

## The effect of acute exercise on endothelial function following a high-fat meal

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**Abstract** The transient impairment of endothelial function following a high-fat meal is well established. Brachial artery flow-mediated dilation (FMD) decreases between 2 and 6 h post ingestion. Whether this impairment can be reduced with acute aerobic exercise has not been investigated. The purpose of this study was to investigate if a single sustained aerobic exercise session can counteract the postprandial attenuation in brachial artery FMD associated with the ingestion of a high-fat meal. Eight apparently healthy adults (five men, three women), age  $25.5 \pm 0.8$  years, performed three treatment conditions in a counter-balanced design: (1) low-fat meal alone (LFM), (2) high-fat meal alone (HFM), and (3) one session of aerobic exercise presented 2 h after ingesting a high-fat meal (HFM-EX). The examination of brachial artery FMD was performed at baseline and 4 h following the ingestion of the meal for each treatment condition. A  $3 \times 2$  (treatment  $\times$  time) repeated measures ANOVA exhibited a significant interaction ( $P = 0.019$ ). Preprandial FMDs were similar ( $P = 0.863$ ) among all three

treatment conditions. The FMDs following the LFM ( $7.18 \pm 1.31\%$ ) and HFM-EX ( $8.72 \pm 0.94\%$ ) were significantly higher ( $P = 0.001$ ) than the FMD following the HFM ( $4.29 \pm 1.64\%$ ). FMD was significantly elevated above preprandial values following the HFM-EX ( $5.61 \pm 1.54$  to  $8.72 \pm 0.94\%$ ,  $P = 0.005$ ) but was unchanged following the LFM ( $6.17 \pm 0.94$  to  $7.18 \pm 1.31\%$ ,  $P = 0.317$ ) and the HFM ( $5.73 \pm 1.23$  to  $4.29 \pm 1.64\%$ ,  $P = 0.160$ ). These findings suggest that a single aerobic exercise session cannot only counteract the postprandial endothelial dysfunction induced by the ingestion of a high-fat meal, but also increase brachial artery FMD in apparently healthy adults.

**Keywords** Aerobic exercise · High-fat diet · Postprandial endothelial dysfunction · Flow-mediated dilation

### Introduction

Atherosclerotic cardiovascular disease is the leading cause of morbidity and mortality in western society (Devaraj and Jialal 1996). The impairment of endothelial function is the primary etiology implicated in the origin and development of atherosclerotic cardiovascular disease (Ross 1999). Since 1992, the non invasive measurement of brachial artery flow-mediated dilation (FMD) has been used to evaluate endothelial function (Celermajer et al. 1992), which is considered a marker of atherosclerotic disease risk (Verma et al. 2003). Among the factors found to compromise endothelial function is the consumption of a high-fat meal (Cuevas et al. 2000). Ingestion of a high-fat meal attenuates endothelial function for up to 6 h with the peak

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dysfunction occurring 4 h following the ingestion (Gaenger et al. 2001; Plotnick et al. 1997; Vogel et al. 1997). It is proposed that postprandial hypertriglyceridemia leads to endothelial dysfunction via enhanced oxidative stress (Bae et al. 2001). In addition, it has been suggested that the repeated postprandial endothelial dysfunction associated with a high-fat meal may lead to atherogenesis (Anderson et al. 2001). Since a significant part of the day is spent in the postprandial state (Sies et al. 2005), strategies that counteract this state may be effective in preventing atherosclerotic cardiovascular disease.

Both acute and chronic exercise have been shown to enhance endothelial function (Harvey et al. 2005; Walther et al. 2004). In addition, acute exercise counteracts hypertriglyceridemia (Katsanos and Moffatt 2004) following a high-fat meal and enhances antioxidant activity (Ji 2002). It is reasonable to anticipate that acute exercise may lessen the postprandial endothelial dysfunction; however only limited research by Gill et al. (2004) has addressed this hypothesis. In their study, subjects walked on a treadmill for 90 min at 50% of  $\dot{V}O_{2\max}$ , 16–18 h prior to the ingestion of the high-fat meal. Peripheral microvascular function after the meal was found to be 15% higher for the exercise condition than for the non-exercise control condition. Whether similar effects occur in the conduit arteries has not been investigated. Thus, the purpose of this study was to investigate if a single sustained aerobic exercise session can counteract the postprandial attenuation in brachial artery FMD associated with the ingestion of a high-fat meal. It was hypothesized that endothelial function, measured by brachial artery FMD, following a high-fat meal in combination with a single session of aerobic exercise would be greater than the FMD following a high-fat meal alone.

## Methods

### Experimental design

A within-subjects experimental design with three treatment conditions, each separated by 2–7 days, was presented to eight apparently healthy adults in a counter-balanced manner. Treatment conditions consisted of (1) ingestion of a low-fat meal alone (LFM), (2) ingestion of a high-fat meal alone (HFM), and (3) one session of aerobic exercise presented 2 h after ingesting a high-fat meal (HFM-EX). Assessment of endothelial function was performed at baseline (0730 h) and 4 h following the ingestion of the meal (1200 h) for each treatment condition. To control for confounding

variables, subjects were instructed to (1) fast for 12 h, (2) abstain from exercise for 24 h, (3) abstain from caffeine, tobacco, and vitamin supplements for 12 h, and (4) awake between 0600 and 0700 h, all prior to each treatment condition (Corretti et al. 2002). Subjects were asked to remain in the laboratory or minimize physical activity between measurements. Procedures were approved by the Indiana University Committee for the Protection of Human Subjects.

### Subjects

Eight apparently healthy physically active young adults (five men, three women) participated in this study. None of the subjects had a history of hypertension, diabetes mellitus, or tobacco use. Exclusion criteria included: (1) cardiovascular, pulmonary or metabolic disease, (2) absolute contraindications to exercise testing as established by the American College of Sports Medicine (American 2005), (3) known gallbladder disease, (4) dietary restrictions regarding the meals provided, (5) vaso-active medications (Corretti et al. 2002), and (6) brachial artery diameter > 5.0 mm (Corretti et al. 2002). Written informed consent was obtained from each subject prior to participation in the study.

### Study procedures

The procedures of the study consisted of risk stratification and screening, performance of a graded maximal exercise test, and completion of the three treatment conditions with pre- and post-assessment of brachial artery FMD.

#### *Risk stratification and screening*

To determine the subject's risk stratification for exercise and eligibility for the study, subjects completed a medical history/health habits questionnaire and underwent a fasting venous blood draw to test for total serum cholesterol and low density lipoprotein cholesterol.

#### *Graded maximal exercise test*

A graded exercise test ( $\dot{V}O_{2\text{peak}}$ ) was performed to determine the individualized target workload for the exercise session (60% of  $\dot{V}O_{2\text{peak}}$ ). The test was performed on a motor driven-treadmill and began at speeds between  $67.0 \text{ m min}^{-1}$  (2.5 mph) and  $134.1 \text{ m min}^{-1}$  (5.0 mph) at 0% grade. The grade was increased 2.5% every two minutes until a maximal

voluntary effort was achieved. Expired gases were measured using the mixing chamber on a Sensor Medics 2900 Metabolic Cart (Sensor Medics Corporation, Yorba Linda, CA, USA). To confirm that maximal effort had been achieved, objective and subjective indicators were used as described by the American College of Sports Medicine (2005).

#### *Treatment conditions*

**Meal interventions** All meals, previously used in other studies (Padilla et al. 2006; Plotnick et al. 1997; Vogel et al. 1997), were presented in the laboratory at 0800 h. The low-fat meal consisted of 154 g of Frosted Flakes (Kellogg Company), 240 ml of skim milk, and 480 ml of orange juice ([3.96 kJ (945 calories)] 0 g fat, 0 g saturated fat, 0 g trans fat, 5 mg cholesterol, 209 g carbohydrates, 23 g protein, 959 mg sodium). The high-fat meal consisted of an Egg McMuffin, a Sausage McMuffin, two hash brown patties (McDonald's Corporation), and water ([3.93 kJ (940 calories)], 48 g fat, 16.5 g saturated fat, 4.5 g trans fat, 280 mg cholesterol, 91 g carbohydrates, 33 g protein, 2,220 mg sodium).

**Exercise intervention** Two hours following the ingestion of one of the high-fat meals, subjects performed a single 45-min continuous bout of treadmill walking at 60% of  $VO_2$  peak. Oxygen uptake ( $VO_2$ ) was measured during the fifth to seventh minute to confirm the exercise intensity. The work rate was adjusted if it was not within  $\pm 10\%$  of the target oxygen uptake. Following the adjustment (if necessary), another gas collection was made after steady state was achieved to confirm the intensity. Heart rate (via Polar monitor), blood pressure (via auscultation) and rating of perceived exertion [using the Borg scale of 6–20 (Borg 1973)] were monitored every 5 min throughout the exercise bout.

#### Brachial artery flow-mediated dilation

Brachial artery FMD was assessed before the meal (0730 h) and 4 h (1200 h) following the meal for each treatment condition. For each FMD measurement, subjects were instructed to lie supine in a dark, climate-controlled room (22–24°C), with their right arm extended out laterally. Each subject underwent an acclimation phase of 20 min to control the hemodynamic response. A blood pressure cuff was placed on the subject's right forearm to induce reactive hyperemia. The brachial artery was imaged longitudinally, 2–10 cm above the antecubital fossa by 2D high reso-

lution Sonoace Pico ultrasound system (Universal Medical Systems, Bedford Hills, NY, USA), using a 7 MHz linear transducer. The placement of the transducer was marked on the skin to ensure the same positioning for all measurements. Once a clear artery image was obtained, a still image was captured on the ultrasound (baseline image). The forearm blood pressure cuff was then inflated to 26.67 kPa (200 mm Hg). After 5 min of occlusion, the pressure was rapidly released to allow for reactive hyperemia to occur. The brachial artery was continuously imaged throughout the entire procedure. A still image was captured at 60 s following the release of the blood pressure cuff. For each still image, five brachial artery diameters were measured in evenly spaced segments, approximately every 0.25 cm using B-mode as previously described (Harris et al. 2006; Padilla et al. 2006). The average of five measurements was used to represent the diameter of the artery. All measurements were taken by the same operator, who was blind to the subject and treatment condition. Flow-mediated dilation was expressed as the percent change in diameter from baseline to post occlusion diameter value. Reproducibility of our FMD measurement was previously investigated using 60 independent images from 5 subjects. Inter-observer reliability yielded an Intra-Class Correlation Coefficient (ICC) of 0.977 with a variation of 2.32%. Intra-observer reliability yielded an ICC of 0.978 and a variation of 2.22%. This reproducibility is acceptable according to the current guidelines for the ultrasound assessment of brachial artery FMD (Corretti et al. 2002).

#### Blood velocity

Blood velocity ( $\text{cm s}^{-1}$ ) was measured using Pulse Doppler at baseline and at peak hyperemia (within 15 s following the release of the blood pressure cuff) with the Doppler flow signal corrected at an insonation angle of 70°. Measurements were performed with the sample volume placed in mid-artery.

#### Statistical analysis

Descriptive statistics were used to summarize the demographic characteristics of the subjects. To test the differences in FMD and peak hyperemic velocity among treatment conditions, a  $3 \times 2$  (treatment  $\times$  time) repeated measures ANOVA was performed (SPSS Inc., Chicago, IL, v.12.0). Tukey's Post Hoc test was used when a significant *F*-ratio was found. All data are presented as mean  $\pm$  standard error of the mean (SEM). Statistical significance was set at  $P < 0.05$ .

**Table 1** Demographic characteristics of the subjects

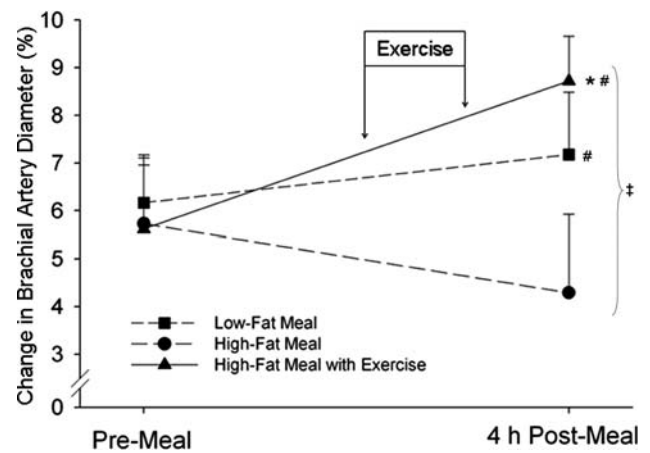
Variable	Value
<i>N</i>	8
Sex (men/women)	5/3
Age (yr)	25.5 ± 0.8
Height (cm)	170.2 ± 3.3
Weight (kg)	66.4 ± 3.4
BMI (kg m <sup>-2</sup> )	22.8 ± 0.6
Total serum cholesterol (mg dl <sup>-1</sup> )	168.2 ± 8.6
Low density lipoprotein cholesterol (mg dl <sup>-1</sup> )	91.0 ± 4.3
VO <sub>2peak</sub> (ml kg <sup>-1</sup> min <sup>-1</sup> )	52.9 ± 2.9

Values are means ± SEM

## Results

Demographic information of the subjects is summarized in Table 1. For the 45-min treadmill walk, the mean VO<sub>2</sub> and heart rate were 32.1 ± 1.8 ml kg<sup>-1</sup> min<sup>-1</sup> (60.7 ± 0.7% of VO<sub>2peak</sub>) and 152 ± 4 beat min<sup>-1</sup>, respectively. Subjects rated the intensity of the walk as 12.3 ± 0.6 (between “fairly light” and “somewhat hard”) on the Borg scale of 6–20 (Borg 1973).

Mean baseline brachial artery diameter, absolute change in diameter, and blood velocity are presented in Table 2. Baseline diameter, baseline velocity, and peak hyperemic velocity were similar among the three treatment conditions ( $P > 0.05$ ). The Fig. 1 illustrates the 4 h FMD response to LFM, HFM, and HFM-EX. A 3 × 2 (treatment × time) repeated measures ANOVA exhibited a significant interaction ( $F_{(2,14)} = 20.64$ ;  $P = 0.019$ ). Preprandial FMDs were similar among treatment conditions ( $F_{(2,28)} = 0.15$ ;  $P = 0.863$ ), whereas postprandial FMDs were significantly different ( $F_{(2,28)} = 8.94$ ;  $P = 0.001$ ). Tukey's Post Hoc analysis indicated that FMDs following the LFM (7.18 ± 1.31%) and HFM-EX (8.72 ± 0.94%) were significantly higher ( $P < 0.05$ ) than the FMD following the HFM (4.29 ± 1.64%); however, the difference between



**Fig. 1** The effects of a low-fat meal, high-fat meal, and high fat meal with exercise on flow-mediated dilation (mean ± SEM). <sup>†</sup>Significant 3 × 2 repeated measures ANOVA interaction ( $P = 0.019$ ). \*Significantly different from pre-meal within treatment type ( $P = 0.005$ ). #Significantly different from 4 h post-high-fat meal ( $P = 0.001$ )

postprandial LFM and HFM-EX was not significant. FMD was significantly elevated ( $P < 0.05$ ) above preprandial values following the HFM-EX (5.61 ± 1.54 to 8.72 ± 0.94%;  $F_{(1,21)} = 9.88$ ;  $P = 0.005$ ) but was unchanged following the LFM (6.17 ± 0.94 to 7.18 ± 1.31%;  $F_{(1,21)} = 1.05$ ;  $P = 0.317$ ) and the HFM (5.73 ± 1.23 to 4.29 ± 1.64%;  $F_{(1,21)} = 2.13$ ;  $P = 0.160$ ).

## Discussion

The purpose of this study was to investigate if a single sustained aerobic exercise session can counteract the postprandial attenuation in brachial artery FMD associated with the ingestion of a high-fat meal. The examination of brachial artery FMD was performed before and 4 h following the ingestion of a low-fat meal alone (LFM), high-fat meal alone (HFM), and high-fat meal followed by one session of aerobic exercise

**Table 2** Preprandial and postprandial artery diameter and blood velocity values at baseline and during hyperemia among treatment conditions

	Time	Baseline artery diameter (mm)	Change in artery diameter (mm)	Baseline blood velocity (cm s <sup>-1</sup> )	Hyperemic blood velocity (cm s <sup>-1</sup> )
Low-Fat Meal	Pre	3.65 ± 0.24	0.23 ± 0.04	11.74 ± 2.63	88.77 ± 7.91
	4 h Post	3.58 ± 0.24	0.25 ± 0.04**	8.23 ± 0.90	79.58 ± 5.20
High-Fat Meal	Pre	3.40 ± 0.28	0.19 ± 0.03	10.33 ± 1.55	85.05 ± 8.33
	4 h Post	3.62 ± 0.33	0.14 ± 0.05	7.87 ± 1.61	79.46 ± 9.69
High-Fat Meal with Exercise	Pre	3.54 ± 0.31	0.19 ± 0.04	12.77 ± 3.23	81.50 ± 8.59
	4 h Post	3.54 ± 0.32	0.30 ± 0.03***	11.98 ± 2.68	90.98 ± 5.12

Values are mean ± SEM

\*Significantly different from pre-meal ( $P < 0.05$ )

\*\*Significantly different from 4 h post-high-fat meal ( $P < 0.05$ )

(HFM-EX). The findings from this investigation suggest that a single aerobic exercise session can not only counteract the postprandial endothelial dysfunction induced by the ingestion of a high-fat meal, but also increase brachial artery FMD in apparently healthy adults.

The design of our investigation was primarily based on the finding that peak endothelial dysfunction in healthy adults is found 4 h following the ingestion of a high-fat meal (Vogel et al. 1997), and that endothelial function is found to increase 1 h after a single bout of exercise (Harvey et al. 2005). The end of the exercise session was timed to conclude 1 h before the expected peak impairment of endothelial function associated with the high-fat meal. This timing would allow an optimal assessment of the potential for exercise to counteract the adverse effect associated with a high-fat meal.

A significant decrease in brachial artery FMD has been reported following a high-fat meal by others (Gaenger et al. 2001; Plotnick et al. 1997; Vogel et al. 1997), yet no significant difference was found between pre- and post-high-fat meal brachial artery FMD in the present study. Although the main purpose of the present study was not to identify the FMD response to a high-fat meal alone, the medium effect size and low power found for this simple main effect ( $F_{(1,21)} = 2.13$ ; partial  $\omega^2 = 0.066$ ; power = 0.285) suggests a lucid trend of endothelial dysfunction. Furthermore, the 4 h FMD following the high-fat meal was significantly lower than the 4 h FMD following the low-fat meal (Fig. 1). The difference between the 4 h FMDs for the high- and low-fat meals clearly illustrates a relative dysfunction associated with the high-fat meal. When exercise was combined with the ingestion of a high-fat meal, increases in FMD were remarkable.

Our findings are similar to Gill and colleagues (Gill et al. 2004), the only other group to investigate the interaction of exercise and a high-fat meal. They investigated the effects of a 90-min treadmill walk at 50% of  $VO_{2max}$ , 16–18 h prior to the ingestion of the high-fat meal on peripheral microvascular function. Our contribution beyond those reported by Gill and colleagues includes (1) the order and timing of the meal in relation to the exercise session, (2) the use of FMD technology, and (3) the exercise stimulus. Gill and colleagues presented the exercise 16–18 h before the meal, whereas we presented the exercise 2 h following the meal. Gill and colleagues utilized microcirculatory techniques to assess endothelial function, whereas we utilized the widely used and standardized technique of brachial artery FMD (Corretti et al. 2002). Gill and colleagues utilized 90 min of treadmill walking at 50% of  $VO_{2max}$ , whereas we utilized 45 min of treadmill

walking at 60%. The duration of exercise in our investigation complies with the current exercise recommendation for prevention and treatment in disease (American College of Sports Medicine 2005).

Although the present study was not intended to elucidate a biological mechanism through which exercise could counteract the deleterious effects of a high-fat meal, possible mechanisms are suggested. First, it is possible for exercise to act through a direct blood flow mechanism. The increased blood flow from exercise may have produced an adequate shear-stress stimulus to release nitric oxide, which could have enhanced vascular endothelial function (Jungersten et al. 1997). Second, exercise may have lessened the endothelial dysfunction associated with the high-fat meal by diminishing the oxidative stress and subsequent inflammatory response (Zhao and Bokoch 2005). An association between an increase in oxidative stress, depletion of endogenous antioxidants and endothelial dysfunction after the ingestion of a high-fat meal has been recently documented (Tsai et al. 2004). This increase in oxidative stress is proposed to produce an inflammatory response. Paradoxically, exercise also induces oxidative stress, which would appear incompatible with its protective effects (Vollaard et al. 2005); however, it is unclear whether this stress induces any harmful cellular damage. In addition, the exercise-induced oxidative stress results in an increase in the production of antioxidant enzyme activity in mice (Meilhac et al. 2001), providing beneficial effects on the endothelium. The increase in antioxidants may be sufficiently strong to not only counteract the oxidative stress from the meal and the exercise, but to improve the overall oxidative balance and as a result enhance endothelial function. As another alternative, skeletal muscle contraction has been shown to release an anti-inflammatory cytokines (Steensberg et al. 2000), which may contribute to the prevention of endothelial dysfunction. Further research on the association among markers of oxidative stress, inflammation, exercise by-products, and endothelial function following the ingestion of a high-fat meal is warranted to provide insight on the possible physiological mechanisms through which exercise counteracts the postprandial endothelial dysfunction. In addition, the role of blood flow must also be investigated.

There are a few limitations to this study. Although the small sample size may appear a limitation of the study, the presence of a statistically significant interaction with a large effect size is indicative of a meaningful treatment effect. It is likely that with an inclusion of more subjects, a statistically significant reduction in FMD following the high-fat meal similar to other

reports in the literature (Gaenger et al. 2001; Plotnick et al. 1997; Vogel et al. 1997) could have been found. The small number of men and women impeded the evaluation of sex differences; thus the effect of sex on the FMD response to acute exercise remains unknown. Nevertheless, sex has been shown to have no effect on the FMD response to a high-fat meal (Plotnick et al. 1997). In addition, because subjects were tested on different days, a change in the menstrual cycle phase can be considered a confounding variable of FMD when examining women. Our sample was composed of apparently healthy physically active young adults; thus the present findings are limited to the population investigated. Similar studies need to be conducted with older adults or clinical populations. In terms of the experimental design, the absence of a fourth treatment day consisting of low-fat meal with exercise impeded the examination of the exercise effect solely; thus, it is unknown to what extent a high-fat meal prevents the positive effect of exercise on endothelial function. From a technological standpoint, the inability to ECG gate and the non-synchronized velocity and diameter measures are limitations of this study (i.e. incapacity to provide estimates of blood flow); however, our laboratory techniques have been shown to generate valid and reproducible data (Harris et al. 2006; Padilla et al. 2006).

The significance of this study is notable. First, the results from this investigation contribute to understanding the protective role of exercise in cardiovascular disease. Although the salutary effects of exercise on the cardiovascular system have been well documented, the mechanism through which exercise produces these beneficial effects remains uncertain (Meilhac et al. 2001). Our results are suggestive of a protective pathway through which exercise is acting. Second, we showed that exercise is effective in counteracting the postprandial endothelial dysfunction when presented 1 h following a high-fat meal; however, further study of the duration of the effect is warranted to determine the clinical relevance of this finding. Since a significant part of the day is spent in the postprandial state (Sies et al. 2005), interventions that reduce the postprandial atherogenic affects may contribute to the prevention of atherosclerotic cardiovascular disease, the leading cause of morbidity and mortality in western society (Devaraj and Jialal 1996).

In conclusion, we found that a single sustained aerobic exercise session can not only counteract the postprandial endothelial dysfunction induced by the ingestion of a high-fat meal, but increase brachial artery FMD in apparently healthy adults. These findings may be of clinical significance because postpran-

dial endothelial function is considered a major factor for atherosclerotic cardiovascular disease. Further investigation is warranted to provide insight into the possible mechanisms through which exercise acts to enhance endothelial function and counteract the deleterious effects of a high-fat meal. In addition, it may be of clinical interest to investigate to what extent a high-fat meal can prevent the improvement of endothelial function following exercise.

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## References

- American College of Sports Medicine (2005) ACSM's guidelines for exercise testing and prescription, 7th edn. Lippincott Williams & Wilkins, Philadelphia
- Anderson RA, Jones CJH, Goodfellow J (2001) Is the fat meal a trigger for acute coronary syndromes? *Atherosclerosis* 159:9–15
- Bae JH, Bassing E, Kim KB, Kim YN, Kim KS, Lee HJ, Moon KC, Lee MS, Park KY, Schewemmer M (2001) Postprandial hypertriglyceridemia impairs endothelial function by enhanced oxidant stress. *Atherosclerosis* 155:517–523
- Borg GA (1973) Perceived exertion: a note on "history" and methods. *Med Sci Sports* 5:90–93
- Celermajer DS, Sorensen KE, Gooch VM (1992) Non-invasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis. *Lancet* 340:1111–1115
- Corretti MC, Anderson TJ, Benjamin EJ, Celermajer D, Charbonneau F, Creager MA, Deanfield J, Drexler H, Gehard-Herman M, Herrington D, Vallance P, Vita J, Vogel R (2002) Guidelines for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of the brachial artery. *J Am Coll Cardiol* 39:257–265
- Cuevas AM, Guasch V, Castillo O, Irribarra V, Mizon C, San Martin A, Strobel P, Perez D, Germain AM, Leighton F (2000) A high-fat diet induces and red wine counteracts endothelial dysfunction in human volunteers. *Lipids* 35:143–148
- Devaraj S, Jialal I (1996) Oxidized low-density lipoprotein and atherosclerosis. *Int J Clin Lab Res* 26:178–184
- Gaenger H, Sturm W, Neumayr G, Kirchmair R, Ebenbichler C, Ritsch A, Foger B, Weiss G, Patsch JR (2001) Pronounced postprandial lipemia impairs endothelium-dependent dilation of the brachial artery in men. *Cardiovasc Res* 52:509–516
- Gill JMR, Al-Mamari A, Ferrell WR, Cleland SL, Packard CJ, Sattar N, Petrie JR, Caslake MJ (2004) Effects of prior moderate exercise on postprandial metabolism and vascular function in lean and centrally obese men. *J Am Coll Cardiol* 44:2375–2382
- Harris RA, Padilla J, Rink LD, Wallace JP (2006) Variability of flow-mediated dilation measurements with repetitive reactive hyperemia. *Vasc Med* 11:1–6
- Harvey PJ, Beverley LM, Kubo T, Picton PE, Su WS, Catherine FN, Floras JS (2005) Hemodynamic after-effects of acute dynamic exercise in sedentary normotensive postmenopausal women. *J Hypertens* 23:285–292

- Ji LL (2002) Exercise-induced modulation of antioxidant defense. *Ann N Y Acad Sci* 959:82–92
- Jungersten L, Ambring A, Wall B, Wennmalm A (1997) Both physical fitness and acute exercise regulate nitric oxide formation in healthy humans. *J Appl Physiol* 82:760–764
- Katsanos CS, Moffatt RJ (2004) Acute effects of premeal versus postmeal exercise on postprandial hypertriglyceridemia. *Clin J Sport Med* 14:33–39
- Meilhac O, Ramachandran S, Chiang K, Santanam N, Parthasarathy S (2001) Role of arterial wall antioxidant defense in beneficial effects of exercise on atherosclerosis in mice. *Arterioscler Thromb Vasc Biol* 21:1681–1688
- Padilla J, Harris RA, Fly DA, Rink LD, Wallace JP (2006) A comparison between active- and reactive-hyperaemia-induced brachial artery vasodilation. *Clin Sci* 110:387–392
- Plotnick GD, Corretti MC, Vogel RA (1997) Effect of antioxidant vitamins on the transient impairment of endothelium-dependent brachial artery vasoactivity following a single high-fat meal. *JAMA* 278:1682–1686
- Ross R (1999) Atherosclerosis—an inflammatory disease. *N Engl J Med* 340:115–128
- Sies H, Stahl W, Sevanian A (2005) Nutritional, dietary and postprandial oxidative stress. *J Nutr* 135:969–972
- Steensberg A, Hall GV, Osada T, Sacchetti M, Saltin B, Pedersen BK (2000) Production of interleukin-6 in contracting human skeletal muscles can account for the exercise-induced increase in plasma interleukin-6. *J Physiol* 537:237–242
- Tsai W, Li Y, Lin C, Chao T, Chen J (2004) Effects of oxidative stress on endothelial function after a high-fat meal. *Clin Sci* 106:315–319
- Verma S, Buchanan MR, Anderson TJ (2003) Endothelial function testing as a biomarker of vascular disease. *Circulation* 108:2054–2059
- Vogel RA, Corretti MC, Plotnick GD (1997) Effect of a single high-fat meal on endothelial function in healthy subjects. *Am J Cardiol* 79:350–354
- Vollaard NBJ, Shearman JP, Cooper CE (2005) Exercise-induced oxidative stress. Myths, realities and physiological relevance. *Sports Med* 35:1045–1062
- Walther C, Gielen S, Hambrecht R (2004) The effect of exercise training on endothelial function in cardiovascular disease in humans. *Exerc Sport Sci Rev* 32:129–134
- Zhao T, Bokoch GM (2005) Critical role of proline-rich tyrosine kinase 2 in reversion of the adhesion mediated suppression of reactive oxygen species generation by human neutrophils. *J Immunol* 174:8049–8055