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Short Communication

The association between muscle strengthening activities and atherogenic index of plasma

Meghan K. Edwards MS [a], Paul D. Loprinzi PhD [b,*]

[a] Physical Activity Epidemiology Laboratory, Department of Health, Exercise Science and Recreation Management, The University of Mississippi, University, MS 38677, United States
[b] Jackson Heart Study Vanguard Center of Oxford, Physical Activity Epidemiology Laboratory, Department of Health, Exercise Science and Recreation Management, The University of Mississippi, University, MS 38677, United States

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ABSTRACT

Atherogenic index of plasma (AIP), calculated as LOG_{10}(triglycerides/high-density lipoprotein-cholesterol), is considered to be a novel indicator of cardiovascular disease (CVD) risk. Muscle strengthening activities (MSA) have been shown to favorably associate with triglycerides and high-density lipoprotein cholesterol (HDL-C). The association between MSA and AIP has yet to be explored in a nationally representative sample of U.S. adults, which was the purpose of this brief report. Data from the 1999–2006 National Health and Nutrition Examination Survey were used ($N = 6694$ adults 20–85 yrs). AIP was obtained from a blood sample and a 2-item questionnaire was implemented to assess MSA participation over the previous 30-days. Individuals meeting MSA guidelines (vs. not) had reduced odds of having an elevated (>0.24) AIP (odds ratio = 0.80; 95% confidence interval: 0.65–0.98; $P = 0.03$). Muscle strengthening activities appear to be inversely associated with AIP. Engaging in MSA may be a strategy to mitigate risk for health outcomes associated with an elevated AIP, such as CVD.

1. Introduction

In 2013, 800.8 thousand adult deaths (30.8% of all deaths) (Mozaffarian et al., 2016) in the United States were the result of cardiovascular disease (CVD), making CVD-specific mortality larger than any other cause of mortality (Murphy et al., 2014). Consequentially, it is important to have accurate and efficient screening procedures available to not only diagnose CVD, but also to identify individuals at a high risk for developing CVD. As such, various indices have been implemented to facilitate and enhance this screening/diagnostic process.

Atherogenic index of plasma (AIP), for instance, is a logarithmically transformed lipid profile ratio calculated using concentrations of triglycerides and high-density lipoprotein cholesterol (HDL-C), LOG_{10}(triglycerides/HDL-C) (Dobiasova & Frohlich, 2001), and has been shown to positively associate with CVD risk (Dobiasova, 2006). The AIP ratio is easily calculated from the lipid profile, making it a feasible measurement to employ in the clinical setting. While HDL-C levels alone are well understood to inversely associate with CVD risk (Dobiasova, 2004; Rader & Hovingh, 2014), the role of triglycerides on CVD risk is equivocal (Dobiasova, 2004). In 1997, Gaziano et al. (1997) first examined the ratio of triglycerides to HDL-C on CVD risk, finding it to be a strong predictor of myocardial infarction. Notably, other studies have similarly demonstrated positive associations between the triglyceride/HDL-C ratio and CVD (Bampi et al., 2009; da Luz et al., 2008). Dobiasova and colleagues, credited with developing and first utilizing AIP as a marker of CVD risk (Dobiasova & Frohlich, 2001), were interested in further exploring the potential health implications of the triglyceride/HDL relationship. They postulated that triglycerides are regulators of lipoprotein interactions, as opposed to independent markers of CVD risk (Dobiasova, 2004), highlighting the associations of an increased plasma concentration of triglycerides with an elevated concentration of low-density lipoproteins (Guerin et al., 2001), enhanced cholesterol esterification/transfer, and HDL remodeling (Murakami et al., 1995). There is evidence to suggest that AIP is a stronger predictor for CVD risk than the triglyceride/HDL-C ratio (Tan et al., 2004), which may be in part due to the strong correlation of AIP with lipoprotein particle size (Dobiasova, 2006). For example, a 2011 study by Raslova et al. (2011) found AIP to explain the most variance in the rate of cholesterol esterification in plasma depleted of apolipoprotein β-containing lipoproteins (FER_{HDL}), when compared to the triglyceride/HDL-C ratio (as well as other markers of CVD-risk). Notably, FER_{HDL} has been demonstrated to be the strongest predictor of positive coronary angiography test results (Frohlich & Dobiasova, 2003), with evidence suggesting it to also be one of the top indicators of change in coronary artery disease progression (Brown et al., 2001; Dobiasova et al., 2011) and overall coronary heart disease risk (Tan et al., 1998). Additionally,

* Corresponding author at: The University of Mississippi, Jackson Heart Study Vanguard Center of Oxford, Physical Activity Epidemiology Laboratory, School of Applied Sciences, Department of Health, Exercise Science, and Recreation Management, 229 Turner Center, University, MS 38677, United States.
E-mail address: pdloprin@olemiss.edu (P.D. Loprinzi).

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previous work has found AIP to be more significantly correlated with CVD risk when compared to other algorithm-generated risk scores (e.g., Castelli Risk Index or Atherogenic Coefficient) (Bhardwaj et al., 2013).

Considering the aforementioned information indicating the potentially unique utility of AIP as an independent marker of CVD risk, and the relatively small body of research examining AIP as an outcome variable, the present study was designed to explore this lipid ratio as the primary outcome of interest. Given the inverse association of physical activity with CVD (Warburton et al., 2006), denoting its potential risk-reducing benefits, we sought to investigate the influences of physical activity on AIP. Notably, recent work has demonstrated an inverse relationship between aerobic exercise and AIP (Stranska et al., 2011). A 2013 study by Venojarvi et al. (2013), however, indicated that distinct modes of exercise training might differently influence AIP. Specifically, a 12-week aerobic training program resulted in significantly decreased AIP in middle-aged men with impaired glucose regulation whereas a 12-week resistance training program did not. Ezeukwu et al. (2015) corroborated these mixed findings, observing a significant decrease in AIP among non-obese young males participating in an 8-week continuous aerobic exercise program and a non-significant increase in AIP among individuals participating in an 8-week interval-based exercise program. These equivocal results, coupled with a substantially smaller volume of work exploring the effects of resistance training (vs. aerobic exercise training) on lipid profile (Mann et al., 2014) and CVD risk (Braith & Stewart, 2006), served as motivation for the present study to evaluate muscle strengthening activity (MSA) participation as the independent variable. Although previous work (Venojarvi et al., 2013) has explored the effects of a resistance training intervention on AIP, the employed sample included only middle-aged men with impaired glucose regulation, making results less generalizable. As such, the purpose of this brief report was to examine the association of MSA participation and AIP among a nationally representative sample of U.S. adults.

2. Methods

2.1. Study design & participants

The 1999–2006 NHANES data was used. Written informed consent was obtained from all participants. The NHANES is an ongoing survey conducted by the Center for Disease Control and Prevention designed to evaluate the health status of U.S. adults through a complex, multistage, stratified clustered probability design. Further details of NHANES can be found elsewhere (http://www.cdc.gov/nchs/nhanes.htm). Participants included 6694 adults (20–85 yrs) with complete data on the study variables.

2.2. Atherogenic index of plasma

AIP was assessed from a blood sample and calculated as: LOG_{10}(triglycerdies/HDL-C), with triglycerides (mg/dL/88.57) and HDL-C (mg/dL/38.67) expressed in mmol/L. AIP was expressed as a continuous variable and also categorized as non-elevated or elevated AIP (>0.24) (Dobiasova, 2006).

2.3. Measurement of muscle strengthening activities

Participants were asked two questions related to engagement in muscular strength activities (MSA): 1) "Over the past 30 days, did you do any physical activities specifically designed to strengthen your muscles such as lifting weights, push-ups or sit-ups?" (response option: *yes* or *no*), and 2) among those answering *yes* to this first question, they were asked, "Over the past 30 days, how many times did you do these activities designed to strengthen your muscles such as lifting weights, push-ups, or sit-ups?" (National Health and Nutrition Examination Survey, 2005–2006). Participants engaging at least 2 MSA sessions/week were considered to meet MSA guidelines. Although these are relatively crude measures of MSA, notably, these NHANES MSA items have provided evidence of convergent validity (e.g., shown to associate lower extremity muscular strength along with various cardiovascular-related parameters) (Dankel et al., 2015; Loprinzi et al., 2015).

2.4. Statistical analysis & covariates

Multivariable linear and logistic regression analysis was employed that evaluated the association between MSA and the AIP (outcome variable). All analyses adjusted for the NHANES complex, multistage probability design. In all models, the following covariates were included: age (continuous; yrs), gender, race-ethnicity (Mexican American, non-Hispanic white, non-Hispanic black, and other), physician-diagnosed hypertension (yes/no), total cholesterol (continuous; mg/dL); LDL-cholesterol (continuous; mg/dL), body mass index (continuous; kg/m^2), self-reported smoking status (current smoker, former smoker, or never a smoker), taking anti-cholesterol medication (yes/no) and meeting aerobic-based moderate-to-vigorous physical activity (MVPA) guidelines (yes/no; ≥2000 MVPA-met-min month, as detailed elsewhere) (Loprinzi, 2015). Notably, previous work has shown the magnitude of the associations between physical activity and health biomarkers to vary by demographic information (e.g., age, gender) (Loprinzi, 2015; Loprinzi & Cardinal, 2012; Loprinzi & Pariser, 2013). Thus, interaction effects of MSA with the demographic parameters (and the other covariates) on AIP were evaluated. Multiplicative interaction was evaluated by creating a cross-product term and including it, along with the main effects and the covariates, in the regression model. Statistical significance was established as $P < 0.05$. Though not the primary focus of this paper, we were also interested in examining the association of MSA with the triglyceride/HDL-C ratio. Consequentially, a multivariable linear regression was performed to assess this.

3. Results

Characteristics of the analyzed sample is shown in Table 1. Participants, on average, were 44 years of age and the sample was equally distributed across gender (52.0% female).

With regard to the main findings, and after adjustment, those meeting MSA guidelines (vs. not) had a lower AIP ($\beta_{adjusted} = -0.03$; 95% CI: -0.05 to -0.01; $P = 0.001$). In a multivariable logistic regression model, those meeting MSA guidelines (vs. not) had reduced odds of having an elevated (>0.24 mmol/L) AIP ($OR_{adjusted} = 0.80$; 95% CI: 0.65–0.98; $P = 0.03$). Notably, there was no evidence of an interaction effect of MSA and age ($P = 0.47$), MSA and gender ($P = 0.39$), MSA and race-ethnicity ($P = 0.40$), MSA and MVPA ($P = 0.67$), MSA and

Table 1
Weighted characteristics of the analyzed sample, 1999–2006 NHANES ($N = 6694$).

Variable	Point estimate	95% CI
AIP, mean	−0.02	−0.03 to −0.009
% elevated (>0.24) AIP	23.2	
% meeting MSA guidelines	22.2	
Age, mean years	44.1	43.3–44.8
% female	52.0	
% white	70.8	
% meeting MVPA guidelines	46.6	
Total cholesterol, mean mg/dL	199.0	197.6–200.4
LDL-cholesterol, mean mg/dL	119.9	118.6–121.1
BMI, mean kg/m^2	28.0	27.7–28.2
% physician-diagnosed hypertension	23.7	
% smoker	23.5	
% on cholesterol medication	8.4	

AIP, Atherogenic Index of Plasma.
BMI, Body mass index.
LDL, Low-density lipoprotein cholesterol.
MSA, Muscle strengthening activities.
MVPA, Moderate-to-vigorous physical activity.