

The longitudinal associations between trajectory of and quantity of alcohol consumption and subsequent changes in blood pressure levels among non-hypertensive adults

Sukyoung Jung,^{1,2} Mi Kyung Kim,^{2,3*} Jinho Shin,⁴ Bo Youl Choi,^{2,3} Young-Hoon Lee,⁵ Dong Hoon Shin,⁶ and Min-Ho Shin⁷

¹*Department of Epidemiology, Milken Institute School of Public Health, George Washington University, Washington, DC, USA*

²*Institute for Health and Society, Hanyang University, Seoul, South Korea*

³*Department of Preventive Medicine, College of Medicine, Hanyang University, Seoul, South Korea*

⁴*Division of Cardiology, Department of Internal Medicine, College of Medicine, Hanyang University, Seoul, South Korea*

⁵*Department of Preventive Medicine & Institute of Wonkwang Medical Science, Wonkwang University College of Medicine, Iksan, South Korea*

⁶*Department of Occupational and Environmental Medicine, Keimyung University Dongsan Medical Center, Daegu, South Korea*

⁷*Department of Preventive Medicine, Chonnam National University Medical School, Gwangju, South Korea*



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***Corresponding author: Mi Kyung Kim**

Department of Preventive Medicine, College of Medicine, Hanyang University

17 Haengdang Dong, Sungdong Gu, Seoul, 133-791, Republic of Korea.

Phone: 82-2-2220-0667 Fax: 82-2-2293-0660 Email: kmkkim@hanyang.ac.kr

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Abstract

Given the dynamic characteristic of an individual's drinking behaviors, comprehensive consideration of alcohol consumption variation using repeated measures may improve insight into the nature of its association with blood pressure (BP) change. We examined the association between longitudinal alcohol consumption (trajectory and quantity) and changes in BP and pulse pressure (PP) among Korean aged ≥ 40 years living in rural areas. Totally, 1682 hypertension-free participants who completed all three health examinations (median, 5.3 years) were included. All three visits were used to determine the cumulative trajectory of and quantity of alcohol consumption and the latest two visits and the last visit were used for the recent trajectory and the most recent quantity of alcohol consumption, respectively. Changes in BP and PP from the baseline to the 3rd visit were used as outcome. In men, ≥ 30 ml/d cumulative average alcohol consumption was associated with the greatest increase in systolic BP (SBP) in both baseline outcome-unadjusted (2.9 mmHg, p-value = 0.032) and -adjusted models (3.6 mmHg, p-value = 0.001) and the given association for the most recent alcohol consumption was observed in the baseline outcome-adjusted model (3.9 mmHg, p-value = 0.003). For PP, similar associations were observed only in the baseline outcome-adjusted model. No meaningful associations in diastolic BP in men and any BP or PP in women existed. The quantity of alcohol consumption than the trajectory may be significantly related to raised SBP and a possible short-term influence of the most recent alcohol consumption may exist when baseline SBP adjusted in men.

Introduction

Elevated blood pressure (BP) is a leading global risk factor for cardiovascular disease and chronic kidney disease and its global prevalence increased continuously between 1990 and 2015 ⁽¹⁾. In 2013, the World Health Organization targeted a 25% relative reduction of the prevalence of elevated BP compared to that in 2010 to be achieved by 2025 for the global prevention and control of non-communicable diseases ⁽²⁾. Since the elevated BP has been appreciated as a lifelong and virtually irreparable condition linked to adverse health outcomes, maintaining normal BP is of critical importance ⁽³⁾. Pulse pressure (PP), which is defined as the difference between systolic BP (SBP) and diastolic BP (DBP), is a marker of arterial stiffness and may be an independent predictor of heart disease ⁽⁴⁾ and stroke ⁽⁵⁾. Yet, there is little evidence of risk factors associated with PP and PP changes.

Alcohol drinking has been extensively examined as a promising risk factor for elevated BP ⁽⁶⁻¹¹⁾ and hypertension ⁽¹²⁻¹⁷⁾ under various study designs. Collective evidence indicated that alcohol consumption had a positive linear association with incident hypertension ⁽¹²⁾ and BP changes in men ⁽⁶⁾ and a modest J-shaped association with no definite protective effect with incident hypertension in women ⁽¹²⁾, however, the given findings may not be enough to fully capture a longitudinal effect of alcohol consumption on BP. For the longitudinal perspective, it is important to note that individual's drinking behaviors are not static and more likely to be dynamic throughout the life course ⁽¹⁸⁾ and even in later life ^(18,19). However, most of the aforementioned studies failed to use the repeated measures of alcohol consumption ^(6,7,9-14,16) and even studies using repeated measures of alcohol consumption have examined at best one time-interval during the relatively long follow-up ⁽⁸⁾, or risk ratio, which cannot provide the extent of BP variation ⁽¹⁷⁾. The randomized controlled clinical trials (RCTs) with a long-term

administration of alcohol may be the best way to demonstrate the causal association, but they are not feasible to conduct due to intrinsic ethical and practical challenges ⁽²⁰⁾.

Given this, a comprehensive consideration of alcohol consumption variation over time using repeated measures may add new insight of the nature of its association with BP change. Therefore, this study aimed to evaluate whether there were longitudinal associations between alcohol consumptions and changes in BP and PP using three repeated measurements and to make comparisons of the associations between different trajectory of and quantity of alcohol consumption groups during the study period under different temporal conditions among Korean adults aged ≥ 40 years living in rural areas.

Materials and methods

Study population

The Korean Multi-Rural communities Cohort (MRCohort) is a population-based cohort of community dwellers from three rural counties (Yangpyeong, Namwon, and Goryeong) in South Korea and a part of the Korean Genome and Epidemiology Study (KoGES), described in detail elsewhere ⁽²¹⁾. At enrollment, we selected villages using multistage cluster sampling in three rural counties and their local residents were encouraged to participate in this study by their community leaders. A total of 8576 participants, who aged ≥ 40 years without a prior physician-diagnosis of heart diseases, stroke, and/or cancer, were recruited between February 2005 and December 2009. They were followed for between 2 and 4 years (mean 2.8 years) from January 2007 to December 2013, with follow-up rates of 79% for the 2nd visit (2007-2013) and 42% for the 3rd visit (2010-2013).

Of 3602 participants who had completed baseline and two follow-up questionnaires and

examinations (median 5.3 years of follow-up), we excluded participants with the following conditions: having a prior physician-diagnosis of hypertension at baseline (taking medication for hypertension or SBP \geq 140 mmHg or DBP \geq 90 mmHg at baseline health examination), diabetes, and/or dyslipidemia (n 1462); starting to take medications for hypertension during the follow-up period (n 337); having missing data on main variables (drinking status, alcohol consumption, and BP levels at each visit), covariates (smoking status, anthropometric measurements, education level, exercise habits, marital status, and job status), and reporting an implausible dietary intake (<500 or >4000 kcal/d) (n 121); The final analysis comprised 1682 participants (men, n 634; women, n 1048).

Ethics

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (Institutional Review Board of Hanyang University) and with the Helsinki Declaration of 1964, as revised in 2000. All participants provided written informed consent to voluntarily participate in this study at all examinations.

Assessment of alcohol consumption

At baseline and at each follow-up visit, alcohol consumption was assessed using questionnaires. The study participants were first asked whether they had ever consumed alcoholic beverages throughout their lifetime. If they answered ‘yes’, they were then asked if they were former or current drinkers of alcohol. For the current drinkers, we collected data on the average frequency of alcoholic beverage consumption (*soju*, *takju*, beer, refined rice wine, wine, and whisky) and the average amount of each beverage consumed per occasion during the past 12

months, using standard units of measure. Standard units for the alcoholic beverages were: 50 ml for *soju* and refined rice wine, 300 ml for *takju*, 200 ml for beer and wine, and 20 ml for whisky, having 10 ml to 15 ml alcohol in these all-standard units. Total daily alcohol consumption was calculated based on the total volume of each alcoholic beverage consumed, expressed in milliliters of alcohol per day (ml/d).

Definition of longitudinal alcohol consumption

As the comprehensive approach to better reflect longitudinal alcohol consumption over time and to compare the effect of each approach, we have presented both the trajectory of and quantity of alcohol consumption over the study period under the two different temporal conditions. First, for the cumulative term perspective (median 5-year), we used alcohol consumption measurements from all three visits under the assumptions and definitions as follows: 1) the trajectory (hereinafter referred to as $\text{alcohol}_{\text{trajectory (baseline, 2nd, 3rd)}}$) indicated the alcohol consumption pattern over the whole study period and was generated based on whether participants have consistently consumed certain levels of alcohol; 2) the quantity (hereinafter referred to as $\text{alcohol}_{\text{average (baseline, 2nd, 3rd)}}$) indicated the cumulative long-term alcohol consumption by considering the possible accrued changes and possible measurement errors⁽²²⁾ and it was calculated by averaging alcohol consumption measures from all three visits. Second, for the recent term perspective (median 3-year), we used alcohol consumption measurements from the latest two visits for the trajectory and the last visit for the quantity under the assumptions and definitions as follows: 1) the trajectory (hereinafter referred to as $\text{alcohol}_{\text{trajectory (2nd, 3rd)}}$) indicated the alcohol consumption pattern during the recent study period and was generated based on whether participants have consistently consumed certain levels of alcohol

between the 2nd and the 3rd visits; 2) the quantity (hereinafter referred to as alcohol_{recent} (3rd)) indicated the short latency effect of alcohol being consumed ⁽²³⁾ and alcohol consumption at the last visit was considered as quantity in the most recent period ^(22,23).

Assessment of covariates

Information on covariates was collected using a structured questionnaire and a comprehensive health examination with a standardized protocol. The list included: age, sex, medical history, education, marital status, job status, exercise habits, smoking status, body mass index (BMI), waist circumference (WC), and menopausal status in women. Higher education was defined as ≥ 12 years of schooling, while regular exercise was defined as exercise undertaken ≥ 3 times per week and ≥ 30 min per session. Smoking status was categorized into current smoking or not at baseline.

Height was measured with a standard height scale to the nearest 0.1 cm, and weight was measured using a metric weight scale to the nearest 0.1 kg, with participants wearing light clothing without shoes. BMI (kg/m^2) was calculated as weight (kg) divided by the square of the height (in meters). WC was measured at a halfway point between the lowest rib margin and the iliac crest. We used a validated food frequency questionnaire comprising 106 food items to obtain information concerning food and nutrient intake ⁽²⁴⁾.

Measurement of blood pressure

Auscultation was used to measure the participants' resting BP in the right arm, with a standard mercury sphygmomanometer and cuff. Two consecutive BP measurements were taken after each participant had been seated at rest for at least 5 minutes. SBP and DBP were measured

using the first and fifth Korotkoff sounds, to the nearest 2 mmHg. If the two SBP or DBP readings were >5 mmHg apart, an additional measurement was performed, and the mean value of the last two measurements was used for subsequent analyses. PP was calculated as the difference between the SBP and the DBP.

Statistical analyses

The demographic and health-related characteristics of study participants were presented as mean and standard deviation for continuous variables and as frequency and the percentage for categorical variables (Supplemental Table 1). All the following analyses were performed in men and women, separately due to the possible difference between two gender⁽¹²⁾. As a criterion for subsequent categorization, we used 30 ml/d of alcohol (2 units) for men based on the previous study⁽²⁵⁾ and above 0 ml/d of alcohol for women because only a few women consumed beyond 30 ml/d (n 13). Accordingly, we classified men into four categories: 1) For alcohol_{trajectory} (baseline, 2nd, 3rd), men consumed certain levels of alcohol persistently across three consecutive visits were defined as each consistent 0 ml/d, consistent >0 to <30 ml/d, or consistent ≥ 30 ml/d, respectively and men consumed varied levels of alcohol across three consecutive visits were defined as inconsistent. For example, if a participant consistently consumed >0 to <30 ml/d of alcohol at baseline and the second visit but consumed ≥ 30 ml/d at the last visit and then he/she was categorized as the inconsistent group. Detailed definitions were presented in Supplemental Table 2. For alcohol_{trajectory} (2nd, 3rd), men consumed certain levels of alcohol persistently during the last two consecutive visits were defined as each consistent 0 ml/d, consistent >0 to <30 ml/d, or consistent ≥ 30 ml/d, respectively and men consumed varied levels of alcohol during the last two consecutive visits were defined as inconsistent. 2) For alcohol_{average} (baseline, 2nd, 3rd), men were

categorized into 0 ml/d, >0 to <15 ml/d, 15 to <30 ml/d, and ≥ 30 ml/d of cumulative average alcohol consumption from all three visits. For alcohol_{recent (3rd)}, men were categorized into 0 ml/d, >0 to <15 ml/d, 15 to <30 ml/d, and ≥ 30 ml/d of the most recent alcohol consumption from the last visit. We classified women into three categories of the trajectory and two categories of the quantity: 1) For alcohol_{trajectory (baseline, 2nd, 3rd)}, women consumed certain levels of alcohol persistently across three consecutive visits were defined as each consistent 0 ml/d or consistent >0 ml/d, respectively and women consumed varied levels of alcohol across three consecutive visits were defined as inconsistent. For alcohol_{trajectory (2nd, 3rd)}, women consumed certain levels of alcohol persistently during the last two consecutive visits were defined as each consistent 0 ml/d or <0 ml/d, respectively and women consumed varied levels of alcohol during the last two consecutive visits were defined as inconsistent. 2) For alcohol_{average (baseline, 2nd, 3rd)}, women were categorized into 0 ml/d or >0 ml/d of cumulative average alcohol consumption from all three visits. For alcohol_{recent (3rd)}, women were categorized into 0 ml/d or >0 ml/d of the most recent alcohol consumption from the last visit.

A primary outcome was change in BP and PP from baseline to the 3rd visit. Changes in BP and PP levels were treated as continuous variables and calculated as the difference between the two measurements ($\Delta SBP_{\text{baseline, 3rd}} = SBP_{3\text{rd}} - SBP_{\text{baseline}}$; $\Delta DBP_{\text{baseline, 3rd}} = DBP_{3\text{rd}} - DBP_{\text{baseline}}$; $\Delta PP_{\text{baseline, 3rd}} = PP_{3\text{rd}} - PP_{\text{baseline}}$).

We assessed potential confounders that differed according to each category of longitudinal alcohol consumption groups using a general linear model (GLM) for continuous variables and categorical variables (Yes = 1/No = 0) and presented in Table 1, Supplemental table 3 to 5. Tukey's post-hoc comparison test was used to identify group differences at $p < 0.05$. We presented two different adjusted models including multivariable (fully adjusted for potential

confounders) and additionally adjusted for BP or PP levels at baseline ⁽²⁶⁾. Regarding the main analysis, we used GLM and Tukey's post-hoc comparison test to assess the longitudinal association between alcohol consumption and subsequent BP and PP levels (BP_{3rd} and PP_{3rd} levels and changes from baseline to the 3rd visit). For the quantities of alcohol consumption, a test for linear trend was conducted using the median value of each category of alcohol consumption as a continuous variable in the multivariable model.

We conducted several sensitivity analyses to assess the robustness of our findings: 1) When analyzing change values using repeated measures, we considered the possible presence of a regression-to-the-mean (RTM) effect ⁽²⁷⁾. Hence, we used a linear regression model to calculate the RTM effect ⁽²⁸⁾, which was taken into account in the analysis ⁽²⁷⁾. RTM-corrected change was calculated as follows: $\Delta RTM-SBP_{\text{baseline}, 3\text{rd}} = SBP_{3\text{rd}} - (a + b * SBP_{\text{baseline}})$, where a and b are the regression coefficients between $SBP_{3\text{rd}}$ and SBP_{baseline} , and the same calculation was applied to $\Delta RTM-DBP$ and $\Delta RTM-PP$ ⁽²⁸⁾. RTM-corrected changes from baseline to the 3rd visit were additionally assessed (data not shown); 2) BP and PP levels at the 3rd visit were also assessed as outcomes (Supplemental table 6 and 7); 3) we repeated the same analyses after excluding former drinkers at least one visit (n 1493) (data not shown).

All statistical analyses were performed using SAS software (Version 9.4, SAS Institute Inc.; Cary, NC, USA) and significance was assessed using an α -level of 0.05 (two-sided probability). Assuming a statistical power of 80% and a two-sided significance level of 0.05, the minimally detectable differences for SBP, DBP, and PP levels at the third visit are 2.52 mmHg, 1.66 mmHg, and 2.06 mmHg, respectively. Under the same assumption, the minimally detectable differences for changes in SBP, DBP, and PP levels are 2.39 mmHg, 1.63 mmHg, and 1.96 mmHg, respectively ⁽²⁹⁾.

Results

At baseline, the mean age of the study participants was 59.2 years, 37.7 % of the study participants were men, and 21.3% of participants had graduated from high school or had been educated to a higher level. 87.7% had married and 60% were farmers. A total of 42.8% ($n = 720$) were current drinkers, 4.2% ($n = 70$) were former drinkers, and the average SBP, DBP, and PP was 115.0 mmHg, 75.1 mmHg, and 39.9 mmHg, respectively (Supplemental Table 1). Men who consistently consumed ≥ 30 ml/d of alcohol across all three visits or consumed ≥ 30 ml/d of cumulative average alcohol engaged in significantly higher proportion of current smoking and similar results were observed when alcohol consumption groups for the recent term were examined (Table 1 and Supplemental table 3 to 5). Women who consumed varied range of alcohol across three visits or consumed >0 ml/d of the cumulative average or the most recent alcohol engaged in significantly higher proportion of regular exercise (Table 1, Supplemental table 3 and 5). The majority of our study participants were likely to maintain their alcohol consumption pattern within median of 5-year (proportion of inconsistent trajectory group: 35.5% in the cumulative term and 9.0% in the recent term for men; 20.3% in the cumulative term and 12.8% in the recent term for women).

Table 2 presents the longitudinal associations of both the trajectory of and the quantity of alcohol consumption groups with subsequent changes in BP ($\Delta BP_{\text{baseline, 3rd}}$) and PP ($\Delta PP_{\text{baseline, 3rd}}$) from the baseline to the 3rd visit in men. In the baseline outcome-unadjusted model, the trajectories of alcohol consumption were not associated with any BP or PP changes. Regarding the quantity, consuming ≥ 30 ml/d of alcohol_{average (baseline, 2nd, 3rd)} was significantly linearly associated with the greatest increase in SBP ($\Delta SBP_{\text{baseline, 3rd}} = 2.9$ mmHg, $p\text{-value} = 0.032$, $p\text{-trend} = 0.022$) and alcohol_{recent (3rd)} has shown an only linear trend with no significant difference

across each group (p-trend = 0.031). No significant or meaningful associations were observed regarding DBP or PP change except for the linear trend of alcohol_{average (baseline, 2nd, 3rd)} with PP change (p-trend = 0.025). In the baseline outcome-adjusted model, alcohol_{trajectory (baseline, 2nd, 3rd)} was not associated with any BP or PP changes but consuming ≥ 30 ml/d of alcohol_{average (baseline, 2nd, 3rd)} was significantly linearly associated with the greatest increase in SBP ($\Delta SBP_{\text{baseline, 3rd}} = 3.6$ mmHg, p-value = 0.001, p-trend = 0.0002) and in PP ($\Delta PP_{\text{baseline, 3rd}} = 7.4$ mmHg, p-value = 0.007, p-trend = 0.001). Both alcohol_{trajectory (2nd, 3rd)} and alcohol_{recent (3rd)} have shown significant linear associations with subsequent changes in SBP (p-value = 0.047 for the trajectory; p-value 0.003, p-trend = 0.0003 for the quantity at the last visit). Alcohol_{recent (3rd)} has shown an only linear trend for DBP (p-trend = 0.034) and consuming ≥ 30 ml/d of alcohol_{recent (3rd)} was significantly linearly associated with the greatest increase in PP ($\Delta PP_{\text{baseline, 3rd}} = 7.3$ mmHg, p-value = 0.022, p-trend = 0.005).

Table 3 has shown longitudinal associations of both the trajectory of and the quantity of alcohol consumption groups with changes in BP ($\Delta BP_{\text{baseline, 3rd}}$) and PP ($\Delta PP_{\text{baseline, 3rd}}$) levels from the baseline to the 3rd visit in women. No significant or meaningful associations of both the trajectory and the quantity of alcohol consumption with any BP or PP changes irrespective of the baseline outcome adjustment.

Discussion

In this longitudinal study of hypertension-free Korean adults, the quantity of alcohol consumption had stronger association with changes in SBP than the trajectory of alcohol consumption in both the cumulative term (median 5-year) and the recent term (median 3-year) in men. Importantly, consuming ≥ 30 ml/d of cumulative average alcohol was significantly

associated with the greatest increase in SBP irrespective of further adjustment for the baseline outcome. The similar SBP changes by the most recent alcohol consumption to cumulative average alcohol consumption were observed in both the baseline outcome-unadjusted and -adjusted model in men. Both the cumulative and the most recent alcohol consumption were significantly associated with PP in men in the baseline outcome-adjusted model. No significant or meaningful associations were observed for DBP in men and any BP or PP in women.

First, our data consistently presented an adverse effect of consuming ≥ 30 ml/d of alcohol on increase in SBP and PP, which is in line with previous findings ^(6,8,9). It is of interest to identify whether a threshold at which alcohol intake became harmful or any beneficial zone of alcohol consumption and its temporal difference is existed. Yet, the existence of such beneficial zone remains unclear, mostly supported the detrimental effect of consuming ≥ 2 drinks per day on BP ^(6,8,9). However, our stronger associations of the quantity of alcohol consumption than the trajectory of alcohol consumption in men could not be directly compared due to the lack of studies simultaneously evaluating these longitudinal variations of alcohol consumption. Considering our approach using the trajectory, the classified categories may not be perfect due to 1) inherent limitations of the categorization method when trajectory defined such as misclassification and loss of power ⁽³⁰⁾, 2) aggregation of too many sub-categories into one inconsistent trajectory group, and 3) lack of sample size for further specification of inconsistent trajectory group. Despite the given challenges need to be addressed in further studies with competent sample size, the quantity may be more informative than the change value or trajectory based on our study.

Another issue in the present finding was that there was the discrepancy in the association between SBP, DBP, and PP. Unlike SBP and PP, there was no association in

subsequent DBP changes. Previously, Framingham heart study among relatively young adults showed an increased change in DBP in those with heavy baseline alcohol consumption levels⁽³¹⁾. As SBP continuously increases with age but DBP decreases after 60 years of age, accordingly PP sharply increases⁽³²⁾. Therefore, increased SBP or PP levels have been suggested to be better predictors of cardiovascular events than DBP in the relatively old age group⁽³³⁾.

The third issue in our finding was that although the cumulative term effect seems to be stronger than the recent term effect on SBP in the baseline outcome-unadjusted model, interestingly, habitual ≥ 30 ml/d alcohol consumption during the recent year showed the similar SBP changes to cumulative consumption in both the baseline outcome-unadjusted and -adjusted model. In the view of not fully understanding the exact latency period yet, it would be meaningful to note that a short term latent positive association may exist between habitual heavy alcohol consumption and SBP changes. Additionally, the longitudinal variation of alcohol consumption can be represented in diverse ways including trajectory, and quantity as well as change value itself. Previous studies using change values of alcohol consumption and BP have suggested that the linear association⁽⁶⁾ or the J-shaped association between alcohol consumption change and BP change⁽⁸⁾, however, our additional analyses using changes in alcohol consumption as continuous, quantiles, or decreased/unchanged/increased categorization did not provide any meaningful association (data not shown). Since change value itself can neglect actual pattern of or total quantity of alcohol consumption over time, our efforts to fully capture the longitudinal alcohol consumption has been made by presenting both the trajectory of and the quantity of alcohol consumption.

In longitudinal analysis using repeated measures, attempts to minimize potential biases should be made to provide more valid findings. When analyzing determinants of change in

health status, the baseline outcome has usually been adjusted under the criteria of confounder⁽²⁶⁾ or to obtain information on the influence of a new exposure under the condition that baseline outcomes are the same. Previous studies have treated baseline BP differently, with adjustment^(15,34-36) or not^(13,37,38) and concerns about adjustment for baseline outcome are related to the RTM bias that may create a pseudo-inverse association between a possible protective risk factor and an outcome^(26,39). To address this issue, we have presented two multivariable adjusted models without and with further baseline outcome adjustment. Since alcohol consumption was considered as harmful factor for BP or PP and the RTM bias may reduce BP changes when adjusting for baseline outcome (data not shown), our findings from the baseline outcome-adjusted models could be considered conservative.

The mechanism through which alcohol increases BP is complex⁽⁴⁰⁾. It has been suggested that increased calcium ions in vascular smooth muscle, increased oxidative stress, and decreased nitric oxide bioavailability influence endothelial dysfunction and alter vascular responsiveness. These mechanisms appear to be more possibly involved in increasing BP than other mechanisms⁽⁴⁰⁾. Habitually consuming heavy quantities of alcohol may lead to an increase in BP through increasing oxidative stress, via increasing sympathetic nervous system activity and through stimulation of the renin-angiotensin aldosterone system⁽⁴⁰⁾.

Our study has some limitations concerning the interpretation of results. First, it is difficult to draw any definite causal inference based on our findings due to observational study design. Second, with the use of cumulative averaging, there was still a possibility that real changes in alcohol consumption habits during follow-up were not reflected. In spite of our efforts to consider both patterns and quantities, real changes in alcohol consumption or important drinking pattern of how frequently they drank or how many drinks per occasion are still not be evaluated.

Third, our results are prone to sick-quitter effect ⁽¹⁴⁾ because some former drinkers during the follow-up (*n* 189) were categorized into the referent group. However, we observed similar associations when we repeated the same analysis after excluding for former drinkers at least once during the whole study period (data not shown, *n* 1493). Fourth, a possible sex difference in the shape of such association may exist due to different ethanol metabolism, however, we could not definitely conclude the existence of such difference because only a few women consumed beyond 30 ml/d (*n* 13). Fifth, because those who were participated to all study examinations but excluded in the final analytic set were older, more likely to engage in higher education, less likely to engage in marriage and farming as an occupation than study participants, interpretation should be made with caution in the view of the applicability to different distributions of demographic, socioeconomic, geographic, and/or ethnic characteristics. Sixth, we may overestimate the strength of the true association by excluding approximately 14% of study participants who started taking hypertension medication during the follow-up period to reduce the possibility of confounding by such drug effect. However, we found similar results when such participants were included (data not shown). Finally, alcohol consumption was measured using an alcohol frequency questionnaire which may lead underreporting of alcohol consumption. Although alcohol questionnaires had shown a relatively high validity and validating the alcohol consumption measure was not within the scope of the current study, the misclassification bias may be existed ⁽⁴¹⁾. Despite these limitations, to date there have been no reports of the longitudinal association between alcohol consumption and BP and PP level changes with comprehensive approaches considering the trajectory and the quantity aspects. Furthermore, to our knowledge, this is the first study attempting to identify the existence of the temporal difference in the given association.

In conclusion, consuming alcohol beyond 30 ml/d was linked with greater increase in SBP and PP and the given association was more evident than the trajectory in Korean men aged ≥ 40 years. Besides the significant positive association of cumulative alcohol consumption with SBP changes, a short-latent positive association of the recent habitual alcohol consumption also seems to exist. There is no definite evidence on beneficial zone of alcohol consumption. Further large-scale studies on longitudinal alcohol consumption and subsequent responses in BP with more repeated measures and longer follow-up period are warranted to provide evidence for primary prevention of hypertension.

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Conflict of interest

The authors declare that there is no conflict of interest.

Author contributions

M.K.K, J.S, B.Y.C, Y.H.L, D.H.S, and M.H.S contributed to the conception or design of the work. S.J and M.K.K contributed to the acquisition, analysis, or interpretation of data for the work. S.J and M.K.K drafted the manuscript and critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Supplementary material

Supplementary material for this article is available online.

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Table 1. Age-adjusted characteristics of study participants according to consistency of alcohol consumption groups during the follow-up¹

| | Men (n 634) | | | | | | | | | Women (n 1048) | | | | | | |
|---|--------------------|-----|--------------------------|-----|-------------------------|-----|------------------------|-----|----------------------|-------------------|-----|-----------------------|-----|-------------------------|-----|----------------------|
| | Consistent 0 | | Consistent >0 and <30 | | Inconsistent | | Consistent ≥30 | | p-value ² | Consistent 0 | | Inconsistent | | Consistent >0 | | p-value ² |
| | Mean or % | SE | Mean or % | SE | Mean or % | SE | Mean or % | SE | | Mean or % | SE | Mean or % | SE | Mean or % | SE | |
| n | 213 | | 106 | | 225 | | 90 | | | 636 | | 213 | | 199 | | |
| Median change in alcohol consumption from initial to last visit (min, max) | 0.0 (0.0, 0.0) | | -1.4 (-27.1, 18.8) | | -2.5 (-318.8, 395.9) | | 0.0 (-388.5, 292.5) | | | 0.0 (0.0, 0.0) | | -0.3 (-46.6, 28.9) | | -0.9 (-465.0, 288.5) | | |
| Follow up period (years) | 5.4 | 0.1 | 5.3 | 0.1 | 5.3 | 0.1 | 5.3 | 0.1 | 0.962 | 5.3 | 0.0 | 5.1 | 0.1 | 5.3 | 0.1 | 0.198 |
| Age (years) | 63.0 ^a | 0.6 | 59.1 ^b | 0.9 | 61.6 ^{ab} | 0.6 | 60.2 ^{ab} | 0.9 | 0.002 | 58.5 ^a | 0.4 | 56.6 ^b | 0.6 | 57.0 ^{ab} | 0.6 | 0.008 |
| Menopause | - | - | - | - | - | - | - | - | | 76.9 | | 78.0 | | 77.7 | | 0.883 |
| Higher education ³ | 32.0 | | 32.1 | | 24.3 | | 20.3 | | 0.057 | 18.6 | | 16.8 | | 15.0 | | 0.418 |
| Married | 96.6 | | 93.8 | | 97.8 | | 96.4 | | 0.326 | 82.9 | | 81.7 | | 81.2 | | 0.820 |
| Farmer | 67.7 | | 69.3 | | 65.5 | | 78.5 | | 0.132 | 51.4 | | 56.5 | | 52.0 | | 0.427 |
| Regular exercise ⁴ | 23.9 | | 19.2 | | 19.6 | | 11.9 | | 0.125 | 18.2 ^a | | 26.0 ^b | | 24.2 ^{ab} | | 0.022 |
| Current smoker | 31.9 ^a | | 30.5 ^a | | 40.0 ^{ab} | | 50.8 ^b | | 0.006 | 1.9 | | 2.6 | | 3.1 | | 0.580 |
| BMI (kg/m ²) | 23.6 | 0.2 | 23.4 | 0.3 | 23.7 | 0.2 | 23.0 | 0.3 | 0.197 | 23.9 | | 24.0 | | 23.9 | | 0.970 |
| WC (cm) | 84.0 | 0.5 | 83.8 | 0.8 | 85.4 | 0.5 | 83.6 | 0.8 | 0.136 | 81.8 | 0.3 | 81.9 | 0.6 | 82.5 | 0.6 | 0.592 |
| Baseline SBP (mmHg) | 115.8 ^a | 0.7 | 117.2 ^{ab} | 1.0 | 117.5 ^{ab} | 0.7 | 120.7 ^b | 1.1 | 0.004 | 113.4 | 0.4 | 112.8 | 0.8 | 114.7 | 0.8 | 0.203 |
| Baseline DBP (mmHg) | 75.9 | 0.5 | 76.6 | 0.7 | 76.3 | 0.5 | 77.5 | 0.8 | 0.413 | 73.8 ^a | 0.3 | 74.2 ^{ab} | 0.5 | 75.9 ^b | 0.5 | 0.003 |
| Baseline PP (mmHg) | 39.9 ^a | 0.6 | 40.7 ^{ab} | 0.9 | 41.2 ^{ab} | 0.6 | 43.2 ^b | 0.9 | 0.028 | 39.6 | 0.3 | 38.6 | 0.5 | 38.8 | 0.6 | 0.189 |
| Total energy (kJ/d) | 7107 | 136 | 7032 | 193 | 7193 | 132 | 7244 | 209 | 0.854 | 6172 | 66 | 6153 | 115 | 6214 | 119 | 0.929 |
| Na intake (mg/d) | 2956 | 117 | 2978 | 166 | 3040 | 113 | 3282 | 180 | 0.482 | 2371 | 56 | 2366 | 97 | 2476 | 100 | 0.637 |
| K intake (mg/d) | 1884 | 41 | 1959 | 59 | 1934 | 40 | 1932 | 63 | 0.721 | 1661 | 22 | 1703 | 39 | 1735 | 40 | 0.239 |

SE, standard error; BMI, body mass index; WC, waist circumference; Na, sodium; K, potassium; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure

¹ All results except each median value were adjusted for sex and age, but sex was adjusted for age and age was adjusted sex. All nutrient intakes are total energy-adjusted values. Values are expressed as the mean ± SE or percentage (%). Mean values with different superscripts (a, b, c) within a row were significantly different among the exposure groups by Tukey's multiple comparison test.² p-value was determined using a general linear model.³ ≥ High school graduation (12 years of education)⁴ ≥3 times/week and ≥30 min/session

Table 2. Multivariable-adjusted changes in blood pressure and pulse pressure during follow-up according to longitudinal alcohol consumption groups in men (*n* 634)¹

| | <i>Trajectory of alcohol consumption</i> | | | | | | | | <i>p</i> -value ² | <i>Quantity of alcohol consumption</i> | | | | | | | | <i>p</i> -value ² | <i>p</i> -trend ³ |
|--|--|-----|------------------------------------|-----|---------------------|-----|-----------------------|-----|------------------------------|--|-----|------------------------|-----|----------------------|-----|------------------|-----|------------------------------|------------------------------|
| | Consistent 0 | | Consistent >0 and <30 | | Inconsistent | | Consistent ≥30 | | | 0 | | >0 to <15 | | ≥15 to <30 | | ≥30 | | | |
| | Mean | SE | Mean | SE | Mean | SE | Mean | SE | | Mean | SE | Mean | SE | Mean | SE | Mean | SE | | |
| <i>Cumulative term effect⁴</i> | | | | | | | | | | | | | | | | | | | |
| <i>n</i> | 213 | | 106 | | 225 | | 90 | | | 213 | | 168 | | 69 | | 184 | | | |
| Changes ⁶ in SBP (mmHg) | | | | | | | | | | | | | | | | | | | |
| Multivariable | 1.1 | 0.9 | -0.8 | 1.3 | 1.5 | 0.9 | 2.0 | 1.4 | 0.445 | 1.1 ^{ab} | 0.9 | -1.3 ^a | 1.0 | 1.5 ^{ab} | 1.6 | 2.9 ^b | 1.0 | 0.032 | 0.022 |
| Multivariable + baseline SBP | 0.1 | 0.9 | -1.2 | 1.3 | 1.4 | 0.8 | 3.4 | 1.3 | 0.061 | 0.1 ^a | 0.9 | -1.7 ^a | 1.0 | 1.9 ^{ab} | 1.5 | 3.6 ^b | 0.9 | 0.001 | 0.0002 |
| Changes ⁶ in DBP (mmHg) | | | | | | | | | | | | | | | | | | | |
| Multivariable | -3.9 | 0.7 | -5.5 | 1.0 | -4.4 | 0.7 | -4.4 | 1.0 | 0.607 | -4.0 | 0.7 | -5.4 | 0.8 | -4.9 | 1.2 | -4.0 | 0.7 | 0.443 | 0.527 |
| Multivariable + baseline DBP | -4.6 | 0.6 | -5.9 | 0.9 | -4.7 | 0.6 | -3.7 | 0.9 | 0.392 | -4.7 | 0.6 | -5.9 | 0.7 | -4.6 | 1.1 | -3.8 | 0.6 | 0.167 | 0.088 |
| Changes ⁶ in PP (mmHg) | | | | | | | | | | | | | | | | | | | |
| Multivariable | 5.1 | 0.8 | 4.7 | 1.1 | 5.9 | 0.7 | 6.3 | 1.2 | 0.641 | 5.0 | 0.8 | 4.1 | 0.9 | 6.4 | 1.3 | 6.9 | 0.8 | 0.088 | 0.025 |
| Multivariable + baseline PP | 4.6 | 0.7 | 4.6 | 1.0 | 6.0 | 0.7 | 7.3 | 1.1 | 0.138 | 4.6 ^a | 0.7 | 4.0 ^a | 0.8 | 6.6 ^{ab} | 1.2 | 7.4 ^b | 0.8 | 0.007 | 0.001 |
| <i>Recent term effect⁵</i> | | | | | | | | | | | | | | | | | | | |
| <i>n</i> | 285 | | 144 | | 57 | | 148 | | | 285 | | 144 | | 57 | | 148 | | | |
| Changes ⁶ in SBP (mmHg) | | | | | | | | | | | | | | | | | | | |
| Multivariable | 1.0 | 0.9 | -0.0 | 1.2 | 0.6 | 1.1 | 2.9 | 1.3 | 0.377 | -0.02 | 0.8 | 0.7 | 1.1 | 2.4 | 1.8 | 2.9 | 1.1 | 0.154 | 0.031 |
| Multivariable + baseline SBP | 0.2 | 0.9 | 0.0 | 1.1 | 0.3 | 1.0 | 3.9 | 1.2 | 0.047 | -0.8 ^a | 0.8 | 0.4 ^{ab} | 1.1 | 2.1 ^{ab} | 1.7 | 3.9 ^b | 1.0 | 0.003 | 0.0003 |
| Changes ⁶ in DBP (mmHg) | | | | | | | | | | | | | | | | | | | |
| Multivariable | -4.3 | 0.7 | -5.8 | 0.9 | -4.0 | 0.8 | -3.8 | 0.9 | 0.350 | -4.7 | 0.6 | -4.7 | 0.8 | -5.0 | 1.3 | -3.5 | 0.8 | 0.646 | 0.235 |
| Multivariable + baseline DBP | -4.9 | 0.6 | -5.7 | 0.8 | -4.3 | 0.7 | -3.7 | 0.8 | 0.303 | -5.3 | 0.5 | -4.8 | 0.7 | -5.2 | 1.2 | -3.4 | 0.7 | 0.182 | 0.034 |
| Changes ⁶ in PP (mmHg) | | | | | | | | | | | | | | | | | | | |
| Multivariable | 5.3 | 0.7 | 5.8 | 1.0 | 4.6 | 0.9 | 6.7 | 1.0 | 0.480 | 4.7 | 0.7 | 5.4 | 0.9 | 7.4 | 1.5 | 6.5 | 0.9 | 0.218 | 0.115 |
| Multivariable + baseline PP | 4.9 | 0.7 | 5.7 | 0.9 | 4.6 | 0.8 | 7.6 | 1.0 | 0.089 | 4.3 ^a | 0.6 | 5.2 ^{ab} | 0.9 | 7.3 ^{ab} | 1.4 | 7.3 ^b | 0.8 | 0.022 | 0.005 |

SE, standard error; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure.

¹ Values are expressed as the mean ± SE. Mean values with different superscripts (a, b, c) within a row are significantly different among the exposure groups by Tukey's multiple comparison test.

² *p*-value for differences across groups was obtained using the general linear model (GLM).

³ p -trend was determined by treating the median value of each group as a continuous variable using GLM.

⁴ For cumulative term effect, alcohol consumption from all three visits was used for both the trajectory and the quantity categorizations.

⁵ For recent term effect, alcohol consumption from the latest two visits (2nd and 3rd) was used for the trajectory categorization and alcohol consumption at the last visit (3rd) was used for the quantity categorization.

⁶ Change values in SBP, DBP, and PP levels represented the difference in SBP, DBP, and PP levels between baseline and the third visit, respectively.

Multivariable: Adjusted for age (years) and current smoking (yes, no).

Table 3. Multivariable-adjusted changes in blood pressure and pulse pressure during follow-up according to longitudinal alcohol consumption groups in women (n 1048)¹

| | <i>Trajectory of alcohol consumption</i> | | | | | | <i>p</i> -value ² | <i>Quantity of alcohol consumption</i> | | | | <i>p</i> -value ² |
|--|--|-----|---------------------|-----|-------------------------|-----|------------------------------|--|-----|--------------|-----|------------------------------|
| | Consistent 0 | | Inconsistent | | Consistent >0 | | | 0 | | >0 | | |
| | Mean | SE | Mean | SE | Mean | SE | | Mean | SE | Mean | SE | |
| <i>Cumulative term effect³</i> | | | | | | | | | | | | |
| <i>n</i> | 636 | | 213 | | 199 | | | 636 | | 412 | | |
| Changes ⁵ in SBP (mmHg) | | | | | | | | | | | | |
| Multivariable | 2.5 | 0.6 | 3.0 | 1.0 | 3.1 | 1.0 | 0.804 | 2.5 | 0.6 | 3.1 | 0.7 | 0.511 |
| Multivariable + baseline SBP | 2.4 | 0.6 | 2.7 | 0.9 | 3.6 | 0.9 | 0.530 | 2.4 | 0.6 | 3.1 | 0.7 | 0.388 |
| Changes ⁵ in DBP (mmHg) | | | | | | | | | | | | |
| Multivariable | -2.8 | 0.4 | -3.0 | 0.6 | -3.8 | 0.7 | 0.408 | -2.8 | 0.4 | -3.4 | 0.5 | 0.304 |
| Multivariable + baseline DBP | -3.0 | 0.4 | -3.0 | 0.6 | -3.0 | 0.6 | 0.998 | -3.0 | 0.4 | -3.0 | 0.4 | 0.951 |
| Changes ⁵ in PP (mmHg) | | | | | | | | | | | | |
| Multivariable | 5.3 | 0.5 | 6.0 | 0.8 | 6.9 | 0.8 | 0.204 | 5.3 | 0.5 | 6.4 | 0.6 | 0.106 |
| Multivariable + baseline PP | 5.4 | 0.5 | 5.6 | 0.7 | 6.6 | 0.8 | 0.383 | 5.4 | 0.5 | 6.1 | 0.5 | 0.323 |
| <i>Recent term effect⁴</i> | | | | | | | | | | | | |
| <i>n</i> | 684 | | 134 | | 230 | | | 754 | | 294 | | |
| Changes ⁵ in SBP (mmHg) | | | | | | | | | | | | |
| Multivariable | - | - | - | - | - | - | - | 2.5 | 0.6 | 3.2 | 0.8 | 0.491 |
| Multivariable + baseline SBP | 1.9 | 0.5 | 2.0 | 1.1 | 2.8 | 0.8 | 0.645 | 2.5 | 0.6 | 3.2 | 0.8 | 0.430 |
| Changes ⁵ in DBP (mmHg) | | | | | | | | | | | | |
| Multivariable | - | - | - | - | - | - | - | -2.9 | 0.4 | -3.4 | 0.5 | 0.399 |
| Multivariable + baseline DBP | -3.3 | 0.3 | -3.5 | 0.7 | -3.5 | 0.5 | 0.905 | -3.0 | 0.4 | -3.1 | 0.5 | 0.901 |
| Changes ⁵ in PP (mmHg) | | | | | | | | | | | | |
| Multivariable | - | - | - | - | - | - | - | 5.4 | 0.5 | 6.6 | 0.7 | 0.131 |
| Multivariable + baseline PP | 5.2 | 0.4 | 5.5 | 0.9 | 6.2 | 0.7 | 0.427 | 5.5 | 0.4 | 6.2 | 0.6 | 0.340 |

SE, standard error; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure.

¹ Values are expressed as the mean ± SE. Mean values with different superscripts (a, b, c) within a row are significantly different among the three groups by Tukey's multiple comparison test.

² *p*-value for differences across groups was obtained using the general linear model (GLM).

³ For cumulative term effect, alcohol consumption from all three visits was used for both the trajectory and the quantity categorizations.

⁴ For recent term effect, alcohol consumption from the latest two visits (2nd and 3rd) was used for the trajectory categorization and alcohol consumption at the last visit (3rd) was used for the quantity categorization.

⁵ Change values in SBP, DBP, and PP levels represented the difference in SBP, DBP, and PP levels between baseline and the third visit, respectively.

Multivariable: Adjusted for age (years) and regular exercise (yes, no) except for the trajectory group for the recent term.