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Regular aerobic exercise protects against impaired fasting plasma glucose-associated vascular endothelial dysfunction with aging

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Abstract

In the present study, we tested the hypothesis that age-associated vascular endothelial dysfunction is exacerbated by IFG (impaired fasting plasma glucose) and that regular aerobic exercise prevents this effect. Data were analysed from a cohort of 131 non-smoking men and women without overt clinical disease. Compared with young adult controls (age=24±1 years, $n = 29$; values are means ± S.E.M.), brachial artery FMD (flow-mediated dilation), a measure of conduit artery EDD (endothelium-dependent dilation), was 33% lower [7.93 ± 0.33 against $5.27 \pm 0.37\% \Delta$ (% change), $P < 0.05$] in MA/O (middle-aged/older) adults with NFG (normal fasting plasma glucose) (99 mg/dl , 62 ± 1 years, $n = 35$). In MA/O adults with IFG ($100\text{--}125 \text{ mg/dl}$, 64 ± 1 years, $n = 28$), FMD was 30% lower ($3.37 \pm 0.35\% \Delta$) than in their peers with NFG and 58% lower than young controls ($P < 0.05$). Brachial artery FMD was greater ($6.38 \pm 0.35\% \Delta$) in MA/O adults with NFG who regularly performed aerobic exercise ($>45 \text{ min/day}$ for 5 days/week, 62 ± 1 years, $n = 23$) compared with their non-exercising peers and only slightly less than young controls ($P < 0.05$). Most importantly, FMD was completely preserved in MA/O adults with IFG who regularly performed aerobic exercise ($6.99 \pm 0.69\% \Delta$, 65 ± 1 years, $n = 16$). In the pooled sample, fasting plasma glucose was inversely related to FMD ($r = -0.42$, $P < 0.01$) and was the strongest independent predictor of FMD ($R^2 = 0.32$). Group differences in FMD were not affected by other subject characteristics or brachial artery properties, including brachial artery dilation to sublingual NTG (nitroglycerine, i.e. endothelium-independent dilation). IFG exacerbates age-associated vascular endothelial dysfunction and this adverse effect is completely prevented in MA/O adults who regularly perform aerobic exercise.

Keywords

aging; flow-mediated dilation; physical fitness; prediabetic state

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Author Contribution: Allison DeVan performed data analysis and interpretation, created all of the Tables and Figures, wrote the initial draft of the paper and edited the final draft; Iratxe Eskurza was involved in the initial study design, performed some measures of primary variables and edited the final draft of the paper; Gary Pierce, Ashley Walker, Kristen Jablonski and Rachelle Kaplon performed some measures of primary variables, performed data entry and edited the final draft of the paper; Douglas Seals was involved in the initial study design, data interpretation, editing the first and final drafts of the paper, and was the primary investigator on the grant funding the study.

Introduction

CVDs (cardiovascular diseases) remain the leading cause of morbidity and mortality in modern societies, and age is the primary risk factor for CVD [1]. Without effective intervention, the rising numbers of older adults will result in a marked increase in the burden of CVD and attendant medical costs [2]. The increase in risk of CVD with aging is attributable in part to the development of vascular endothelial dysfunction, as indicated by impaired EDD (endothelium-dependent dilation) [3,4]. Therefore understanding the factors that influence endothelial function with aging has important clinical implications for preventing projected increases in age-associated CVD.

IFG (impaired fasting plasma glucose), defined as fasting plasma glucose concentrations of 100–125 mg/dl (5.6–6.9 mmol/l) [5], is considered a ‘prediabetic state’ as it increases the likelihood of developing Type 2 diabetes mellitus [6]. Adults with IFG often demonstrate impaired vascular endothelial function (i.e., reduced EDD) when compared with individuals with NFG (normal fasting plasma glucose) [7–10]. Importantly, the prevalence of IFG increases with age [11] and the presence of IFG worsens the risk of CVD with aging [6]. However, it is not known whether IFG exacerbates vascular endothelial dysfunction with age and, therefore, may contribute to the associated increase in CVD risk.

Regular aerobic exercise is an effective lifestyle behaviour for maintaining overall vascular health with aging [12,13]. EDD is largely preserved in healthy normoglycaemic MA/O (middle-aged/older) adults who perform aerobic exercise when compared with young adults [13–17]. However, it is unknown whether endothelial function is maintained better in MA/O adults with IFG who regularly engage in aerobic exercise, i.e. if exercise can protect against the combined adverse effects of aging and IFG.

Accordingly, we first tested the hypothesis that the age-associated reduction in vascular endothelial function is greater in otherwise healthy MA/O adults with IFG compared with age-matched adults with NFG. We then tested the hypothesis that MA/O adults with IFG who perform regular aerobic exercise (‘trained’) demonstrate better endothelial function than their non-exercising peers with IFG. To do so, we assessed values for brachial artery FMD (flow-mediated dilation), a well-established measure of conduit artery EDD and vascular endothelial function [18], in young adult controls and groups of MA/O adults with normal or IFG and who were either regularly performing aerobic exercise or not. We also took the opportunity to gain insight into the relationship between endothelial function and fasting plasma glucose among individuals differing in age and habitual exercise status.

Materials and Methods

Subjects

A cohort of non-smoking men and women (age, 18–79 years) free from overt clinical disease from our laboratory database ($n = 131$) previously assessed for FMD were used for the analysis. Subjects were assigned to groups based on their fasting plasma glucose concentrations (< 99 mg/dl or 100–125 mg/dl), age (18–30 years or 50–79 years) and reported physical activity (< 30 min/day for ≤ 2 days/week or > 45 min/day for ≥ 5 days/week of aerobic exercise for the past 2 years). All subjects had BP (blood pressure) $< 150/90$ mmHg at rest and a BMI (body mass index) of < 32 kg/m². Subjects refrained from all dietary supplements for > 2 weeks prior to vascular measures. All subjects were not taking prescription medication and did not take non-prescription medications during the 48 h prior to testing. All procedures were approved by the Institutional Review Board at the University of Colorado at Boulder. The nature, benefits and risks of the study were explained to the volunteers, and their written informed consent was obtained before participation.

Procedures

All measurements were performed at the University of Colorado at Boulder CTRC (Clinical Translational Research Center) after an overnight fast from food and caffeine and 24-h abstention from alcohol and exercise. Premenopausal women were tested during the early-follicular phase of the menstrual cycle.

Subject Characteristics

BMI, and waist and hip circumferences were measured by anthropometry [19]. Arterial BP was measured over the brachial artery during rest using a semi-automated device (Dinamap Pro 100; GE Healthcare), which also provided resting HR (heart rate). Maximal oxygen consumption was measured during incremental treadmill exercise using open-circuit spirometry as previously described [20]. A CTRC bionutritionist analysed a 3-day diet record recorded by subjects, as described previously [21].

Fasting plasma glucose was measured by enzymatic methods (Roche Diagnostic Systems) and plasma insulin by RIA (Diagnostic Systems Laboratory). IR (insulin resistance) was estimated with the HOMA-IR (homoeostasis model assessment of insulin resistance) by the formula $[\text{fasting plasma glucose (mg/dl)} \times \text{fasting plasma insulin (milli-units/ml)}] / 405$ [22]. The HOMA-IR has been validated against other measures of insulin sensitivity (e.g. intravenous glucose tolerance test) as a reliable estimate of insulin sensitivity [23]. Serum cholesterol and TAG (triacylglycerol) concentrations were determined by the CTRC core laboratory using standard assays. Circulating CRP (C-reactive protein) was measured using a high-sensitivity chemistry-immuno analyser (AU400e; Olympus Diagnostic Systems).

Brachial Artery Dilation

Duplex ultrasonography was used to assess brachial artery FMD as described previously [24,25]. Brachial artery FMD was expressed as millimetre change (mm Δ) and percentage change (% Δ) from baseline diameter, and the peak shear stimulus was assessed in a subset of subjects as described previously [24–26]. Brachial artery FMD was not normalized to peak shear stimulus [27] because values for shear rate were available only on a subset of subjects. In the pooled subset of subjects on which data were available, shear rate was not significantly related to brachial FMD ($r = 0.22$, $P = 0.28$). Endothelium-independent dilation, a measure of vascular smooth muscle sensitivity to nitric oxide, was assessed only in a subset of subjects whose baseline BP was sufficient to safely tolerate the vasodilation produced by sublingual NTG (nitroglycerine) [24–26].

Data Analyses

Statistical analyses were performed with IBM SPSS (version 19). Differences among groups were assessed by one-way ANOVA with LSD (least significant difference) post-hoc tests and a general linear model with univariate analysis when controlling for covariates. In the case of missing waist/hip ratio, HR and blood lipid values ($n = 2–4$ out of a total of 131), the group mean was substituted. Bivariate correlations (two-tailed) and stepwise linear regression analyses (backwards method) were used to identify significant determinants of brachial artery FMD. Significance was set at $P < 0.05$ for all statistical analyses. All results are expressed as means $\pm$ S.E.M.

Results

Subject Characteristics

The MA/O groups did not differ in age, and the regularly exercising subjects had higher maximal oxygen consumption and lower resting HRs than the non-exercising age-matched

groups (Table 1). Fasting plasma glucose was higher in the IFG groups compared with the NFG groups (Table 2). The MA/O adults with IFG had higher waist/hip ratio, plasma insulin and HOMA-IR compared with the other groups. In general, serum CRP concentrations were higher in non-exercising MA/O groups compared with their trained peers and the young controls. Estimated total energy intake was greater in the young adults and trained groups compared with the MA/O sedentary groups (Table 3). No other differences in diet composition were observed.

Brachial Artery FMD

Brachial artery FMD was 33%(% Δ) to 34%(mm Δ) lower in the non-exercising MA/O adults with NFG compared with the young adult controls ($P < 0.05$) (Figure 1 and Table 4). Brachial artery FMD was reduced by an additional 30 (% Δ) to 36% (mm Δ) in non-exercising MA/O adults with IFG compared with their peers with normal glucose and was 58% lower than the mean value of the young adult controls ($P < 0.05$).

Brachial artery FMD was greater in MA/O trained adults with NFG compared with the non-exercising MA/O NFG and IFG groups ($P < 0.05$), and only slightly lower (– 12 %) than in the young controls ($P < 0.05$). Most importantly, in contrast with the markedly impaired brachial artery FMD of their non-exercising peers, MA/O trained adults with IFG had levels of FMD that were well preserved and not significantly different from those of either their exercising peers with NFG or the young controls. These group differences in brachial artery FMD were unaffected and remained highly significant ($P < 0.05$) after co-varying for baseline diameter, subject characteristics including sex (Table 1), plasma lipids, and CRP (Table 2).

Brachial artery endothelium-independent dilation was not related to age ($r = 0.04$, $P = 0.73$) or exercise status ($r = 0.18$, $P = 0.10$). Covarying for endothelium-independent dilation did not alter group differences in FMD.

Relationships between brachial artery FMD and plasma glucose and insulin

In the pooled sample, brachial artery FMD was inversely related to fasting plasma glucose concentrations ($r = -0.42$, $P < 0.01$, $n = 131$) and HOMA-IR ($r = -0.24$, $P = 0.01$, $n = 102$), whereas there was only a trend for a relationship with fasting plasma insulin ($r = -0.18$, $P = 0.07$, $n = 102$). Among all clinical characteristics (Tables 1 and 2), fasting plasma glucose was the strongest independent predictor of brachial artery FMD in the overall sample ($R^2 = 0.32$ for model with age and peak oxygen consumption). The relationship between FMD and fasting plasma glucose was due primarily to a significant inverse relationship among the non-exercising MA/O groups (Figure 2a), as there was no significant relationship among trained MA/O adults and young controls (Figure 2b).

Discussion

There were two novel and biomedically important findings from the present study. First, our results show that MA/O adults with IFG have greater vascular endothelial dysfunction than their peers with NFG and markedly impaired function when compared with normal values observed in healthy young adults. Secondly, MA/O adults with IFG who regularly perform aerobic exercise have preserved vascular endothelial function despite the potent combined adverse influence of older age and IFG.

Age, IFG and Vascular Endothelial Dysfunction

The reduced brachial artery FMD in MA/O adults with NFG observed in the present study (compared with healthy young controls) is consistent with previous findings from our

laboratory reporting that vascular endothelial function is reduced even in MA/O adults free of clinical disease [14,17,25,28]. The present findings extend our past observations in part by showing that IFG is not required for the development of age-associated vascular endothelial dysfunction. More importantly, the present results demonstrate for the first time that vascular endothelial dysfunction with aging is exacerbated by the presence of IFG. Indeed, compared with values in healthy young adults, the impairment in brachial artery FMD in MA/O adults with IFG was essentially twice as great as their peers with NFG. These observations are in agreement with our recent results showing that MA/O adults with even borderline high concentrations of LDL (low-density lipoprotein)-cholesterol have significantly lower brachial artery FMD than age-matched individuals with optimal/near optimal LDL-cholesterol [29]. Collectively these findings indicate that the addition of even modest (subclinical) elevations in selective risk factors for CVD leads to further vascular endothelial dysfunction with aging and could represent an important intermediary event in the associated increases in CVD risk in these groups. The results of our study also support recent findings of others that demonstrate that prediabetic states are associated with impaired conduit artery vascular endothelial function in humans [8–10], while extending these past observations to show the additive effect of aging and IFG.

Aerobic Exercise and Age- And IFG-Related Vascular Endothelial Dysfunction

Our finding that, among MA/O adults with NFG, those performing regular aerobic exercise have enhanced brachial artery FMD is in agreement with previous observations from our laboratory and others [14,15,30,31]. However, our results here demonstrate for the first time that not only does aerobic exercise largely preserve vascular endothelial function with aging in the setting of NFG, but also protects the vascular endothelium from the additional negative impact of IFG. This novel finding is in agreement with our recent observation that regular aerobic exercise appears to protect against the potentially harmful effects of elevated LDL-cholesterol [29]. Middle-aged adults who perform regular aerobic exercise also appear to be partly protected from impairments in brachial artery FMD in response to acute ischaemia/reperfusion injury [31]. Taken together, these findings support the concept that aerobic exercise may confer resistance to the negative effects of a wide variety of adverse factors that would otherwise act to worsen age-associated vascular endothelial dysfunction. The present results also are consistent with previous reports showing improved vascular function with aerobic exercise interventions in patients with prediabetes [9] and Type 2 diabetes mellitus [32]. Considered together, the results of the present study and these earlier observations suggest that the protective effects of aerobic exercise/fitness against CVD and cardiovascular events with aging and/or elevated fasting plasma glucose [32] may be mediated in part via vascular endothelial-preserving actions.

Relationship between Endothelial Function and Fasting Plasma Glucose

In the present analysis, brachial artery FMD was inversely related to fasting plasma glucose in the overall sample. Moreover, fasting plasma glucose concentrations were the strongest independent correlate of FMD in the pooled group. However, the overall correlation appeared to be based primarily on a relationship between FMD and glucose in the non-trained MA/O subjects, as no significant correlation was observed in young subjects or trained MA/O adults. As such, habitual aerobic exercise and young age appear to be at least two factors that exert a protective influence on the vasculature against potentially harmful influences [13,29].

Possible Mechanisms and Limitations

The limitations of retrospective analysis of a large and diverse sample of subjects did not allow us to investigate the mechanisms by which IFG exacerbated and regular aerobic exercise prevented vascular endothelial dysfunction with aging and IFG. Mean group

concentrations of circulating CRP, a marker of systemic inflammation, suggested a possible anti-inflammatory effect associated with younger age and regular exercise. However, CRP was not a significant predictor of FMD and controlling for CRP did not alter group differences in FMD. Previous work by our laboratory and others support the view that aging leads to endothelial dysfunction via development of vascular oxidative stress and that aerobic exercise prevents this effect [14,15,28,33]. Similarly, there is compelling evidence that elevations in plasma glucose in settings of prediabetes and Type 2 diabetes mellitus are associated with vascular oxidative stress [8,10,34–36]. As such, in the present study, it is conceivable that aging- and IFG-induced endothelial dysfunction and the protection afforded by aerobic exercise against this were, at least in part, mediated through different modulating effects on oxidative stress.

There are limitations in the present analysis. The number of men and women in the MA/O IFG group was smaller compared with the other groups due to difficulty in finding such subjects. This also limited our ability to assess possible sex-related differences between groups. However, ANCOVA (analysis of co-variance) showed no effect of sex, and a separate analysis with only men produced the same group differences as observed in the overall sample. The absence of a young IFG group is another limitation of the analysis. Such a group could have provided insight into the potential impact of IFG on brachial artery FMD in young adults, without the added effect of older age. We do not believe that this limitation affects the conclusions based on the results of the five groups presented. Moreover, we have previously shown that brachial artery FMD is not impaired in otherwise young healthy adults with a single cardiovascular risk factor [29]. Our measurements of endothelial function were limited to large conduit artery dilation to a flow stimulus (i.e., brachial artery FMD), and data on shear stress and NTG-induced dilation were limited. However, neither of these factors was significantly related to FMD in the present sample, nor have we observed age- or aerobic exercise-related group differences in previous studies [17,30,37–39]. Importantly, the non-shear rate normalized expressions of FMD used in the present study (i.e., % Δ and mm Δ), and not FMD corrected for shear rate, predict risk of future cardiovascular events [40,41]. Nevertheless, we recognize that shear rate is an important indicator of the stimulus for dilation and, as such, the lack of data on all of the subjects in our groups is a notable limitation of the analysis.

Summary and Conclusions

In summary, the present findings show for the first time that IFG significantly exacerbates age-associated vascular endothelial dysfunction and that this adverse effect is completely prevented in MA/O adults who regularly perform aerobic exercise. Our results also suggest that these divergent effects on vascular endothelial function with aging may help explain how IFG worsens and aerobic exercise protects against age-associated clinical CVD and cardiovascular events.

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Abbreviations

BP	blood pressure
BMI	body mass index
CRP	C-reactive protein
CTRC	Clinical and Translational Research Center
CVD	cardiovascular disease
EDD	endothelium-dependent dilation
FMD	flow-mediated dilation
HOMA-IR	homoeostasis model assessment of insulin resistance
HR	heart rate
IFG	impaired fasting plasma glucose
LDL	low-density lipoprotein
MA/O	middle-aged/older
NFG	normal fasting plasma glucose
NTG	nitroglycerine

Clinical Perspectives

- Lifestyle behaviours such as regular aerobic exercise prevent or lessen the vascular dysfunction that occurs with aging alone. However, it is unknown whether regular aerobic exercise can mitigate age-related vascular endothelial dysfunction in the presence of IFG (impaired fasting plasma glucose), a risk factor for cardiovascular disease and Type 2 diabetes and a common impairment with aging.
- The results of the present study show that MA/O (middle-aged and older) adults with IFG have greater conduit artery endothelial dysfunction than their age-matched normoglycaemic peers, but that this dysfunction is not observed in MA/O adults with IFG who perform aerobic exercise 5 days or more per week.
- These findings provide new evidence that regular aerobic exercise preserves vascular health in MA/O adults with additional risk factors, and reinforces the important role of aerobic exercise in the prevention of age-related cardiovascular diseases.

Figure 1. Brachial artery FMD (%Δ) in groups divided by exercise training status, age and fasting plasma glucose concentrations

Values are means $\pm$ S.E.M. * $P < 0.05$ against non-exercising young NFG; † $P < 0.05$ against non-exercising MA/O NFG; ‡ $P < 0.05$ against trained MA/O NFG; and § $P < 0.05$ against trained MA/O IFG.

Figure 2. Influence of age and training status on the relationships between glucose and FMD (%Δ)

(a) Non-exercising MA/O adults with NFG and IFG concentrations. **(b)** Non-exercising young and trained MA/O adults with NFG and IFG.

Table 1

Subject characteristics

Characteristic	Non-exercising		Non-exercising		Non-exercising		Trained	
	young	NFG	MA/O	NFG	MA/O	IFG	MA/O	NFG
Age (years)	24±1		62±1 [*]		64±1 [*]		62±1 [*]	
Men/women (n)	26/3		30/5		24/4		21/2	
Body mass (kg)	74±2		80±2 [*]		83±2 ^{‡§}		72±2 [‡]	
BMI (kg/m ²)	23±1		26±1 [*]		27±1 ^{‡§}		23±1 [‡]	
Waist/hip ratio	0.83±0.01		0.90±0.01 ^{‡§}		0.94±0.02 ^{‡§}		0.86±0.01	
Systolic BP at rest (mmHg)	111±2		121±2 [*]		122±3 [*]		116±2	
Diastolic BP at rest (mmHg)	60±1		75±1 ^{‡§}		75±2 ^{‡§}		72±2 [*]	
HR at rest (beats/min)	58±2		62±2		59±1 [§]		54±2 [‡]	
$\dot{V}O_{2peak}$ [ml.min ⁻¹ . (kg of body weight) ⁻¹]	47±1		31±1 [*]		29±1 ^{‡§}		42±2 [‡]	

Values are means± S.E.M.

^{*} $P < 0.05$ against non-exercising young NFG[‡] $P < 0.05$ against non-exercising MA/O NFG[‡] $P < 0.05$ against trained MA/O NFG[§] $P < 0.05$ against trained MA/O IFG. $\dot{V}O_{2peak}$, peak oxygen consumption.

Table 2
Fasting blood glucose, insulin, lipid profile and CRP

Parameter	Non-exercising		Non-exercising		Non-exercising		Trained	
	young NFG	MA/O NFG	MA/O IFG	MA/O IFG	MA/O NFG	MA/O IFG	MA/O NFG	MA/O IFG
Plasma glucose (mg/dl)	87±1	90±1	105±1 ^{***}	103±2 ^{***}	87±1	103±2 ^{***}	87±1	103±2 ^{***}
Plasma insulin (milli-units/ml) //	5.6±0.5	5.8±0.5	8.9±1.2 ^{***§}	4.5±0.5	4.5±0.5	5.8±1.0	4.5±0.5	5.8±1.0
HOMA-IR //	1.2±0.1	1.3±0.1	2.3±0.3 ^{***§}	1.0±0.1	1.0±0.1	1.5±0.3	1.0±0.1	1.5±0.3
Serum total cholesterol (mg/dl)	166±6	199±5 [*]	202±5 [*]	193±6 [*]	116±6	211±7 [*]	193±6 [*]	211±7 [*]
Serum LDL-cholesterol (mg/dl)	100±5	126±5 [*]	127±6 [*]	125±8 [*]	116±6	125±8 [*]	116±6	125±8 [*]
Serum HDL-cholesterol (mg/dl)	47±2	50±2	53±3 ^{‡§}	60±2 [‡]	85±5 [‡]	65±6 [‡]	85±5 [‡]	96±11
Serum TAG (mg/dl)	92±6	115±7 [*]	120±7 ^{‡§}	85±5 [‡]	85±5 [‡]	96±11	85±5 [‡]	96±11
Serum CRP (mg/l) ¶	0.59±0.09	1.20±0.17 ^{***§}	1.01±0.16 [§]	0.58±0.08	0.58±0.08	0.54±0.12	0.58±0.08	0.54±0.12

Values are means ±S.E.M.

^{*} $P<0.05$ against non-exercising young NFG;

[‡] $P<0.05$ against non-exercising MA/O NFG;

[‡] $P<0.05$ against trained MA/O NFG;

[§] $P<0.05$ against trained MA/O IFG. HDL, high-density lipoprotein; TAG, triacylglycerol.

// Non-exercising young NFG ($n=22$); non-exercising MA/O NFG ($n=32$); non-exercising MA/O IFG ($n=18$); trained MA/O NFG ($n=17$); trained MA/O IFG ($n=13$).

¶ Log-transformed for statistics; non-exercising young NFG ($n=12$); non-exercising MA/O NFG ($n=27$); non-exercising MA/O IFG ($n=14$); trained MA/O NFG ($n=12$); trained MA/O IFG ($n=9$).

Table 3

Dietary intake //

Parameter	Non-exercising		Non-exercising		Non-exercising		Trained	
	young NFG	MA/O NFG	MA/O NFG	MA/O IFG	MA/O IFG	MA/O NFG	MA/O NFG	MA/O IFG
Total (kcal/day)	2957±111	2079±100 ^{*,†}	2148±117 [*]	2453±95 [*]	2341±161 [*]			
Carbohydrates (% of total kcal)	49±1	49±2	48±2	52±2	51±2			
Protein (% of total kcal)	15±1	17±1	17±1	16±1	15±1			
Fat (% of total kcal)	36±1	35±2	34±2	33±2	31±2			
Vitamin C (mg)	156±15	162±19	125±12	170±21	181±26			
Vitamin E (units)	16±2	13±1	11±1	14±2	16±3			

Values are means ± S.E.M.

^{*} $P<0.05$ against non-exercising young NFG;

[†] $P<0.05$ against trained MA/O NFG. 1 kcal≈4,184 kJ.

// Non-exercising young NFG ($n = 24-25$); non-exercising MA/O NFG ($n = 27-30$); non-exercising MA/O IFG ($n = 18-21$); trained MA/O NFG ($n = 19-21$); trained MA/O IFG ($n = 12-14$).

Table 4

Brachial artery parameters

Parameter	Non-exercising young NFG	Non-exercising MA/O NFG	Non-exercising MA/O IFG	Trained MA/O NFG	Trained MA/O IFG
FMD change in diameter (mm)	0.32±0.01	0.21±0.01 ^{*§}	0.15±0.02 ^{*†‡§}	0.24±0.01 [*]	0.27±0.02 [*]
FMD baseline diameter (mm)	4.00±0.09	3.98±0.09	4.40±0.13 ^{*†‡§}	3.79±0.09	3.94±0.15
FMD peak diameter (mm)	4.32±0.09	4.18 ± 0.09	4.55±0.14 ^{†‡}	4.03±0.09	4.21±0.14
NTG-mediated dilation (%Δ) //	21.5±1.1	21.6±0.09	19.2±1.1 ^{‡§}	26.4±1.2 ^{*†}	23.9 ±2.0

Values are means ±S.E.M.

^{*} $P<0.05$ against non-exercising young NFG;

[†] $P<0.05$ against non-exercising MA/O NFG;

[‡] $P<0.05$ against trained MA/O NFG;

[§] $P<0.05$ against trained MA/O IFG.

// Non-exercising young NFG ($n = 21$); non-exercising MA/O NFG ($n = 25$); non-exercising MA/O IFG ($n = 23$); trained MA/O NFG ($n = 14$); trained MA/O IFG ($n = 10$).