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Calf exercise-induced vasodilation is blunted in healthy older adults with increased walking performance fatigue

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ABSTRACT

Vascular aging as measured by central arterial stiffness contributes to slow walking speed in older adults, but the impact of age-related changes in peripheral vascular function on walking performance is unclear. The aim of this study was to test the hypothesis that calf muscle-specific vasodilator responses are associated with walking performance fatigue in healthy older adults. Forty-five older (60–78 yrs) adults performed a fast-paced 400 m walk test. Twelve of these adults exhibited fatigue as defined by slowing of walking speed ($\geq$0.02 m/s) measured during the first and last 100 m segments of the 400 m test. Peak calf vascular conductance was measured following 10 min of arterial occlusion using strain-gauge plethysmography. Superficial femoral artery (SFA) vascular conductance response to graded plantar-flexion exercise was measured using Doppler ultrasound. No difference was found for peak calf vascular conductance between adults that slowed walking speed and those that maintained walking speed ($p > 0.05$); however, older adults that slowed walking speed had a lower SFA vascular conductance response to calf exercise (at highest workload: slowed group, 2.4 $\pm$ 0.9 vs. maintained group, 3.6 $\pm$ 0.9 ml/kg/min/mm Hg; $p < 0.01$). Moreover, the initial increase in SFA vascular conductance from rest to exercise was positively correlated with the change in walking speed for all adults (rho = 0.41, $p = 0.005$). In conclusion, these results suggest that calf exercise hemodynamics are associated with walking performance fatigability in older adults.

1. Introduction

Understanding the mechanisms that contribute to loss of physical function with age has significant implications for improving health and quality of life for older adults. Walking speed has proven to be an informative measure of physical function. Not only does it represent the ability of older adults to perform activities related to independent living (Verghese et al., 2011), but walking speed also predicts future disability and all-cause mortality (Newman et al., 2006; Studenski et al., 2011). Walking speed at a normal or fast pace decreases with advancing age (Ko et al., 2010). Outside of severe clinical conditions (e.g., stroke) where walking speed can fall abruptly, the vast majority of older adults experience a progressive decline in walking speed (Guralnik et al., 2001). This indicates that the underlying physiological deficits that impair walking ability manifest slowly. Older adults may compensate for these deficits by altering walking performance to maintain function (Rantakokko et al., 2013), which may present as an inability to sustain walking speed (i.e., fatigue) during an endurance walk test (Simonsick et al., 2014).

Increased fatigability during walking may occur if aged arteries have a reduced ability to deliver oxygen and nutrients to active muscle for energy utilization. Leg muscle oxidative capacity (e.g., capillary density, oxidative enzyme activity) is strongly associated with walking speed in normally active, non-endurance trained older adults (Coen et al., 2013; Nicklas et al., 2008). Muscle blood flow is related to the oxidative potential of muscle (Laughlin and Armstrong, 1985), which declines with age (Yu et al., 2007); thus, lower muscle blood flow during exercise may reflect reduced muscle oxidative capacity in older adults. However, aging is also associated with a decline in vascular function that manifests as a reduced ability of peripheral arteries to dilate (Celermajer et al., 1994) and increase blood flow (Westby et al., 2011). Indeed, lower muscle blood flow responses to leg exercise have been observed in healthy older adults as compared to younger adults (Donato et al., 2006; Proctor et al., 2003a). Interestingly, drug therapy in older adults to increase vascular function (arterial vasodilatory capacity) improves blood flow responses to leg exercise that result in greater muscle oxygen consumption (Chen et al., 1999) and faster walking speed (Cowley et al., 1990). Therefore, it is possible that age-related changes in muscle blood flow may be a physiological deficit that plays a role in walking performance fatigue in older adults.

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The aim of this study was to determine if calf muscle blood flow and vasodilation are associated with walk test fatigability in healthy, normally active older adults. We hypothesized that older adults unable to sustain walking speed during a fast-paced 400 m walk test would have i) a lower ability to maximally dilate calf muscle vasculature, and/or ii) smaller muscle blood flow and vascular conductance responses to plantar-flexion exercise as compared to adults able to maintain walking speed.

2. Methods

2.1. Participants

Forty-five older adults (25 women and 20 men) between the ages of 60 and 78 yrs provided written informed consent to participate in this study. These participants were screened to identify factors well known to alter vascular function independent of aging. Exclusion criteria included a personal history of physician-diagnosed cardiovascular disease, diabetes, and pulmonary disease. In addition, adults were not eligible to participate if taking medications for high blood pressure, cholesterol, or hormone replacement to avoid drug influence on vasodilatory capacity. Lastly, participants were excluded if obese (body mass index >29 kg/m^2), had a resting seated brachial blood pressure $>149/99$ mm Hg as measured by auscultation, or a fasting blood glucose >115 mg/dl as measured by finger-prick (Accu-Chek Active, Roche Diagnostics) after 8–12 h of fasting. The Human Research Protection Program at Texas Tech University provided ethics approval for this study.

2.2. Study protocol

Participants were asked to refrain from caffeine for ≥ 12 h, and to avoid food and vitamins/supplements for 4 h prior to two study visits. On the first day, body composition was assessed using dual-energy X-ray absorptiometry (Lunar Prodigy, GE Medical Systems) for measurement of percent total body fat and calf lean mass. Maximal isometric grip strength was measured using a Lafayette hand dynamometer (model 78010) and was defined as the highest value from three individual efforts in each hand. Participants rested in the supine position for 10 min prior to measurement of maximal calf vasodilatory capacity. Lastly, participants were familiarized with the 400 m walk test. On the second visit, muscle blood flow was measured during single-leg graded light-intensity calf exercise. Lastly, walking performance was assessed using a 400 m walk test.

2.3. Maximal calf blood flow and dilation

Post-occlusive reactive hyperemia was measured using strain-gauge plethysmography (EC6, Hokanson) on the right calf muscle under supine conditions. The strain-gauge was placed around the widest portion of the calf with the leg elevated above the heart level approximately 12 cm to promote venous drainage. A thigh cuff was inflated for 10 min at 240 mm Hg on the upper leg approximately 1 cm above the knee to occlude arterial blood flow. Following cuff deflation, calf blood flow was measured every 15 s for 3 min (12 flow measurements) by rapidly inflating (7 s inflation, 8 s release) the thigh cuff to 50 mm Hg to occlude venous outflow. An ankle cuff was inflated to 240 mm Hg to occlude foot circulation during measurement of calf blood flow. Beat-by-beat blood pressure was measured using a validated automated device (CNAP monitor, CNSystems). The measurement site (finger cuff) was placed at the level of the elevated calf. Vascular conductance was calculated by dividing calf blood flow by mean blood pressure. Peak calf blood flow was defined as the highest measurement taken during the 3 min post-occlusive reactive hyperemia.

2.4. Calf exercise blood flow

Diameter and blood velocity were measured in the right superficial femoral artery (SFA) at rest and during plantar flexion exercise using Doppler ultrasound (Vivid 7, General Electric) with a 5–13 MHz linear transducer probe. Plantar flexion of the right foot was performed while the participant was in a seated reclined position. Exercise consisted of three light-intensity stages (0.5, 1.0, 1.5 kg) of 3 min duration each. Participants were instructed to move their foot through a full range of motion at a cadence of 40 contractions per minute as set by an audio metronome. Blood velocity was sampled in real time (1000 Hz) using a data acquisition system (Powerlab 8SP, ADInstruments). Diameter was determined using an automated edge detection system (Brachial Analyzer, Medical Imaging Applications). Blood velocity (30 s sample) and diameter (20 s clip) were analyzed from samples recorded during the last minute of each stage of exercise. Blood flow was calculated by multiplying the cross-sectional area (πr^2) of the SFA artery with mean blood velocity. Mean blood flow was normalized to calf lean mass. Blood pressure in the left arm was measured continuously during exercise using an automated device (CNAP monitor, CNSystems). The measurement site (finger cuff) was placed at the level of the heart. Vascular conductance was calculated by dividing blood flow with mean blood pressure.

2.5. Walking performance fatigability

Participants completed a fast-paced 400 m walk test (Simonsick et al., 2001). Two traffic cones were placed 65.5 ft apart in a long flat-surfaced hallway. Participants were instructed to "select a pace that you can comfortably maintain for 10 laps but you feel that you can complete in your best time." Walking speed (m/s) was calculated based on time to complete the first 100 m (0–100 m) and last 100 m (300–400 m) of the 400 m walk test. Performance fatigue was defined as slowing of walking speed from the first to the last 100 m segment. The change in walking speed was rounded up to the next hundredth when the thousandth place was ≥ 0.005 m/s. We set the criteria for a significant decline in walking speed at ≥ 0.02 m/s since the standard error of the change in walking speed for the entire sample in this study was ~0.01 m/s.

2.6. Statistical analysis

Participants were divided into two groups based on assessment of walking fatigue (see Results). Independent-sample *t*-tests were used to compare participant characteristics between groups. Repeated measures two-way analysis of covariance (group $\times$ stage) was used to compare blood flow and vascular conductance responses to exercise between groups after adjusting for age and sex. If a significant interaction was detected, a Tukey post-hoc test was used for multiple pairwise comparisons between groups. All outcome variables were normally distributed as determined by a Kolmogorov–Smirnov test. The change in walking speed failed normality, therefore a Spearman rho correlation was used to assess the relationship between the change in walking speed and vascular function. Significance was considered $p \leq 0.05$.

3. Results

3.1. Walking performance fatigue

Twelve adults (26%) slowed walking speed during the walk test while all other adults either sustained or increased walking speed. Adults that did not slow walking speed were categorized into one maintained walking speed group for comparison purposes. Characteristics for each group are shown in Table 1. Adults that slowed walking speed were of similar age, body fat, resting blood pressure, fasting blood glucose, and maximal grip strength as compared to the maintained