Evaluation of Racial Differences in Resting and Postprandial Endothelial Function in Postmenopausal Women Matched for Age, Fitness and Body Composition

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Objective: We investigated endothelial function at rest and after a high-fat meal challenge in African American (AA) and Caucasian postmenopausal women matched for age, body mass index, percent fat and fitness level.

Design: Pilot study.

Setting: University of Virginia General Clinical Research Center. Participants: Eight AA and 8 Caucasian postmenopausal women.

Intervention: Participants underwent a VO_2 peak treadmill protocol, percent fat assessment, and brachial artery flow-mediated dilation measurements (baseline and 4 hours following a high-fat meal).

Main outcomes measures: Baseline and postprandial flow mediated dilation (FMD) following a high-fat meal.

Results: FMD values were similar in AA (5.4%, 95% CI: 3.3, 7.4) and Caucasian women (4.0%, 95% CI: 2.0, 6.1). There was no significant change in FMD from baseline to four hours following the meal challenge within groups (AA: .9%, $P=.397$, Caucasian: 2.3%, $P=.063$) or between groups ($P=.449$), despite a significant increase in triglycerides (AA: 81.8 mg/dL, $P<.001$, Caucasian: 99.7 mg/dL, $P=.004$).

Conclusions: The present pilot study found that when postmenopausal AA and Caucasian women are matched for age, fitness and body composition, reported racial differences in resting endothelial function were not observed. Additionally, there were no racial differences in postprandial endothelial function or metabolism following a high-fat meal. (*Ethn Dis.* 2013; 23[1]:43–48)

Key Words: Flow-mediated Dilation, Postmenopausal, Racial Differences, African American, Postprandial, Endothelial Function

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Introduction

Endothelial dysfunction is believed to be an early event in atherogenesis, and is an independent risk factor for cardiovascular events[1] and hypertension[2] in postmenopausal women. Similar to the epidemiological data showing racial differences in cardiovascular risk, endothelial function is reduced in African American (AA) compared to Caucasian women.[3] This risk is exacerbated by the deleterious cardiometabolic consequences of menopause[4] and aging,[5] both of which have been shown to further reduce endothelial function. This is likely due to the increased presence of cardiovascular disease (CVD) risk factors,[6] aging related changes in the artery itself,[7] reduced physical activity/exercise participation,[8] and the decline in endogenous estrogen levels following menopause.[5] Loehr et al[3] found that AA postmenopausal women had lower (−.54%) flow mediated dilation (FMD) values compared to Caucasians. Based on data from a recent meta-analysis,[9] this racial difference in FMD corresponds to approximately a 7% increased risk in CVD in AA women. However, it is possible that this difference could be confounded by aerobic fitness and obesity, as they have not been measured in previous studies finding racial differences in endothelial function.[3,10–13] This may be an important consideration as exercise capacity is a strong predictor of mortality,[14] endothelial function is associated with fitness and obesity levels,[15] exercise training improves FMD,[16] and racial differences in body fat have been reported in postmenopausal women.[17]

Postprandial endothelial dysfunction may be an important component of CVD risk, as humans spend much of their time in a postprandial state.[18] Although racial differences in fasting endothelial function have been reported previously,[3,10–13] little data exist to our knowledge evaluating racial differences in endothelial function following a meal challenge. Since AA individuals exhibit greater oxidative stress in response to postprandial lipemia compared to Caucasians,[19] it is plausible that following a high-fat meal, AA could have greater reduction in endothelial function. However, there are no data to our knowledge whether racial differences are present in postprandial endothelial function specifically following a high-fat meal challenge.

Since AA individuals exhibit greater oxidative stress in response to postprandial lipemia compared to Caucasians,[19] it is plausible that following a high-fat meal, AA could have greater reduction in endothelial function.

The purpose of our study was to obtain pilot data regarding racial differences in endothelial function at rest and 4 hours following a high-fat meal challenge in postmenopausal AA and Caucasian women who were matched for age, aerobic fitness, percent body fat, and body mass index.

METHODS

Participants

Participants in our study were obtained from a larger prospective exercise training study, and were matched for age, percent fat, body mass index, and VO_2 peak. Postmenopausal healthy volunteers were recruited from the Charlottesville, Virginia area. The study protocol was approved by the institutional review board and each participant provided written informed consent. Follicle stimulating hormone (FSH) levels were measured to confirm postmenopausal status, however duration of menopause was not determined. Potential participants were excluded if they were taking ace-inhibitors, cholesterol lowering medications, estrogen replacement therapies, participating in aerobic exercise more than 2 times per week, had type 1 or 2 diabetes, were pre-menopausal, hypertensive or had other medical conditions that contraindicated treadmill exercise testing. This allowed us to match eight pairs of postmenopausal women. All participants were non-smokers, were not taking antioxidant supplements, and refrained from caffeine consumption for 2 hours prior to exercise testing and 12 hours prior to the meal challenge.

Body Fat

Percentage body fat was measured using air displacement plethysmography (BodPod, Life Measurement Instruments, Concord, Calif) corrected for thoracic gas volume as described previously.[20]

Determination of VO_2 Peak

Each participant began walking at an initial velocity of 60 m/min with velocity increasing by 10 m/min every 3 min (the duration of each stage) until volitional exhaustion. Metabolic measures were obtained through standard open circuit spirometry (Viasys Vmax 229, Yorba Linda, Calif). VO_2 peak was determined as the highest one-min oxygen consumption value obtained.

Baseline Measurements and Meal Challenge

Participants were admitted to the General Clinical Research Center (GCRC) after an overnight fast and rested in bed for 15 minutes prior to obtaining a fasting blood sample and the baseline measurement of FMD. Additionally, participants refrained from acute exercise for 24 hours prior to the GCRC admission. All meal challenges were initiated between 0700 and 0800h, were prepared by the GCRC metabolic kitchen, and had a caloric density of 550 kcal. The meal consumed was a breakfast meal consisting of sausage links, orange juice, eggs (with cheese), and whole milk. The macronutrient composition of the meal was approximately 57% fat, 25% protein, and 18% carbohydrate. The fatty acid composition of the meal was approximately 49% saturated, 35% monounsaturated, and 5% polyunsaturated fatty acids. We based this meal challenge on previous data from our laboratory that showed a decrease in postprandial FMD at 4 hours with a similar meal in adults with the metabolic syndrome.[21]

Endothelial Function

Flow mediated dilation was evaluated at rest and 4 hours following the high-fat meal challenge. Brachial artery assessments were obtained using 2D and Doppler ultrasound measurements (HDI 5000, Philips Ultrasound, Andover, Mass). Artery diameter was assessed using Brachial Analyzer Software (Brachial Analyzer, Medical Imaging Applications, Iowa City, Iowa), and the brachial artery mean blood velocity was measured using a pulse-wave Doppler with on-line angle correction and analysis software. All imaging was performed in the long axis approximately 4 cm proximal from the antecubital fold in the anterior/medial plane. Arterial diameters (mm) were calculated as the mean distance between the anterior and posterior wall at the vessel-blood interface. Baseline diameters measurements were triggered to the R-wave of the cardiac cycle. Mean baseline diameter was determined by averaging diameters over 1 min ($\sim$ 12 images). Flow-mediated dilation measurements were defined as the percent change in vessel diameter from rest to peak dilation.[22] We did not measure shear rate as data indicate that shear rate area under the curve is not related to FMD in older participants.[23] The same individual analyzed the data from all the FMD studies.

Prior to baseline measurements, participants were asked to rest in a supine position for 15 min. A blood pressure cuff was placed 4–5 cm distal from the antecubital fold and inflated to 50 mm Hg above resting systolic blood pressure for 5 min. The cuff was then rapidly deflated (reactive hyperemia) and measurements were obtained for peak blood flow velocity for approximately 15 seconds and ultrasound images were taken for an additional 1 minute 45 seconds to determine peak dilation (usually 60 to 90 s after cuff release).

Evaluation of fitness level and postprandial FMD measurements occurred on separate days in order to eliminate potential confounding effects of acute aerobic exercise on FMD.[24]

Blood Sampling Procedures

Three fasting blood samples were obtained (15 minutes apart) for analysis of baseline blood glucose, insulin and triglycerides. Adiponectin was measured from one blood sample obtained at baseline. Four hours following the high fat-meal challenge, we obtained a blood sample which was analyzed for triglycerides, glucose and insulin. Serum glucose concentrations were measured

Table 1. Baseline participant characteristics. Results are presented as mean ± SD

	African American (*n*=8)	Caucasian (*n*=8)
Age, years	55.0 ± 1.7	57.6 ± 5.2
Height, cm	163.4 ± 4.1	162.1 ± 6.7
Weight, kg	82.1 ± 16.5	76.7 ± 13.8
BMI, kg/m^2	30.8 ± 6.2	29.3 ± 5.1
VO_2 peak, mL/kg/min	22.1 ± 3.4	21.5 ± 3.4
Body Fat, %	43.4 ± 7.8	43.2 ± 7.8
Adiponectin, ng/mL	14556.31 ± 4561.5	16464.42 ± 6527.9
Fasting plasma insulin, μIU/mL	6.92 ± 6.4	4.52 ± 4.4
Fasting glucose, mg/dL	92.5 ± 11.3	95.00 ± 10.9
Triglycerides, mg/dL	63.8 ± 17.0	141.6 ± 119.0
HOMA-IR	1.61 ± 1.5	1.42 ± 1.3
QUICKI	.35 ± .1	.38 ± .4
Brachial artery diameter, mm	2.9 ± .5	2.8 ± .5
Peak blood flow velocity, cm/sec	99.9 ± 29.7	99.9 ±22.6

in duplicate using a glucose oxidase method (YSI Instruments 2300 STAT Plus, Yellow Springs, Ohio). Serum insulin concentrations were measured using a solid-phase chemiluminescent immunometric assay (Diagnostic Products Corporation, Immulite 2000, Los Angeles, CA); the assay sensitivity was 2 μIU/mL^{-1} and the mean intra- and interassay coefficients of variation were 4.1% and 5.1% for insulin. Serum adiponectin concentrations were measured using a commercially available ELISA method (Linco, St. Charles, MO); the assay sensitivity was 780 ng/mL^{-1} and the mean intra- and interassay coefficients of variation were 6.7% and 13.4%. Triglycerides were measured at the University of Virginia clinical lab through a glycerol phosphate oxidase method. The homeostasis model assessment–insulin resistance (HOMA-IR: [fasting glucose (mg/dl) × fasting Insulin (μU/mL)] / 405) and quantitative insulin-sensitivity check index (QUICKI: 1/[log fasting insulin (μU/mL) + log fasting glucose (mg/dl)]) were calculated.

Statistical Analysis

Statistical analyses were performed with SAS version 9.1 (SAS Institute Inc., Cary, NC). The baseline demographic data including participant: age, body weight, body mass index, height, percent body fat, peak VO_2, and blood measures (baseline insulin, glucose, adiponectin, triglycerides) were compared between the AA and Caucasian study groups with a Wilcoxon rank-sum test. Pearson correlations were used to evaluate the relationship between baseline blood analyses (triglycerides, insulin and glucose, HOMA-IR, QUICKI) with baseline FMD. In addition, we evaluated the correlation of the change in postprandial triglycerides values with change in FMD at 4 hours.

Endothelial function at rest and change in FMD (baseline to 4 hours) following the high-fat meal challenge between AA and Caucasian participants were evaluated with an analysis of covariance (ANCOVA). For endothelial function at rest, FMD at baseline was compared between AA and Caucasian participants with adjustments for triglycerides at baseline. For change in endothelial function following the meal challenge (4 hour FMD-baseline FMD), the analyses were adjusted for baseline FMD, baseline triglycerides, and change in triglycerides. In addition, we examined the effects of the meal challenge on change in postprandial triglycerides, insulin, glucose, brachial artery diameter, and peak blood flow velocity (2 × 2 ANCOVA with adjustments baseline value). The results are presented in adjusted least square means with 95% confidence intervals.

RESULTS

Demographic data are displayed in Table 1. The AA group had a mean ± SD age of 55.0 ± 1.7 yr, percent fat of 43.4 ±7.8%, and VO_2 peak of 22.1 ± 3.4 mL/kg/min. The Caucasian group had a mean age of 57.6 ± 5.2 yr, a body fat of 43.2 ± 7.8% and VO_2 peak of 21.5 ± 3.4 mL/kg/min. No significant differences in baseline characteristics were found between AA and Caucasian participants. However, the difference in triglycerides at baseline approached significance between AA (63.8 mg/dL) and Caucasian (141.6 mg/dL) participants (P=.083). The correlation between baseline FMD and baseline triglycerides, insulin, adiponectin, insulin, glucose, HOMA or QUICKI values were not significant (all P>.05).

Endothelial Function

Brachial diameter and peak blood flow following occlusion were similar between AA and Caucasian participants (Table 1). Baseline FMD was similar between AA (5.4%, CI: 3.3, 7.4) and Caucasians participants (4.0%, CI: 2.0, 6.1). As shown in Figure 1, there was no significant change in FMD from baseline to four hours within groups in AA (.9%, P=.397) or Caucasian (2.3%, P=.063) participants or between groups (P=.449). Additionally, there were no significant changes in brachial artery diameter or peak blood flow velocity following the meal challenge (P>.05) (Table 2).

Change in Postprandial Triglycerides, Glucose, and Insulin

The change in triglycerides, glucose and insulin are shown in Table 2. Within group analysis showed that postprandial triglycerides were significantly elevated following the meal challenge in AA (81.8 mg/dL, P<.001) and Caucasian (99.7 mg/dL, P=.004) participants with no significant differences in change in triglycerides (P=.579). The correlation between

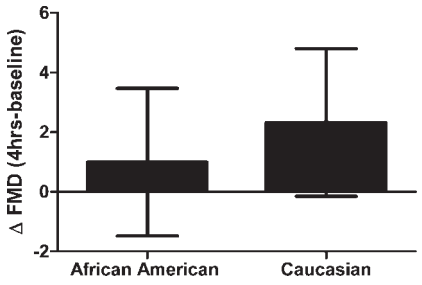

Fig 1. Change in FMD in AA and Caucasian postmenopausal women following a high fat meal challenge (57% fat, 25% protein, 18% carbohydrate). Results are presented as adjusted least square means with 95% confidence intervals

change in triglycerides and change in FMD was not significant (r=.15, P=.570). Additionally, no significant changes in insulin or glucose values within or between groups were found following the meal challenge (all P>.05).

DISCUSSION

The results of our pilot study indicate that no racial differences in baseline FMD or change in FMD following a high-fat meal were evident in postmenopausal women matched for age, fitness and body composition. Due to the fact that these are pilot data, a larger study is necessary to confirm these findings. However, to our knowledge, no studies exist evaluating the effects of a high-fat meal on endothelial function in AA compared to Caucasians individuals.

The major findings of our pilot study indicate that, in postmenopausal women matched for age, fitness and body composition, no racial differences in baseline FMD or change in FMD were evident following a high-fat meal challenge.

Table 2. Change in blood analyses and vascular function measurements following the high fat meal challenge. ANCOVA was adjusted for baseline value

	African American	Caucasian	*P* (Comparison Between Groups)
Δ Glucose (mg/dL)	1.11	−1.98	.340
Δ Insulin (mg/dL)	1.00	1.34	.908
Δ Triglyceride (mg/dL)	81.78[a]	99.80[a]	.579
Δ Brachial Artery diameter (mm)	.06	.09	.763
Δ Peak blood flow velocity (cm/sec)	9.81	13.05	.747

[a] Denotes significant change within groups. A P<.05 was used as the criterion for significance.

Previously reported racial differences in endothelial function have been proposed secondary to several potential etiologies. These include elevated oxidative stress,[25] endothelin-1 (ET-1)[10] and asymmetric demethylarginine (ADMA) levels.[11] However, many of these factors are also affected by fitness level and exercise training. Exercise training has been shown to improve antioxidant capacity,[26] thus potentially reducing the vasoconstricting effects of oxidants on nitric oxide availability.[5] Evidence from smaller training studies have found that exercise training improves ET-1 and ADMA levels.[27,28] African American individuals have been shown to have lower fitness levels compared to Caucasians,[29,30] which may be related to a lower percentage or total number of oxidative muscle fibers.[30] Zeno et al[31] found that in healthy adults (n=142), the majority of AA participants (57.1%) had low or fair fitness (determined through a treadmill VO_2 max test) compared to Caucasians (31.4%). Recent epidemiological data suggest that exercise capacity may reduce mortality in a similar manner in AA and Caucasian individuals. Kokkinos et al[32] found that for each metabolic equivalent increase in exercise capacity during a Bruce protocol treadmill test, there was a similar reduction in all-cause mortality risk in AA (14%) and Caucasian (12%) men. Therefore, future studies in this area should consider that the reported racial impairment in endothelial function could be due to reduced fitness.

Similarly, we found no racial differences in postprandial endothelial function between AA and Caucasian participants following a high-fat meal challenge. Our results support the data of Muniyappa et al[33] who found no racial differences in postprandial endothelial function following a meal challenge (20% protein, 40% fat, and 40% carbohydrate), despite lower insulin sensitivity in AA participants. However, it should be noted that contrary to previous findings,[34–36] we did not observe a significant impairment in postprandial endothelial function in either group despite a similar increase in triglyceride levels in both groups. The total caloric content of the meal challenges in previous studies evaluating postprandial FMD have ranged from 596–1480 kcals and from 30–99% fat with those studies providing >45% fat kcal resulting in a decline in FMD at 4 hours.[37] Since the size and fat content of our meal (550 kcal; ~35 g fat) were less than previous reports,[34–36] this may have resulted in an insufficient fat load. A critical kcal load, or fat content of the meal, may be necessary to induce postprandial impairment in FMD. Strey et al,[38] for example, reported no

impairment in endothelial function in women with type 2 diabetes after consuming a 660-kcal meal containing 40g fat. In contrast, Steer et al[39] reported significant impairment in endothelium-dependent vasodilation in women and men after consuming a meal containing only 26–34g fat (although total energy content of the meal was 700–900 kcal). Additionally, other factors such as the diurnal rhythm of endothelial function, and the FMD procedure itself[24] may have countered the potential impairment of our high-fat meal in the present study. Thus, our pilot data suggest no racial differences in the change in FMD or other blood measures (triglycerides, glucose or insulin) following the meal challenge, and no racial differences in postprandial endothelial function in participants matched for age, body composition and fitness level.

It is important to note that there are several limitations in this investigation. Due to the pilot nature of this investigation, we had a small sample of postmenopausal women ($n=16$). In addition, we did not have a fasting control condition that would have allowed us to determine the magnitude of the diurnal rhythm in FMD, and whether this differed by race. Secondly, we had a wide range of baseline triglyceride levels in the Caucasian participants compared to the AA participants (approached significance between groups), which may affect racial differences in FMD at baseline. Since the reported triglyceride levels at baseline were the average value of three samples obtained prior to the meal challenge, it is unlikely that the wider distribution seen in the Caucasian group was due to measurement error. Lastly, FMD values were not corrected for shear rate area under the curve. However, there is evidence that shear stress normalization may only be appropriate for young adults, as Thijssen et al[23] observed no significant correlation between FMD and various methods of shear stress correction in older adults. Additionally, previous studies have observed significant relationships between FMD uncorrected for shear and cardiovascular disease risk.[1,40]

CONCLUSIONS

The results of the present pilot study indicate that baseline and postprandial endothelial function is similar in AA and Caucasian postmenopausal women matched for age, fitness and body composition. Our results may suggest that fitness and body composition should be taken into account when examining differences in endothelial function between AA and Caucasians individuals. Future research should investigate the possible racial differences following meals composed of other macronutrient compositions, and the effect of previous FMD measurements on postprandial endothelial dysfunction.

ACKNOWLEDGMENTS

We would like to thank the University of Virginia General Clinical Research Center, and NIH grant RR00847 for the resources to complete this project.

REFERENCES

1. Rossi R, Nuzzo A, Origliani G, Modena MG. Prognostic role of flow-mediated dilation and cardiac risk factors in post-menopausal women. *J Am Coll Cardiol*. 2008;51(10):997–1002.
2. Rossi R, Chiurlia E, Nuzzo A, Cioni E, Origliani G, Modena MG. Flow-mediated vasodilation and the risk of developing hypertension in healthy postmenopausal women. *J Am Coll Cardiol*. 2004;44(8):1636–1640.
3. Loehr LR, Espeland MA, Sutton-Tyrrell K, Burke GL, Crouse JR, Herrington DM. Racial differences in endothelial function in postmenopausal women. *Am Heart J*. 2004;148(4):606–611.
4. Taddei S, Virdis A, Ghiadoni L, et al. Menopause Is Associated With Endothelial Dysfunction in Women. *Hypertension*. 1996;28(4):576–582.
5. Seals DR, Jablonski KL, Donato AJ. Aging and vascular endothelial function in humans. *Clin Sci*. 2011;120(9–10):357–375.
6. Matthews KA, Kuller LH, Sutton-Tyrrell K, Chang Y-F, Tietjen GE, Brey RL. Changes in cardiovascular risk factors during the perimenopause and postmenopause and carotid artery atherosclerosis in healthy women: premenopausal risk continuum for carotid atherosclerosis after menopause. *Stroke*. 2001;32(5):1104–1111.
7. Brandes RP, Fleming I, Busse R. Endothelial aging. *Cardiovasc Res*. 2005;66(2):286–294.
8. Poehlman ET, Toth MJ, Gardner AW. Changes in energy balance and body composition at menopause: a controlled longitudinal study. *Ann Intern Med*. 1995;123(9):673–675.
9. Inaba Y, Chen J, Bergmann S. Prediction of future cardiovascular outcomes by flow-mediated vasodilatation of brachial artery: a meta-analysis. *Int J Cardiovasc Imaging*. 2010;26(6):631–640.
10. Campia U, Cardillo C, Panza JA. Ethnic differences in the vasoconstrictor activity of endogenous endothelin-1 in hypertensive patients. *Circulation*. 2004;109(25):3191–3195.
11. Melikian N, Wheatcroft SB, Ogah OS, et al. Asymmetric dimethylarginine and reduced nitric oxide bioavailability in young Black African men. *Hypertension*. 2007;49(4):873–877.
12. Perregaux D, Chaudhuri A, Rao S, et al. Brachial vascular reactivity in Blacks. *Hypertension*. 2000;36(5):866–871.
13. Campia U, Choucair WK, Bryant MB, Waclawiw MA, Cardillo C, Panza JA. Reduced endothelium-dependent and -independent dilation of conductance arteries in African Americans. *J Am Coll Cardiol*. 2002;40(4):754–760.
14. Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise capacity and mortality among men referred for exercise testing. *N Engl J Med*. 2002;346(11):793–801.
15. Palmieri EA, Palmieri V, Innelli P, et al. Aerobic exercise performance correlates with post-ischemic flow-mediated dilation of the brachial artery in young healthy men. *Eur J Appl Physiol*. 2005;94(1):113–117.
16. Green DJ, Maiorana A, O'Driscoll G, Taylor R. Effect of exercise training on endothelium-derived nitric oxide function in humans. *J Physiol*. 2004;561(1):1–25.
17. Kanaley JA, Giannopoulou I, Tillapaugh-Fay G, Nappi JS, Ploutz-Snyder LL. Racial differences in subcutaneous and visceral fat distribution in postmenopausal Black and White women. *Metabolism*. 2003;52(2):186–191.
18. Zilversmit D. Atherogenic nature of triglycerides, postprandial lipidemia, and triglyceride-rich remnant lipoproteins. *Clin Chem*. 1995;41(1):153–158.
19. Lopes HF, Morrow JD, Stoijiljkovic MP, Goodfriend TL, Egan BM. Acute hyperlipidemia increases oxidative stress more in African Americans than in White Americans. *Am J Hypertens*. 2003;16(5):331–336.

20. Dempster P, Aitkens S. A new air displacement method for the determination of human body composition. *Med Sci Sports Exerc*. 1995;27(12):1692–1697.
21. Brock DW, Davis CK, Irving BA, et al. A high-carbohydrate, high-fiber meal improves endothelial function in adults with the metabolic syndrome. *Diabetes Care*. 2006;29(10): 2313–2315.
22. Corretti MC, Anderson TJ, Benjamin EJ, et al. Guidelines for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of the brachial artery: a report of the international brachial artery reactivity task force. *J Am Coll Cardiol*. 2002;39:257–265.
23. Thijssen DHJ, Bullens LM, van Bemmel MM, et al. Does arterial shear explain the magnitude of flow-mediated dilation?: a comparison between young and older humans. *Am J Physiol Heart Circ Physiol*. 2009;296(1): H57–H64.
24. Zhu W, Zeng J, Yin J, et al. Both flow-mediated vasodilation procedures and acute exercise improve endothelial function in obese young men. *Eur J Appl Physiol*. 2010;108(4): 727–732.
25. Kalinowski L, Dobrucki IT, Malinski T. Race-specific differences in endothelial function: predisposition of African Americans to vascular ciseases. *Circulation*. 2004;109(21): 2511–2517.
26. Powers SK, Ji LL, Leeuwenburgh C. Exercise training-induced alterations in skeletal muscle antioxidant capacity: a brief review. *Med Sci Sports Exerc*. 1999;31(7):987–997.
27. Maeda S, Miyauchi T, Kakiyama T, et al. Effects of exercise training of 8 weeks and detraining on plasma levels of endothelium-derived factors, endothelin-1 and nitric oxide, in healthy young humans. *Life Sci*. 2001;69(9):1005–1016.
28. Mittermayer F, Pleiner J, Krzyzanowska K, Wiesinger G, Francesconi M, Wolzt M. Regular physical exercise normalizes elevated asymmetrical dimethylarginine concentrations in patients with type 1 diabetes mellitus. *Wien Klin Wochenschr*. 2005;117(23):816–820.
29. LaMonte MJ, Durstine JL, Yanowitz FG, et al. Cardiorespiratory fitness and C-reactive protein among a tri-ethnic sample of women. *Circulation*. 2002;106(4):403–406.
30. Hunter GR, Weinsier RL, Darnell BE, Zuckerman PA, Goran MI. Racial differences in energy expenditure and aerobic fitness in premenopausal women. *Am J Clin Nutr*. 2000;71(2):500–506.
31. Zeno SA, Kim-Dorner SJ, Deuster PA, Davis JL, Remaley AT, Poth M. Cardiovascular fitness and risk factors of healthy African Americans and Caucasians. *J Natl Med Assoc*. 2010;102(1):28–35.
32. Kokkinos P, Myers J, Kokkinos JP, et al. Exercise capacity and mortality in Black and White men. *Circulation*. 2008;117(5):614–622.
33. Muniyappa R, Sachdev V, Sidenko S, et al. Postprandial Endothelial Function Does Not Differ in Women by Race: An Insulin Resistance Paradox? *Am J Physiol Endocrinol Metab*. 2012;302(2):E218–E225.
34. Padilla J, Harris R, Fly A, Rink L, Wallace J. The effect of acute exercise on endothelial function following a high-fat meal. *Eur J Appl Physiol*. 2006;98(3):256–262.
35. Plotnick GD, Corretti MC, Vogel RA. Effect of antioxidant vitamins on the transient impairment of endothelium-dependent brachial artery vasoactivity following a single high-fat meal. 1997;278(20):1682–1686.
36. Vogel RA, Corretti MC, Plotnick GD. Effect of a single high-fat meal on endothelial function in healthy subjects. *Am J Cardiol*. 1997;79(3):350–354.
37. Wallace JP, Johnson B, Padilla J, Mather K. Postprandial lipaemia, oxidative stress and endothelial function: a review. *Int J Clin Pract*. 2010;64(3):389–403.
38. Strey CH, Young J, Collier M, Florkowski CM, Shand BI, Scott RS. The postprandial state does not impair endothelial function in women with type 2 diabetes irrespective of glycaemic control. *Diabetologia*. 2004;47(10): 1838–1846.
39. Steer P, Sarabi DM, Karlström B, et al. The effect of a mixed meal on endothelium-dependent vasodilation is dependent on fat content in healthy humans. *Clin Sci*. 2003;105(1):81–87.
40. Benjamin EJ, Larson MG, Keyes MJ, et al. Clinical correlates and heritability of flow-mediated dilation in the community: the Framingham Heart Study. *Circulation*. 2004;109(5):613–619.

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