Prevalence and cardiovascular risk factors of carotid plaque in rural-dwelling adults: a population-based study in Shandong, China

Jie Zhang
  Shandong Provincial Hospital Affiliated to Shandong First Medical University

Yuanyuan Xiang
  Shandong Provincial Hospital Affiliated to Shandong First Medical University

Xiaokang Ji
  Shandong University School of Public Health

Shaowei Sang
  Shandong University Qilu Hospital

Sai Shao
  Shandong Medical Imaging Research Institute

Xiang Wang
  Shandong Provincial Hospital Affiliated to Shandong First Medical University

Xiaohui Liu
  Shandong Provincial Hospital Affiliated to Shandong First Medical University

Guangbin Wang
  Shandong Medical Imaging Research Institute

Ming Lv
  Shandong University Qilu Hospital

Fuzhong Xue
  Shandong University School of Public Health

Yifeng Du
  Shandong Provincial Hospital Affiliated to Shandong First Medical University

QinJian Sun (✉ sqj1210@163.com)
  Shandong Provincial Hospital   https://orcid.org/0000-0002-9323-9154

Research article

Abstract

Background

The association between carotid plaque (CP) and cardiovascular risk factors (CRFs) remains elusive. And few studies focus on CRFs associated with multiple CPs and irregular CP. We aimed to investigate CRFs associated with the presence, number and irregular surface morphology of CP in rural-dwelling Chinese population.

Methods

This population-based study included 2021 participants who were aged ≥ 40 and free of stroke. Data were collected via interviews, clinical examinations, and laboratory tests. Carotid plaque was estimated by ultrasonography. Binary logistic and multinomial logistic regression models were used to analyze data.

Results

Of the 2021 participants, 774 (38.3%) were detected with CP. The multi-adjusted odds ratio (95% confidence interval) of CP was 1.75 (1.40−2.19) for hypertension, 1.62 (1.03−2.55) for low high-density lipoprotein cholesterol (HDL-C), 1.55 (1.20−2.01) for high hypersensitive C-reactive protein (hs-CRP), 1.41 (1.07−1.87) for diabetes mellitus (DM), 1.39 (1.00-1.93) for high total cholesterol and 1.38 (1.03−1.85) for high low-density lipoprotein cholesterol (LDL-C). When the number and surface morphology of CP were analyzed, hypertension, high hs-CRP, DM and high LDL-C were associated with multiple CPs; hypertension, high hs-CRP and high total cholesterol were associated with irregular CP.

Conclusions

Carotid plaque is common amongst middle-aged and older people living in rural China. Hypertension, low HDL-C, high hs-CRP, DM, high total cholesterol and high LDL-C may be associated independently with CP.

Background

Carotid plaque (CP) is associated with an increased risk of ischemic stroke, which is a major cause of human death and long-term disability [1, 2]. Previous studies indicated that CP was highly prevalent in China, approximately 40.3%-60.3% of Chinese aged ≥ 40 years were affected [3−5], and more than 70% of CP occurred in rural areas [6]. With demographic ageing, the number of individuals with CP will further increase, which might be indicative of considerable burden of ischemic stroke in the future. Compared with carotid intima-media thickening, CP assessed by ultrasound is a stronger and more accurate

predictor of ischemic stroke [1]. Therefore, identifying the modified cardiovascular risk factors (CRFs) associated with CP is essential for the prevention and treatment of ischemic stroke.

The CRFs associated with CP have been explored by previous studies, but association between CP and CRFs remains elusive [7, 8]. However, few studies have focused on the correlation between CRFs and CP characteristics such as number and surface irregularity, which increase the risk of cardio-cerebrovascular disease [2, 9].

Therefore, this study aimed to investigate the CRFs associated with the presence, number and surface morphology of CP in middle-aged and older adults living in rural communities in China.

Methods

Study design and population

This study was based on the Kongcun Town Asymptomatic Intracranial Artery Stenosis study, which has been described previously in detail [10, 11]. Briefly, this is an ongoing, population-based study targeting a total of 2311 rural residents aged ≥40 years and with no history of stroke. Of the 2311 participants, 2027 completed questionnaires [11], laboratory blood tests and imaging examinations. In this study, 6 participants were excluded due to missing information on smoking habits (n=5) and drinking habits (n=1). Finally, the data of 2021 eligible participants were analyzed. Due to the missing information for surface morphology (n=21) and the number (n=7) of CP, 2000 and 2014 participants were involved in the analysis, respectively.

Collection and Assessment of variables

As previous described [10, 11], data on demographics, CRFs, medical history, anthropometrics and blood biochemical markers were collected. Hypertension was defined as blood pressure ≥140/90 mmHg, use of antihypertensive drugs, or self-reported hypertension. Diabetes mellitus (DM) was defined as fasting plasma glucose ≥7.0 mmol/L, use of blood glucose-lowering drugs, insulin injection or self-reported history of diabetes. Dyslipidemia was defined as total cholesterol ≥6.20 mmol/L or triglyceride ≥1.80 mmol/L or high-density lipoprotein-cholesterol (HDL-C) <1.11 mmol/L or low-density lipoprotein-cholesterol (LDL-C) ≥3.36 mmol/L, or use of cholesterol-lowering medication or self-reported hyperlipidemia. Smoking habits were defined as consuming at least one cigarette per day for more than one year and were dichotomized as never vs. ever. Alcohol intaking habits were defined as drinking at least once a week for more than 6 months, and were categorized as never vs. ever.

Carotid ultrasonography examination

Carotid plaque was detected by ultrasonography examination which has been proved to have high sensitivity and specificity [12]. The measurement and assessment of CP have been described in detail previously [11]. Carotid plaque was defined as focal intimal-middle film thickness ≥1.5 mm [13]. The surface morphology and number of CP were also observed by two experienced physicians through

ultrasonography, and CP was divided into regular CP group and irregular CP group according to the surface morphology.

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences software version 22.0 for Windows (IBM Corp., Released 2013, Armonk, NY: IBM Corp). Demographic and clinical information of participants were presented as mean (standard deviation) for continuous variables and frequency (%) for categorical variables. Differences between participants with and without CP were compared using t-test for continuous variables and the chi-squared test for categorical variables. Binary logistic and multinomial logistic regression models were used to estimate the odds ratio and 95% confidence interval of the related CRFs for the presence, surface morphology and number of CP. The variables included in multiple-adjusted model were age, gender, hypertension, DM, total cholesterol, triglyceride, LDL-C, HDL-C, hypersensitive C-reactive protein (hs-CRP), body mass index (BMI), smoking habits, alcohol intaking habits. All statistical tests were two-tailed, and the significance level was set at p<0.05.

Results

Characteristics of study participants

Demographic and clinical characteristics of study participants are shown in (Table 1). Of the 2021 participants, 774 (38.3%) suffered from CP. Compared with participants without CP, participants with CP were older and had higher levels of total cholesterol, triglyceride, LDL-C, BMI and hs-CRP. In addition, participants with CP were also more likely to suffer from hypertension, DM and dyslipidaemia. Moreover, the proportion of smokers and drinkers was significantly higher in participants with CP than in those without CP.

Association between CRFs and CP

Hypertension, DM, high total cholesterol (≥6.20 mmol/L), high LDL-C (≥3.36 mmol/L), low HDL-C (<1.11 mmol/L) and high hs-CRP (≥2.00 mg/L) were significantly associated with an increased odds ratio of CP, even when multiple potential confounders were controlled (Table 2). After adjusting for multiple potential confounders, hypertension, DM, high LDL-C and high hs-CRP were significantly associated with an increased likelihood of multiple CPs (Table 3). In the multiple-adjusted model, hypertension, high total cholesterol and high hs-CRP were associated with an increased likelihood of irregular CP (Table 4).

Discussion

In this population-based study, we found that the prevalence of CP was 38.3% among rural-dwelling adults aged ≥ 40 years in Shandong China. Hypertension, DM, high total cholesterol, high LDL-C, high hs-CRP and low HDL-C were positively associated with the presence of CP. Moreover, hypertension, DM, high

LDL-C and high hs-CRP were associated with multiple CPs; hypertension, high total cholesterol and high hs-CRP were associated with irregular CP.

Previous population-based cohort studies have showed the prevalence of CP in different areas. The Tromso study found that the prevalence of CP was 35% in men and 27% in women among inhabitants aged 40 to 87 years in Northern Norway [14]. In the Northern Manhattan Study, the prevalence of CP among participants ≥ 39 years of age was 57% [15]. In China, the Asymptomatic Polyvascular Abnormalities Community study found that the prevalence of CP was 54.1% among inhabitants ≥ 40 years of age in Tangshan city [4] and another study found that the prevalence of CP was 40.3% among inhabitants ≥ 45 years old in Tianjin city [3]. Although previous studies indicated that extracranial atherosclerosis was more common in white patients compared with Asians [16, 17], the above three studies conducted in China suggested that CP was more common in Chinese. Therefore, identifying the modified CRFs associated with CP is essential for the future prevention and treatment of ischemic stroke in China.

This study found that DM was associated with the presence of CP and multiple CPs, which was consistent with previous studies [3, 18, 19]. The underlying mechanisms of the correlation between diabetes and carotid atherosclerosis may be explained by the decrease in the bioavailability of the main anti-atherosclerotic factor endothelium-derived nitric oxide [20], and abnormal platelet activity caused by insulin insufficient and/or resistance [21].

In this study, we found that the association of hypertension with the presence of CP and multiple CPs, which was consistent with previous studies [18, 19]. Previous studies have shown that hypertension may be the most prominent risk factor for carotid atherosclerosis [22, 23]. The association between hypertension and surface morphology of CP was also examined by our study. The present study found that hypertension was not only related to regular CP, but also to irregular CP. Hypertension increases the pulling stress imposed on the carotid artery. Some studies found that the carotid artery wall material of hypertensive patients was less elastic at the site of the plaque than upstream and in the area affected by plaque, carotid artery was strained inwardly, which may generate a high level of stress concentrations and fatigue [24], leading to plaque rupture and irregular plaque surface formation. In addition, a four-year follow-up study suggested that hypertension was associated with new intraplaque hemorrhage [25], which was found to co-exist with disruption of the plaque surface [26].

Some studies have examined the association between lipid profiles and CP, but got inconsistent results [19, 27–29]. High LDL-C was found to be associated with the presence of CP [19, 27, 29], which was consistent with our findings. However, an Algeria study failed to prove the association between high LDL-C and CP [28]. In this study, high LDL-C was also found to be related to multiple CPs, which was in line with a previous study [19]. Consistent with other previous studies [28, 29], low HDL-C was also associated with CP in the present study, which suggested that HDL-C may be a protective factor for carotid atherosclerosis. It is worth noting that in this study, high total cholesterol was not only associated with the presence of CP, but also with irregular CP. The relationship between total cholesterol and the presence

of CP also has been found in some studies [27, 30]. To our knowledge, the association between total cholesterol and the surface morphology of CP has not been studied yet. Plasma cholesterol was considered to be the most important determinant of the putatively thrombogenic lipid core, thus high total cholesterol may be related to the rupture proneness of atherosclerotic lesions [25, 31], which may explain the association between total cholesterol and irregular CP.

Consistent with previous studies [32–34], we found that high hs-CRP was associated with the presence of CP. Moreover, the association of hs-CRP with multiple CPs or irregular CP were also found in the present study. Hs-CRP, a clinical marker of inflammation, is mainly produced by hepatocytes in response to increased interleukin-6 [35]. Previous studies indicated that hs-CRP may participate in the pathogenesis of atherosclerosis, including promoting vascular remodeling, endothelial cell dysfunction [36] and low-density lipoprotein cholesterol deposition [37]. The underlying mechanism of the association between hs-CRP and CP is still elvsive. Some studies indicated that CRP levels were positively associated with the number of new vessels in the plaque [38], and new microvessels at the base of the plaque are independently associated with plaque rupture [39], which may partly explain the relationship between hs-CRP and CP with irregular surface.

To our knowledge, this is the first study not only to explore the CRFs associated with the presence of CP, but also to investigate the CRFs associated with multiple CPs and irregular CP, which may increase the risk of ischemic stroke [2, 9]. Secondly, we used ultrasound to examine the plaques, which may be less accurate than magnetic resonance imaging (MRI) or computed tomography (CT). However, a study on the accuracy of ultrasound, CT and MRI in the diagnosis of CP morphology found that ultrasound had higher accuracy for the diagnosis of CP morphology than that of CT or MRI [12]. In addition, compared to CT or MRI, ultrasound is non-invasive, easily available and inexpensive. Thirdly, compared with the city dwellers, rural populations receive fewer medical interventions due to the backward economic and medical level, which provides more accurate information for carotid atherosclerosis.

However, there are several limitations in the present study. Firstly, this study is an ongoing cohort study, it is impossible to make causal conclusions. Secondly, this study was conducted on the middle-aged and elderly populations living in China rural area. Therefore, caution should be taken when generalizing our findings to other ethnical groups.

Conclusions

This study suggested that hypertension, DM, high total cholesterol, high LDL-C, high hs-CRP and low HDL-C may be independently associated with the presence of CP. Moreover, hypertension, DM, LDL-C and hs-CRP might be associated with multiple CPs, and hypertension, total cholesterol and hs-CRP might be associated with irregular CP.

Abbreviations

BMI, body mass index; CP, carotid plaque; CT, computed tomography; DM, Diabetes mellitus; HDL-C, high-density lipoprotein cholesterol; hs-CRP, hypersensitive C-reactive protein; LDL-C, low-density lipoprotein cholesterol; MRI, magnetic resonance imaging.

Declarations

Ethics approval and consent to participate

The Ethics Committee of the Shandong Provincial Hospital affiliated to Shandong First Medical University approved the study protocol, and the study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

Consent for publication

All participants provided their informed consent.

Availability of data and materials

The datasets obtained during this study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

QJS, YFD and FZX conceived and designed the research. JZ, YYX, XW, XKJ, SWS, SS, and XHL acquired the data. YYX, WX, SS, XHL and GBW analyzed and interpreted the data. JZ and YYX draft the manuscript. XW, ML, FZX, YFD and QJS made critical revisions of the manuscript. All authors approved the final manuscript.

Acknowledgements

Author details

[1]Department of Neurology, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, Shandong, China. [2]Department of Biostatistics, School of Public Health, Shandong University, Jinan, Shandong, China. [3]Department of Clinical Epidemiology, Qilu Hospital, Cheeloo College of Medicine, Shandong University, Jinan, Shandong, China. [4]Department of Radiology, Shandong Medical Imaging Research Institute, Cheeloo College of Medicine, Shandong University, Jinan, Shandong, China.

[1]Jie Zhang, E-mail: 642606603@qq.com [1]Yuanyuan Xiang, E-mail: 15168889383@126.com [2]Xiaokang Ji, E-mail: jxk@sdu.edu.cn [3]Shaowei Sang, E-mail: sangshaowei1@163.com [1]Xiang Wang, E-mail: higherwx@163.com [1]Xiaohui Liu, E-mail: liuxiaohui0315@sina.com [4]Guangbin Wang, E-mail: cjr.wangguangbin@vip.163.com [3]Ming Lv, E-mail: lvming@sdu.edu.cn [2]Fuzhong Xue, E-mail: xuefzh@sdu.edu.cn [1]Yifeng Du, E-mail: duyifeng2013@163.com [1]Qinjian Sun, E-mail: sqj1210@163.com

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Tables

Table 1 Demographic and clinical characteristics of participants by carotid plaque (n=2021)

Characteristics	All participants (N=2021)	Normal (n=1247, 61.7%)	CP (n=774, 38.3%)	[a]P-value
Age (years), mean (SD)	57.6 (10.4)	54.1 (9.0)	63.2 (9.9)	<0.001
Male, n (%)	965 (47.7)	575 (46.1)	390 (50.4)	0.061
Hypertension, n (%)	1159 (57.3)	603 (48.4)	556 (71.8)	<0.001
DM, n (%)	310 (15.3)	142 (11.4)	168 (21.7)	<0.001
Dyslipidaemia, n (%)	803 (39.7)	438 (35.1)	365 (47.2)	<0.001
Total cholesterol (mmol/L), mean (SD)	5.36 (1.00)	5.25 (0.93)	5.55 (1.07)	<0.001
Triglyceride (mmol/L), mean (SD)	1.37 (0.93)	1.31 (0.88)	1.46 (0.99)	0.001
LDL-C (mmol/L), mean (SD)	2.99 (0.68)	2.90 (0.64)	3.14 (0.72)	<0.001
HDL-C (mmol/L), mean (SD)	1.63 (0.39)	1.64 (0.38)	1.61 (0.39)	0.144
Hs-CRP (mg/L), mean (SD)	1.54 (3.50)	1.35 (3.56)	1.85 (3.37)	0.002
BMI (kg/m^2), mean (SD)	25.12 (3.34)	25.33 (3.34)	24.79 (3.32)	<0.001
Smoking habits, n (%)	718 (35.5)	390 (31.3)	328 (42.4)	<0.001
Alcohol intaking habits, n (%)	783 (38.7)	455 (36.5)	328 (42.4)	0.008

Abbreviations: CP, carotid plaque; DM, diabetes mellitus; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; BMI, body mass index; hs-CRP, hypersensitive C-reactive protein.

[a]P comparison between the participants with and without carotid plaque.

Table 2 Association of carotid plaque associated with CRFs (n=2021)

CRFs	n/N	Odds ratio (95% confidence interval)	
		[a]Model 1	[b]Model 2
Hypertension	552/1155	1.82 (1.47-2.25)[‡]	1.75 (1.40-2.19)[‡]
DM	167/309	1.72 (1.31-2.25)[‡]	1.41 (1.07-1.87)[*]
High total cholesterol (≥6.20 mmol/L)	195/379	1.73 (1.35-2.22)[‡]	1.39 (1.00-1.93)[*]
High triglyceride (≥1.80 mmol/L)	168/401	1.30 (1.02-1.67)[*]	0.94 (0.71-1.23)
High LDL-C (≥3.36 mmol/L)	271/559	1.69 (1.35-2.10)[‡]	1.38 (1.03-1.85)[*]
Low HDL-C (<1.11 mmol/L)	55/115	1.69 (1.11-2.57)[*]	1.62 (1.03-2.55)[*]
High hs-CRP (≥2.0 mmol/L)	199/382	1.65 (1.28-2.12)[‡]	1.55 (1.20-2.01)[†]
High BMI (≥24 kg/m^2)	470/1288	1.10 (0.89-1.36)	0.90 (0.73-1.13)
Smoking habits	327/717	1.35 (0.98-1.84)	1.37 (0.98-1.90)
Alcohol intaking habits	327/782	1.07 (0.80-1.44)	0.96 (0.70-1.31)

Abbreviations: CRFs, cardiovascular risk factors; DM, diabetes mellitus; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; hs-CRP, hypersensitive C-reactive protein; BMI, body mass index.

[a]Model 1 adjusted for age, gender.

[b]Model 2 adjusted for age, gender, hypertension, diabetes mellitus, total cholesterol, triglyceride, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, hypersensitive C-reactive protein, body mass index, smoking habits, alcohol intaking habits.

n/N indicates number of cases with carotid artery plaque/number of participants.

[*]P<0.05.

[†]P<0.01.

Table 3 Association of single and multiple carotid plaques associated with CRFs (n=2014)

CRFs	Normal (n=1243)	Single CP (n=319)	Multiple CPs (n=452)
	Reference	OR (95% CI)[a]	OR (95% CI)[a]
Hypertension	1.00	1.44 (1.10-1.90)[†]	2.28 (1.71-3.04)[‡]
DM	1.00	1.28 (0.89-1.83)	1.65 (1.19-2.29)[†]
High total cholesterol (≥6.20 mmol/L)	1.00	1.46 (0.96-2.22)	1.36 (0.91-2.03)
High triglyceride (≥1.80 mmol/L)	1.00	0.90 (0.63-1.27)	1.03 (0.74-1.44)
High LDL-C (≥3.36 mmol/L)	1.00	1.12 (0.77-1.63)	1.67 (1.17-2.40)[†]
Low HDL-C (<1.11 mmol/L)	1.00	1.43 (0.81-2.52)	1.73 (1.00-2.99)
High hs-CRP (≥2.0 mmol/L)	1.00	1.43 (1.03-1.98)[*]	1.75 (1.29-2.38)[‡]
High BMI (≥24 kg/m^2)	1.00	1.07 (0.80-1.41)	0.81 (0.61-1.06)
Smoking habits	1.00	1.65 (1.08-2.52)[*]	1.17 (0.78-1.76)
Alcohol intaking habits	1.00	0.96 (0.65-1.41)	0.95 (0.65-1.38)

Abbreviations: CRFs, cardiovascular risk factors; OR, odds ratio; CI, confidence interval; CP, carotid plaque; DM, diabetes mellitus; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; hs-CRP, hypersensitive C-reactive protein; BMI, body mass index.

[a]Model adjusted for adjusted for age, gender, hypertension, diabetes mellitus, total cholesterol, triglyceride, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, hypersensitive C-reactive protein, body mass index, smoking habits, alcohol intaking habits.

[*]P<0.05.

[†]P<0.01.

[‡]P<0.001.

Table 4 Association of regular and irregular carotid plaques associated with CRFs (n=2000)

CRFs	Right			Left		
	OR (95% CI)[a]			OR (95% CI)[a]		
	normal	Regular CP	Irregular CP	normal	Regular CP	Irregular CP
Hypertension	1.00	2.05 (1.56-2.69)[‡]	1.80 (1.12-2.88)[*]	1.00	1.69 (1.31-2.19)[‡]	1.88 (1.20-2.95)[†]
DM	1.00	1.28 (0.94-1.74)	1.44 (0.88-2.36)	1.00	1.54 (1.13-2.08)[†]	1.41 (0.88-2.27)
High total cholesterol (≥6.20 mmol/L)	1.00	1.12 (0.77-1.62)	1.78 (0.92-3.46)	1.00	1.13 (0.78-1.62)	1.99 (1.06-3.73)[*]
High triglyceride (≥1.80 mmol/L)	1.00	1.05 (0.77-1.44)	1.05 (0.61-1.81)	1.00	1.01 (0.74-1.38)	0.81 (0.47-1.37)
High LDL-C (≥3.36 mmol/L)	1.00	1.68 (1.20-2.34)[†]	1.00 (0.53-1.87)	1.00	1.57 (1.13-2.17)[†]	0.97 (0.53-1.76)
Low HDL-C (<1.11 mmol/L)	1.00	2.25 (1.38-3.67)[†]	1.98 (0.84-4.64)	1.00	1.09 (0.65-1.84)	1.74 (0.78-3.87)
High hs-CRP (≥2.0 mmol/L)	1.00	1.49 (1.12-1.99)[†]	1.87 (1.20-2.91)[†]	1.00	1.41 (1.06-1.88)[*]	1.58 (1.03-2.43)[*]
High BMI (≥24 kg/m^2)	1.00	1.00 (0.77-1.30)	0.82 (0.54-1.25)	1.00	0.77 (0.60-0.99)[*]	0.83 (0.56-1.24)
Smoking habits	1.00	1.27 (0.87-1.87)	1.62 (0.85-3.10)	1.00	1.21 (0.84-1.75)	1.69 (0.92-3.12)
Alcohol intaking habits	1.00	1.13 (0.79-1.62)	0.69 (0.39-1.21)	1.00	0.85 (0.61-1.20)	0.97 (0.57-1.67)

Abbreviations: CRFs, cardiovascular risk factors; OR, odds ratio; CI, confidence interval; CP, carotid plaque; DM, diabetes mellitus; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; hs-CRP, hypersensitive C-reactive protein; BMI, body mass index.

[a]Model adjusted for adjusted for age, gender, hypertension, diabetes mellitus, total cholesterol, triglyceride, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, hypersensitive C-

reactive protein, body mass index, smoking habits, alcohol intaking habits.

*P<0.05.

†P<0.01.

‡P<0.001.