European Journal of Applied Physiology (2019) 119:1663–1669
https://doi.org/10.1007/s00421-019-04154-1

ORIGINAL ARTICLE

Prior cycling exercise does not prevent endothelial dysfunction after resistance exercise

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Received: 24 January 2019 / Accepted: 27 April 2019 / Published online: 4 May 2019
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Abstract

Purpose Resistance exercise impairs endothelial function acutely. Therefore, it becomes important to devise an effective strategy for preventing acute endothelial dysfunction after resistance exercise. Herein, we tested the hypothesis that resistance exercise-induced temporal endothelial dysfunction is prevented by prior cycling.

Methods Twelve young healthy subjects completed two randomized experimental trials: (1) resistance exercise only trial (RE trial), (2) resistance exercise with prior cycling trial (C + RE trial). Following baseline brachial artery flow-mediated dilation (FMD), the subjects maintained the supine position for 45 min in the RE trial; the subjects performed a 45 min of cycling (67.0 ± 1.7% HRmax) in the C + RE trial. After 45 min of resting or cycling, the subjects performed resistance exercise (69.7 ± 4.0 kg) at the same time points. Following the resistance exercise, they were asked to rest in the supine position for 60 min. Then FMD were repeated at 10, 30 and 60 min after the resistance exercise in both trials.

Results The increased blood flow and shear rate after resistance exercise did not differ between trials, and these changes disappeared following resting in the supine position for 60 min. There was no significant interaction in %FMD responses. Both trials caused impairment in %FMD after the resistance exercise, and statistical significance was observed at 30 and 60 min after resistance exercise in the RE trial.

Conclusion The present study revealed that cycling for 45 min prior to resistance exercise was not sufficient to prevent the acute endothelial dysfunction after resistance exercise.

Keywords Vascular function · Resistance exercise · Aerobic exercise · Flow-mediated dilation

Abbreviations

FMD	Flow-mediated dilation
NO	Nitric oxide
ET-1	Endothelin-1
1RM	One repetition maximum
RPE	Perceived exertion
HR	Heart rate
AUC	Area under the curve
ANOVA	Analysis of variance
ANCOVA	Analysis of covariance
SE	Standard error
$\dot{V}O_2$max	Maximal oxygen uptake

Communicated by Guido Ferretti.

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Introduction

Endothelial dysfunction is implicated in the etiology of cardiovascular disease (Harrison et al. 1987; Ross. 1999; De Jongh et al. 2002; Jambrik et al. 2004; Patti et al. 2005; Yoshida et al. 2006). Flow-mediated dilation (FMD) is a frequently used, noninvasive technique that measures the bioactivity of endothelium-derived nitric oxide (NO) (Koojman et al. 2008) in conduit arteries and predicts the risk of cardiovascular events (Gokce et al. 2002; Kuvin et al. 2001; Modena et al. 2002; Perticone et al. 2001). Although the prevalence of recommending resistance exercise as an exercise prescription has augmented in the last few decades, resistance exercise induces temporal endothelial dysfunction (Buchanan et al. 2017; Morishima et al. 2018). However, an effective strategy to prevent the resistance exercise-induced acute endothelial dysfunction remains to be elucidated, and has, therefore, become a focus of recent research.

We have recently demonstrated that high-intensity resistance exercise with low repetitions prevents acute endothelial

dysfunction as assessed by FMD (Morishima et al. 2018). In addition, a subsequent study has indicated that a 10 min of cycling after resistance exercise restored impaired endothelial function (Morishima et al. 2019). Cycling after resistance exercise offers a realistic and practical method to restore acute endothelial dysfunction; however, there is an important limitation in this previous study as temporal endothelial dysfunction immediately after resistance exercise is unavoidable. In this regards, it remains unknown whether resistance exercise-induced temporal endothelial dysfunction can be prevented by prior cycling. It is possible that the shear stress-induced augmentation of NO synthesis caused by prior cycling may be sufficient to offset the subsequent vascular effects of resistance exercise. For example, the prior augmentation of NO synthesis may attenuate the resistance exercise-induced production of vasoconstrictors, including endothelin-1 (ET-1) (Yanagisawa et al. 1988; Okamoto et al. 2008; Nishiyama et al. 2017).

Accordingly, the present study tested the hypothesis that resistance exercise-induced acute endothelial dysfunction can be prevented by prior cycling. Specifically, brachial artery endothelial functions were assessed via FMD prior to and following resistance exercise under two conditions: where a resistance exercise was preceded by a 45 min bout of cycling and where a resistance exercise was preceded by a time-matched period of supine rest. The duration of 45 min of cycling was used as this duration of cycling was previously reported to prevent an impaired endothelial function caused by sitting (Morishima et al. 2017; Ballard et al. 2017). We hypothesize that resistance exercise-induced acute endothelial dysfunction would be prevented by a 45 min of cycling.

Methods

Subjects

Twelve young, untrained, male subjects (age: 20.4 ± 0.3 years, height: 174.6 ± 2.3 cm, weight: 64.1 ± 2.5 kg, body mass index: 17.5 ± 2.4 kg/m^2) participated in the present study. The subjects were not participating in any training programs at the start of this study. The subjects were non-smokers, with no history or symptoms of cardiovascular, pulmonary, metabolic, or neurological disease. No subjects reported taking medications. All subjects were informed about the purpose of the present study and experimental procedure, and provided written informed consent. The study was approved by the Ethics Committee for Human Experiments at Sports Research Center, Hosei University, Japan [ID: 2017-003].

Experimental procedures

The subjects visited the laboratory three times throughout the experimental period. During the first visit, the subject's one repetition maximum (1RM) for leg extension was assessed using weight-stack machines. Prior to measuring 1RM, the subjects performed warm-up sets with ten repetitions at 50% and 70% of the predicted 1RM and stretching of the major muscle groups that were subjected to the exercises. The intensity was increased until the subjects were unable to perform a lift. A schematic of the study design is presented in Fig. 1. The order of experimental visits was randomized and each visit was separated by at least 7 days to avoid the acute influences of exercise in the second visit (i.e., energy metabolism, muscle fatigue, etc.) on the third visit. The two experimental visits consisted of the following conditions: (1) resistance exercise only trial (RE trial); (2) resistance exercise with prior cycling trial (C + RE trial). Subjects were instructed to eat a light meal two or more hours prior to arriving to the laboratory. In addition, subjects were asked to refrain from caffeine and alcohol for at least 10 h as well as from exercise for 24 h prior to the study visit. All experimental timing was kept constant among visits. All studies were performed in a temperature-controlled room kept at 23 °C. Upon arrival to the laboratory, the subjects were placed in a supine position. Subjects were instrumented with an automated sphygmomanometer (Omron Cooperation, Kyoto, Japan) for periodic measurements of systolic and diastolic blood pressure after resting quietly for 10 min. All vascular measurements in the brachial artery were performed in the right arm. Brachial artery is the most popular artery for assessment of FMD. In addition, brachial artery FMD after exercise reflects whole-body endothelial function even though the arm is not working muscle. In fact, several studies used this method (Buchanan et al. 2017; Iwamoto et al. 2018; Morishima et al. 2018). Brachial artery diameter and blood velocity were measured using duplex-Doppler

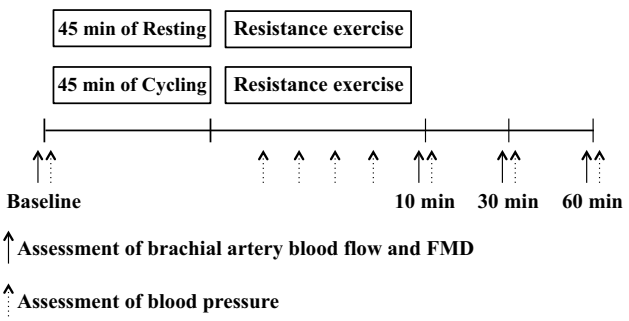

Fig. 1 Experimental design. The intensity of resistance exercise was ten repetitions for five sets at 70% of 1RM. The workload of cycling was individualized for each subject to target a RPE of 11–13

ultrasound (Aixplorer, Supersonic Imagine, France). A 10 MHz linear array transducer was placed over the brachial artery just distal to the brachial fossa. We marked the landmark to measure same point repeatedly. Simultaneous diameter and velocity signals were obtained in duplex mode at a pulsed frequency of 30 MHz and corrected with an insonation angle of 60°. The brachial artery FMD was assessed as previously described (Boyle et al. 2013; Fairfax et al. 2015). Briefly, a cuff was placed on the lower arm. Two minutes of baseline hemodynamics were recorded and then the cuff was inflated to a pressure of 220 mmHg for 5 min (MIST-1000, SARAYA, Osaka, Japan). Continuous diameter and blood velocity measures were recorded for 3 min following cuff deflation. The recordings of all vascular variables were analyzed offline using specialized edge-detection software (S-13037 ver. 2.0.1, Takei Kiki Kogyo, Japan).

Following baseline measurement, the subjects in the RE trial maintained the supine position for 45 min; subjects in the C + RE trial performed a 45 min of leg cycling on a stationary bike (Aerobike 75XLIII, Combi wellness Co, Tokyo, Japan) (Fig. 1). During cycling, the subjects maintained a cycling cadence of 60 rpm. The workload was individualized for each subject to target a rate of perceived exertion (RPE) of 11–13 (Borg Scale, 6–20). Heart rate (HR) and RPE were monitored throughout the exercise bout. The %HRmax was calculated from the age-predicted HRmax ([the average HR during cycling/(220 − age) × 100]). After 45 min of resting or cycling, the subjects performed resistance exercise (leg extension) at the same time points in both trials. The exercise intensity consisted of ten repetitions for five sets at 70% of 1RM. The resting period between all sets was 60 s. The intensity during the resistance exercise was adjusted to allow the subjects to complete ten repetitions in each set (approximately 70% of 1RM for the first set). The subjects were asked to lift and lower the weight in 1 s and 2 s, respectively. In addition, the subjects were instructed to breath out and in when they lift and lower the weight, respectively. During the resting period between sets, systolic and diastolic blood pressures were measured. Following the resistance exercise, the subjects were placed back into the supine position. FMD and blood pressure assessments were then repeated at 10, 30 and 60 min after resistance exercise.

Data analysis

Blood flow was calculated from the continuous diameter and mean blood velocity recordings at each of the experimental time points using the following equation: 3.14 × (diameter/2)^2 × mean blood velocity × 60. The brachial artery FMD percent change was calculated using the following equation: %FMD = (peak diameter − base diameter)/(base diameter) × 100. The brachial artery FMD delta change from baseline was calculated using the following equation: ΔFMD = %FMD at 10, 30 and 60 min − %FMD at baseline. The shear rate, an estimate of shear stress without blood viscosity, was calculated as 4 × mean blood velocity/diameter. The hyperemic shear rate area under the curve (AUC) up to the peak diameter was calculated as stimulus for FMD, as described previously (Boyle et al. 2013; Thijssen et al. 2009).

Statistical analysis

Before the statistical analysis, we confirmed that all data have normal distribution. A two-way (time × trial) repeated measures analysis of variance (ANOVA) with Tukey post hoc testing was performed on all dependent variables. FMD was also adjusted for basal diameter and hyperemic shear rate AUC via analysis of covariance (ANCOVA) to statistically control for the influence of basal diameter and shear stimulus on FMD response. The ANCOVA and ANOVA tests were performed using SPSS software (version 23). Significance was accepted at $P \leq 0.05$. Data are expressed as means ± standard error (SE).

Results

The average workload during cycling was 83.7 ± 3.0 W and the absolute and relative exercise intensity was 119.3 ± 5.0 bpm and 67.0 ± 1.7% HRmax. The average RPE during cycling was 12.8 ± 0.2. The average workload during resistance exercise was 69.7 ± 4.0 kg.

Following resistance exercise, brachial artery blood flow ($P < 0.001$ in both trials) and shear rate ($P = 0.01$ in the both trials) were significantly increased relative to baseline in both trials (Fig. 2, Table 1). This initial increase in blood flow and shear rate caused by resistance exercise disappeared after 30 min of rest in the supine position. No statistical

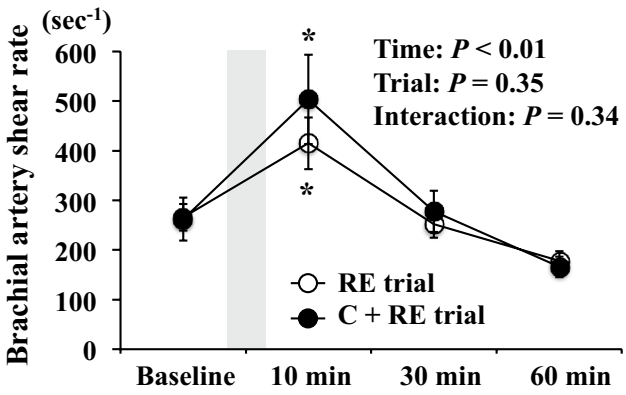

Fig. 2 Brachial artery shear rate in the RE trial and C + RE trial. The shaded box indicates the duration of cycling. Data are expressed as means ± SE. *$P < 0.05$ vs. baseline

Table 1 Brachial artery hemodynamics before, during and after resistance exercise

		Supine	Duration of resistance exercise				Supine	Supine	Supine	ANOVA
		Baseline	1st set	2nd set	3rd set	4th set	10 min	30 min	60 min	
Basal diameter (cm)	RE trial	0.38 ± 0.01					0.39 ± 0.01	0.39 ± 0.01	0.4 ± 0.01	Time: $P = 0.45$ Trial: $P = 0.38$ Interaction: $P = 0.13$
	C + RE trial	0.38 ± 0.01					0.39 ± 0.01	0.39 ± 0.01	0.37 ± 0.01	
Blood flow (ml/min)	RE trial	86.2 ± 8.5					130.9 ± 14.1*	83.8 ± 10.8	60.4 ± 5.2	Time: $P < 0.01$ Trial: $P = 0.27$ Interaction: $P = 0.31$
	C + RE trial	85.8 ± 9.9					161.8 ± 25.2*	106.8 ± 10.7	55.5 ± 4.4	
Hyperemic shear rate AUC (arbitrary units)	RE trial	97,054 ± 15,205					139,804 ± 15,135	95,215 ± 10,327	77,366 ± 7501	Time: $P < 0.01$ Trial: $P = 0.49$ Interaction: $P = 0.57$
	C + RE trial	102,748 ± 16,384					128,063 ± 17,753	79,345 ± 8575	78,253 ± 6248	
ANCOVA-corrected FMD (%) (covariate: hyperemic shear rate AUC)	RE trial	7.7 ± 0.7					5.3 ± 0.7	4.1 ± 0.7*	4.2 ± 0.7*	Time: $P < 0.01$ Trial: $P = 0.49$ Interaction: $P = 0.62$
	C + RE trial	7.6 ± 0.7					6.7 ± 0.7	5.6 ± 0.7	5.6 ± 0.7	
ANCOVA-corrected FMD (%) (covariate: basal diameter)	RE trial	7.7 ± 0.7					5.5 ± 0.7	4.1 ± 0.7*	4.1 ± 0.7*	Time: $P < 0.01$ Trial: $P = 0.47$ Interaction: $P = 0.66$
	C + RE trial	7.6 ± 0.7					6.9 ± 0.7	5.5 ± 0.7	5.5 ± 0.7	
Mean arterial pressure (mmHg)	RE trial	86 ± 1	101 ± 2*	98 ± 1*	97 ± 2	100 ± 3	88 ± 2	85 ± 1	88 ± 1	Time: $P < 0.01$ Trial: $P = 0.68$ Interaction: $P = 0.27$
	C + RE trial	88 ± 1	104 ± 3*	99 ± 2*	101 ± 3	94 ± 3	92 ± 1	84 ± 2	86 ± 2	

Mean ± SE. *$P < 0.05$ vs. baseline

All baseline and post-measurements were collected in the supine position

ANCOVA-corrected flow-mediated dilation (FMD) data are adjusted for basal diameter and hyperemic shear rate area under the curve (AUC)

differences in blood flow or shear rate were detected at any time point between the trials ($P > 0.05$, Fig. 2, Table 1).

Both trials caused impairment in brachial artery %FMD after the resistance exercise (Fig. 3a), and statistical significance was observed at 30 and 60 min post-resistance exercise in the RE trial. The reduction of %FMD in the C + RE trial did not reach statistical significance. However, there was no significant interaction in brachial artery %FMD responses between trials. The %FMD corrected for basal diameter and hyperemic shear rate AUC by ANCOVA did not affect the interpretation of the main findings as there were no significant interactions in %FMDs between trials (Table 1). The ΔFMD from baseline did not differ between trials. Although subjects in the C + RE trial tended to higher levels of ΔFMD at 10, 30 and 60 min compared with those in the RE trial, the differences were not statistically significant ($P = 0.34$, $P = 0.07$ and $P = 0.26$, respectively, Fig. 3b). No changes were observed in brachial artery diameter over time, and no differences among the visits were detected across time points (Table 1).

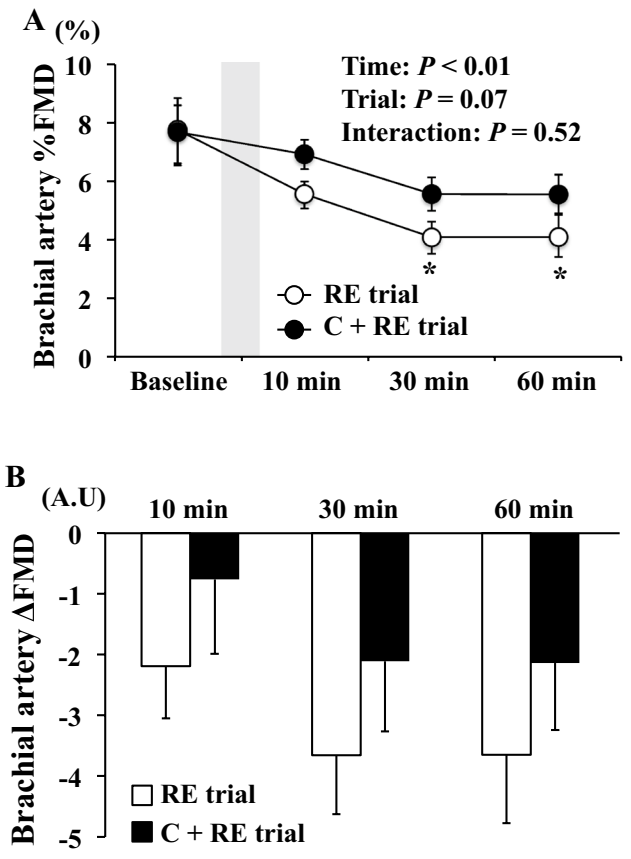

Fig. 3 Brachial artery %FMD (**a**) and ΔFMD relative to baseline (**b**) in the RE trial and C + RE trial. The shaded box indicates the duration of cycling. Data are expressed as means ± SE. *$P < 0.05$ vs. baseline

The mean arterial pressure was significantly elevated during the resistance exercise ($P < 0.01$ in both trials) but returned to baseline levels there after (Table 1). There were no significant differences in mean arterial pressure over time between the trials (Table 1).

Discussion

The novel finding of the present study is that a 45 min of prior cycling did not inhibit the acute endothelial dysfunction caused by subsequent resistance exercise. Indeed, we found that there is no significant interaction in %FMD between trials. The findings do not support the hypothesis that temporal endothelial dysfunction after resistance exercise can be prevented by prior aerobic exercise. However, the findings reported in this study provide an important evidence of a practical strategy that is effective order of exercises for maintaining endothelial function after resistance exercise.

The present study examined whether cycling for 45 min prior to resistance exercise prevents resistance exercise-induced acute endothelial dysfunction. However, prior cycling was not found to have a significant preventative effect. The C + RE trial showed marginal attenuation of the decline of %FMD after the resistance exercise because we did not observe the significant reduction of %FMD after the resistance exercise in the C + RE trial. However, there was no significant interaction in %FMD responses between trials. This suggested that the beneficial effect of prior cycling was attenuated by the subsequent resistance exercise. In support of this idea, a previous study demonstrated that running prior to resistance exercise for 8 weeks did not prevent the resistance exercise-induced increase in arterial stiffness (Okamoto et al. 2007). As our previous study reported that cycling for 10 min after resistance exercise rescued the acute endothelial dysfunction after resistance exercise (Morishima et al. 2019), it was suggested that the FMD response could be markedly affected by the last performed exercise. This series of studies provide important evidence regarding the order of resistance and aerobic exercise; performing aerobic exercise after resistance exercise, rather than before, is recommended to maintain endothelial function. However, performing aerobic exercise after resistance exercise cannot avoid temporal impairment of endothelial function. Therefore, further investigations are required to clarify the beneficial strategy that achieves the prevention of resistance exercise-induced temporal endothelial dysfunction.

The endothelium exerts several vascular protective effects, which are largely mediated by NO. These include anti-oxidative effects and anti-inflammatory effects. Endothelial dysfunction is an early, reversible step in cardiovascular disease and is characterized by a reduction in NO bioavailability (Davignon and Ganz 2004;

Forstermann and Muzel 2006; Mudau et al. 2012). In this regards, a single bout of aerobic exercise has been shown to increase in NO bioavailability in humans (Goto et al. 2007). However, we did not find a significant interaction in blood flow or shear rate in the present study, suggesting that the shear stress-induced augmentation of NO synthesis was similar between the two trials. One possibility is that the cycling intensity used in the present study (67.0 ± 1.7% HRmax) may be low to prevent the impact of subsequent resistance exercise. As the exercise-induced increase in NO bioavailability depends on exercise intensity (Goto et al. 2007), high-intensity exercise would be appropriate as a prior aerobic exercise. There is precedence in the literature supporting the idea that high-intensity exercise is effective to enhance NO bioavailability. For example, previously published studies in animals and humans demonstrated that high-intensity interval training increased the release and synthesis of NO (Hasegawa et al. 2018; Izadi et al. 2018). Based on these findings, it is reasonable to speculate that increasing aerobic exercise intensity as the next stage of investigation in this study area is to clarify the novel strategy to offset the vascular effect of resistance exercise.

There are several limitations in the present study. First, we used RPE to determine the cycling intensity. However, we need to measure HRmax or maximal oxygen uptake ($\dot{V}O_2$max) to set the aerobic exercise intensity accurately in the future studies. Second, it is difficult to conclude the chronic arterial adaptation after long-tem resistance training from the present results since we focused on the acute FMD response to a single bout of resistance exercise.

In conclusion, the present study revealed that cycling for 45 min prior to resistance exercise was not sufficient to prevent the effects of the resistance exercise on endothelial function. This study provides the first evidence, to best our knowledge that the vascular effects of resistance exercise are not offset by prior aerobic exercise. Accordingly, individuals should perform aerobic exercise subsequent to resistance exercise, rather than before, to maintain endothelial function acutely. The results of the present study may assist in providing a practical strategy to prevent acute endothelial dysfunction after resistance exercise.

Acknowledgements The authors appreciate the time and effort put in by all volunteer subjects. The authors also appreciate Dr. Jaume Padilla for his advice about data analysis.

Author contributions TM and EO: conceptualized and designed the study; TM, MT, and EO: performed the experiments; TM: analyzed data; TM, MT, and EO: interpreted the results of experiments; TM: prepared figures and table. TM and EO: drafted the manuscript; TM, MT, and EO: edited and revised the manuscript; TM, MT, and EO: approved the final version of manuscript.

Funding This work was supported by The Japan Society for the Promotion of Science Grant-in-Aid for Scientific Research [Grant number 18K17834 (to T.M.), 18K10832 (to E.O.)].

Compliance with ethical standards

Conflict of interest No conflicts of interest, financial or otherwise, are declared by the authors.

References

Ballard KD, Duguid RM, Berry CW, Dey P, Bruno RS, Ward RM, Timmerman KL (2017) Effects of prior exercise on sitting-induced vascular dysfunction in healthy men. Eur J Appl Physiol 117:2509–2518

Boyle LJ, Credeur DP, Jenkins NT, Padilla J, Leidy HJ, Fadel Thyfault JP, PJ. (2013) Impact of reduced daily physical activity on conduit artery flow-mediated dilation and circulating endothelial microparticles. J Appl Physiol 115(1519–1525):2013

Buchanan CE, Kadlec AO, Hoch AZ, Gutterman DD, Durand MJ (2017) Hypertension during weight lifting reduces flow-mediated dilation in nonathletes. Med Sci Sports Exerc 49(4):669–675

Davignon J, Ganz P (2004) Role of endothelial dysfunction in atherosclerosis. Circlation 109(23):27–32

De Jongh S, Lilien MR, Bakker HD, Hutten BA, Kastelein JJ, Stroes ES (2002) Family history of cardiovascular events and endothelial dysfunction in children with familial hypercholesterolemia. Atherosclerosis 163(1):193–197

Fairfax ST, Padilla J, Vinna LC, Holwerda SW, Davis MJ, Fadel PJ (2015) Myogenic responses occur on a beat-to-beat basis in the resting human limb. Am J Physiol Heart Circ Physiol 308(5):H59–H67

Forstermann U, Muzel T (2006) Endothelial nitric synthase in vascular disease: from marvel to menace. Circulation 113(13):1708–1714

Gokce N, Keaney JF Jr, Hunter LM, Watkins MT, Menzoian JO, Vita JA (2002) Risk stratification for postoperative cardiovascular events via noninvasive assessment of endothelial function: a prospective study. Circulation 105:1567–1572

Goto C, Nishioka K, Umemura T, Jitsuiki D, Sakagutchi A, Kawamura M, Chayama K, Yoshizumi M, Higashi Y (2007) Acute moderate-intensity exercise induces vasodilation through an increase in nitric oxide bioavailability in humans. Am J Hypertens 20:825–830

Harrison DG, Freiman PC, Armstrong ML, Marcus ML, Heistad DD (1987) Alterations of vascular reactivity in atherosclerosis. Circ Res. 61(5 Pt 2):1174–1180

Hasegawa N, Fujie S, Horii N, Miyamoto-Mikami E, Tsuji K, Uchida M, Hamaoka T, Tabata I, Iemitsu M (2018) Effects of different exercise modes on arterial stiffness and nitric oxide synthesis. Med Sci Sports Exerc 50(6):1177–1185

Iwamoto E, Bock JM, Casey DP (2018) High-intensity exercise enhances conduit artery vascular function in older adults. Med Sci Sports Exerc 50(1):124–130

Izadi MR, Ghardashi Afousi A, Asvadi Fard M, Babaee Bigi MA (2018) High-intensity interval training lowers blood pressure and improves apelin and NOx plasma levels in older treated hypertensive individuals. J Physiol Biochem 74:47–55

Jambrik Z, Venneri L, Varga A, Rigo F, Borges A, Picano E (2004) Peripheral vascular endothelial function testing for diagnosis of coronary artery disease. Am Heart J 48(4):684–689

Kooijman M, Thijssen DH, de Groot PC, Bleeker MW, van Kuppevelt HJ, Green DJ, Rongen GA, Smits P, Hopman MT (2008)

Flow-mediated dilatation in the superficial femoral artery is nitric oxide mediated in humans. J Physiol 586:1137–1145
Kuvin JT, Patel AR, Sliney KA, Pandian NG, Rand WM, Udelson JE, Karas RH (2001) Peripheral vascular endothelial function testing as a noninvasive indicator of coronary artery disease. J Am Coll Cardiol 38:1843–1849
Modena MG, Bonetti L, Coppi F, Bursi F, Rossi R (2002) Prognostic role of reversible endothelial dysfunction in hypertensive postmenopausal women. J Am Coll Cardiol 40:505–510
Morishima T, Restaino RM, Walsh LK, Kanaley JA, Padilla J (2017) Prior exercise and standing as strategies to circumvent sitting-induced leg endothelial dysfunction. Clin Sci. 131(11):1045–1053
Morishima T, Tsuchiya Y, Iemitsu M, Ochi E (2018) High-intensity resistance exercise with low repetitions maintains endothelial function. Am J Physiol Heart Circ Physiol 315:H681–H686
Morishima T, Iemitsu M, Ochi E (2019) Short-term cycling restores endothelial dysfunction after resistance exercise. Scand J Med Sci Sports. https://doi.org/10.1111/sms.13434
Mudau M, Genis A, Lochner A, Strijdom H (2012) Endothelial dysfunction: the early predictor of atherosclerosis. Cardiovasc J Afr 23(4):222–231
Nishiyama SK, Zhao J, Wray DW, Richardson RS (2017) Vascular function and endothelin-1: tipping the balance between the vasodilation and vasoconstriction. J Appl Physiol 122(2):354–360
Okamoto T, Masuhara M, Ikuta K (2007) Combined aerobic and resistance training and vascular function: effect of aerobic exercise before and after resistance training. J Appl Physiol 103(5):1655–1661
Okamoto T, Masuhara M, Ikuta K (2008) Relationship between plasma endothelin-1 concentration and cardiovascular responses during high-intensity concentric and eccentric exercise. Clin Physiol Func Imaging 28(1):43–48
Patti G, Pasceri V, Melfi R, Goffredo C, Chello M, D'Ambrosio A, Montesanti R, Di Sciascio G (2005) Impaired flow-mediated dilation and risk of restenosis in patients undergoing coronary sent implantation. Circulation 111(1):70–75
Perticone F, Ceravolo R, Pujia A, Ventura G, Iacopino S, Scozzafava A, Ferraro A, Chello M, Mastroroberto P, Verdecchia P, Schillaci G (2001) Prognostic significance of endothelial dysfunction in hypertensive patients. Circulation 104:191–196
Ross R (1999) Atherosclerosis—an inflammatory disease. N Engl J Med 340:115–126
Thijssen DH, Dawson EA, Tinken TM, Cable NT, Green DJ (2009) Retrograde flow and shear rate acutely impair endothelial function in humans. Hypertension 53:986–992
Yanagisawa M, Kurihara H, Kimura S, Tomobe Y, Kobayashi M, Mitsui Y, Yazaki Y, Goto K, Masaki T (1988) A novel potent vasoconstrictor peptide produced by vascular endothelial cells. Nature 332:411–415
Yoshida T, Kawano H, Miyamoto S, Motoyama T, Fukushima H, Hirai N, Ogawa H (2006) Prognostic value of flow-mediated dilation of the brachial artery in patients with cardiovascular disease. Intern Med 45(9):575–579

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