.3 (−4.8, +3.0)	−2.3 (−5.1, +1.2)	−4.9 (−8.2, -2.9)*	0.007
Decrease in eGFR (n, %)	44 (42.3)	17 (56.7)	14 (87.5)	<0.001
Demographic data				
Age (years)	67.0 (64.0, 70.0)	68.0 (65.0, 69.0)	63.5 (59.5, 66.5)	0.104
Male (n, %)	32 (30.8)	22 (73.3)	16 (100.0)	<0.001
Body mass index (kg/m^2)	23.1 (21.2, 24.8)	24.1 (22.2, 25.3)	25.2 (21.6, 26.5)	0.041
Systolic BP (mmHg)	124.0 (114.0, 136.0)	129.0 (118.0, 136.0)	128.0 (120.5, 136.0)	0.279
Diastolic BP (mmHg)	73.0 (67.0, 80.0)	77.5 (71.0, 82.0)	74.5 (69.0, 84.0)	0.105
Social history				
Smoking history (pack-years)	0.0 (0.0, 15.0)	3.3 (0.0, 30.0)	35.5 (0.5, 43.0)*	<0.001
Current smoking (n, %)	9 (8.7)	5 (16.7)	8 (50.0)	<0.001
Past medical history				
Hypertension (n, %)	40 (38.5)	10 (33.3)	11 (68.8)	0.095
Diabetes mellitus (n, %)	14 (13.5)	1 (3.3)	0 (0.0)	0.036
Dyslipidemia (n, %)	51 (49.0)	7 (23.3)	9 (56.3)	0.512
Cerebrovascular accident (n, %)	3 (2.9)	3 (10.0)	0 (0.0)	0.748
Heart disease (n, %)	6 (5.8)	1 (3.3)	0 (0.0)	0.278
Hyperuricemia (n, %)	4 (3.8)	3 (10.0)	3 (18.8)	0.018
Blood test				
eGFR (mL/min/1.73 m^2)	72.4 (65.7, 77.5)	68.9 (63.5, 75.8)	73.1 (69.3, 82.1)	0.728
Hemoglobin (g/dL)	13.6 (12.9, 14.8)	15.1 (14.0, 15.5)*	14.9 (14.4, 15.2)*	<0.001
FBG (mg/dL)	98.5 (93.0, 107.0)	102.0 (94.0, 109.5)	101.0 (95.0, 104.5)	0.225
HbA1c (%)	5.7 (5.4, 5.9)	5.6 (5.3, 5.8)	5.6 (5.4, 5.9)	0.196
HDL cholesterol (mg/dL)	60.0 (50.0, 73.5)	63.0 (50.0, 72.0)	57.0 (49.5, 66.5)	0.599
LDL cholesterol (mg/dL)	116.5 (104.0, 138.0)	124.0 (102.0, 142.0)	119.5 (101.5, 130.5)	0.986
Triglycerides (mg/dL)	86.0 (61.5, 116.5)	86.5 (75.0, 122.0)	111.5 (81.5, 291.0)*	0.008
Total cholesterol (mg/dL)	198.0 (175.5, 217.5)	205.0 (174.0, 230.0)	195.5 (177.5, 222.5)	0.570
AST (U/L)	22.0 (19.0, 25.0)	23.0 (21.0, 26.0)	26.0 (23.5, 33.0)*†	0.001
ALT (U/L)	16.0 (13.0, 20.5)	17.5 (15.0, 21.0)	24.5 (20.0, 28.0)*†	0.001
GGT (U/L)	20.0 (15.0, 30.0)	33.0 (20.0, 54.0)*	42.5 (32.0, 83.5)*	<0.001
Uric acid (mg/dL)	4.8 (4.1, 5.8)	6.1 (5.1, 6.5)*	6.2 (5.9, 7.3)*	<0.001
Urine test				
UACR (mg/g)	5.3 (3.9, 8.8)	5.5 (3.7, 7.2)	7.0 (4.1, 16.4)	0.695

eGFR, estimated glomerular filtration rate ; BP, blood pressure ; FBG, fasting blood glucose ; HbA1c, hemoglobin A1c ; HDL, high density lipoprotein ; LDL, low density lipoprotein ; AST, aspartate transaminase ; ALT, alanine transaminase ; GGT, γ-glutamyltransferase ; UACR, urine albumin-to-creatinine ratio.
*adjusted $P < 0.05$ vs. none-to-low and † adjusted $P < 0.05$ vs. intermediate after the Bonferroni correction.

discrepancy of the impact of alcohol consumption on renal function remains controversial. Drinking habits are influenced by cultural and genetic backgrounds over the world[30,31]. Although polyphenols show anti-atherosclerotic effects, amounts of polyphenols differs according to the types of beverages (wine, beer, etc.)[32]. As to genetic background, an allele of rs671 in aldehyde dehydrogenase 2 (ALDH2), a functional variant involved in alcohol metabolism, is specifically prevalent among East Asian populations[33,34]. A meta-analysis of genome-wide association studies for kidney function-related traits revealed that some loci including ALDH2 are associated with kidney function[35]. Thus, the impact of alcohol intake should be further elucidated, taking account of the type of beverages and characteristics of the study population. In addition, according to a large-scale Mendelian randomization analysis, an allele of rs1229984 in alcohol dehydrogenase 1B (ADH1B), a genetic variant associated with none or minimal alcohol intake, expresses a cardiovascular-protective profile[36].

Table 2. Logistic regression analysis for decreased estimated glomerular filtration rate (75 events / 150 participants).

Alcohol intake	Odds ratio	95% confidence interval	*P* value
Unadjusted model			
Intermediate (vs. none-to-low)	1.783	0.785-4.050	0.167
High (vs. none-to-low)	9.545	2.063-44.163	0.004
Adjusted model 1			
Intermediate (vs. none-to-low)	1.682	0.699-4.048	0.246
High (vs. none-to-low)	8.274	1.583-43.250	0.012
Adjusted model 2			
Intermediate (vs. none-to-low)	1.972	0.741-5.248	0.174
High (vs. none-to-low)	11.418	1.554-83.879	0.017

Adjusted model 1 : adjusted for age and sex.
Adjusted model 2 : adjusted for age, sex, body mass index, current smoking, hypertension, diabetes mellitus, dyslipidemia, estimated glomerular filtration rate, and urine albumin-to-creatinine ratio.

Since the current study was based on specific health checkups performed in a single town, the number of participants was relatively small. Thus, our results should be considered preliminary, and further studies or meta-analyses are necessary to confirm our findings. The amount of alcohol intake in 2016 was self-reported and changes in alcohol intake over the three years were not considered. In addition, taking into account the situations in which one typically drinks alcohol, the salt and protein from snacks consumed while drinking may have had an effect on the participants' renal function. However, these data were not available in the database used for our study.

In conclusion, a high amount of alcohol intake is associated with a decrease in eGFR in a Japanese cohort with normal renal function.

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Conflict of interest disclosure

None.

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