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Binge Drinking Impairs Vascular Function in Young Adults

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Objectives The aim of this study was to assess whether young binge drinkers (BD) have impaired macrovascular and microvascular function and cardiovascular disease risk factors compared with age-matched alcohol abstainers (A).

Background Binge drinking rates are highest on college campuses and among those age 18 to 25 years; however, macrovascular and microvascular endothelial function in young adults with histories of repeated binge drinking (≥5 standard drinks in 2 h in men, ≥4 standard drinks in 2 h in women) has not been investigated.

Methods Cardiovascular profiles, brachial artery endothelial-dependent flow-mediated dilation (FMD), and flow-independent nitroglycerin (NTG)–mediated dilation and vasoreactivity of resistance arteries (isolated from gluteal fat biopsies) were evaluated in A and BD.

Results Men and women (18 to 25 years of age; A, n = 17; BD, n = 19) were enrolled. In the BD group, past-month mean number of binge episodes was 6 ± 1, and the mean duration of binge drinking behavior was 4 ± 0.6 years. FMD and NTG-mediated dilation were significantly lower in the BD group (FMD: 8.4 ± 0.7%, p = 0.022; NTG-mediated dilation: 19.6 ± 2%, p = 0.009) than in the A group (FMD: 11 ± 0.7%; NTG-mediated dilation: 28.6 ± 2%). Acetylcholine-induced and sodium nitroprusside–induced dilation in resistance arteries was not significantly different between the A and BD groups. However, endothelin-1–induced constriction was significantly enhanced in the BD group compared with the A group (p = 0.032). No differences between groups were found in blood pressure, lipoproteins, and C-reactive protein.

Conclusions Alterations in the macrocirculation and microcirculation may represent early clinical manifestations of cardiovascular risk in otherwise healthy young BD. This study has important clinical implications for screening young adults for a repeated history of binge drinking. (J Am Coll Cardiol 2013;62:201–7) © 2013 by the American College of Cardiology Foundation

Regular heavy episodic alcohol use (or "binge drinking") is one of the most serious public health problems confronting American colleges (1). More than half of college student drinkers engage in regular binge drinking, which is broadly defined as consuming more than 4 or 5 standard drinks (13 g alcohol/drink) in a 2-h period (2–4). Results from retrospective studies enrolling adults ranging in age from 40 to 60 years have found that binge drinking is associated with a heightened risk for cardiovascular (CV) events, such as stroke, sudden death, myocardial infarction, and increased mortality after myocardial infarction (5–8). Others have reported that an alcohol binge drinking pattern is associated with progression of carotid atherosclerosis (9). Several mechanisms may underlie the increased risk for adverse CV events; however, a central mechanism may be changes in vascular biology, such as endothelial dysfunction.

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The endothelium is a key regulator of vascular function. Endothelial dysfunction is an early indicator of blood vessel damage and atherosclerosis and a strong prognostic factor

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Abbreviations and Acronyms

A = alcohol abstainers
ACh = acetylcholine
BD = binge drinkers
BP = blood pressure
CRP = C-reactive protein
CV = cardiovascular
EC_{50} = half maximal effective concentration
ET = endothelin
FMD = flow-mediated dilation
L-NAME = N-nitro-L-arginine methyl ester
NO = nitric oxide
NTG = nitroglycerin
SNP = sodium nitroprusside

for future CV events (10,11). Impaired endothelium-independent dilation, reflective of smooth muscle dysfunction, is also linked to the development of atherosclerosis. Flow-mediated dilation (FMD) and nitroglycerin (NTG)–mediated dilation of the brachial artery are commonly used to evaluate endothelial-dependent and endothelial-independent function, respectively. To our knowledge, endothelial function in young adults with repeated histories of binge drinking has not been investigated, nor have studies simultaneously evaluated macrovascular and microvascular endothelial function. Endothelial cells can differ in structure and physiologic function, depending on the vasculature bed, making it clinically important to study vascular function at multiple vascular sites. This study was designed to test the hypothesis that young binge drinkers (BD) have impaired macrovascular and microvascular function compared with age-matched alcohol abstainers (A).

Methods

Study subjects and protocol. Thirty-eight nonsmoking healthy subjects were recruited from an urban university setting into this study: A (10 men, 9 women) and BD (11 men, 6 women). BD were defined as those who consumed ≥5 standard drinks (12 oz beer, 5 oz table wine, 1.5 oz 80-proof spirits, or 8 to 9 oz malt liquor) in a 2-h period in the past 2 weeks if male and ≥4 standard drinks in a 2-h period in the past 2 weeks if female (2). A were defined as those who consumed no more than 1 to 5 standard drinks in the past year. Exclusion criteria were history of diabetes, hypertension, pregnancy, CV disease or events, thyroid disease, pituitary tumor, a genetic disease causing disability, gout, illicit drug use, and body mass index ≥30 kg/m^2. The study was approved by the Office of Protection of Research Subjects and Institutional Review Board, and written consent was obtained from all subjects.

In all subjects, the following tests were performed: fasting lipid panel (total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglycerides), insulin and glucose, complete blood count differential, C-reactive protein (CRP), and blood alcohol levels (Alverno Clinical Laboratories, Hammond, Indiana). Venous samples were drawn into a serum tube and an ethylenediaminetetraacetic acid–containing tube. Also measured were resting blood pressure (BP), heart rate, oxygen saturation, and temperature. Gluteal fat pad biopsies were performed, and resistance arteries were isolated for isolated perfused microvessel experiments.

All subjects completed questionnaires about medical history, diet, and alcohol beverage consumption. The Block Brief 2000 Food Frequency Questionnaire (NutritionQuest, Berkeley, California) was used to obtain information about diet. Alcohol consumption (pattern and frequency) was estimated using a modified version of the 6-item set of questions on binge drinking (12). Three additional questions were included on binge drinking that addressed the type of alcohol consumed, history of familial alcohol abuse, and duration of binge drinking. For BD, the rate of alcohol consumption (grams per hour) was calculated on the basis of their most recent binge drinking episode (rate = total grams of alcohol consumed/time spent consuming alcohol).

Measurement of FMD. All imaging studies were performed in the morning after an overnight fast. Similar to previously reported protocols and methods, ultrasound imaging was conducted using the MicroMaxx ultrasound machine (SonoSite, Seattle, Washington) (13). Imaging of the brachial artery was performed in a longitudinal plane, at approximately 5 cm proximal to the antecubital fossa of the right arm, abducted approximately 80° from the body, with the forearm supinated. The ultrasound probe (11 MHz) was positioned at a 60° insonation angle to visualize the anterior and posterior lumen-intima interfaces, to measure diameter or central flow velocity (pulsed Doppler). After baseline ultrasound imaging, Doppler readings of peak flow and mean flow were performed for at least 5 s. A BP cuff was placed on the forearm, distal to the antecubital fossa of the imaged arm, and inflated to 60 mm Hg above baseline systolic BP for 5 min. Once the cuff was released, BP and heart rate measurements in the opposite arm were taken, along with Doppler readings of the first 10 s after cuff release. The brachial artery was then imaged continuously to capture 30 s, 1 min, 2 min, and 3 min after BP cuff release. The response to NTG was used for the determination of endothelium-independent vasodilation. After obtaining a baseline (resting) brachial artery image, a sublingual NTG tablet (0.4 mg) was administered, and brachial artery images and measurements were repeated and obtained as detailed earlier.

Images were digitally recorded using Brachial Imagery (Medical Imaging, Iowa City, Iowa) and analyzed as previously described (13). Four hundred fifty frames were captured, digitized, and analyzed from the M-line (the border between the intima and media of the brachial artery) of the same location of blood vessel using visible landmarks with edge detection software. Approximately 75 frames (7.5 frames/s for 10 s) were analyzed for each baseline and time point measurement through a mean of brachial artery diameters over the entire RR interval. FMD and the response to NTG were calculated using the averaged minimal mean brachial artery diameter at baseline compared with the largest mean values obtained after release of the forearm occlusion or administration of NTG.