Acute Exhaustive Rowing Exercise Reduces skin Microvascular Dilator Function in Young Adult Rowing Athletes

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European Journal of Applied Physiology (2018) 118:461–474
https://doi.org/10.1007/s00421-017-3790-y

ORIGINAL ARTICLE

Acute exhaustive rowing exercise reduces skin microvascular dilator function in young adult rowing athletes

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Received: 13 July 2017 / Accepted: 12 December 2017 / Published online: 21 December 2017

Abstract

Purpose The effect of acute exhaustive exercise session on skin microvascular reactivity was assessed in professional rowers and sedentary subjects. A potential involvement of altered hemodynamic parameters and/or oxidative stress level in the regulation of skin microvascular blood flow by acute exercise were determined.

Methods Anthropometric, biochemical, and hemodynamic parameters were measured in 18 young healthy sedentary men and 20 professional rowers who underwent a single acute exercise session. Post-occlusive reactive hyperemia (PORH), endothelium-dependent acetylcholine (ACh), and endothelium-independent sodium nitroprusside (SNP) microvascular responses were assessed by laser Doppler flowmetry in skin microcirculation before and after acute exercise. Serum lipid peroxidation products and plasma antioxidant capacity were measured using spectrophotometry.

Results At baseline, rowers had significantly lower diastolic blood pressure (DBP) and heart rate (HR), and higher stroke volume (SV), PORH, and endothelium-dependent vasodilation than sedentary. Acute exercise caused a significant increase in systolic blood pressure, DBP, HR, and SV and a decrease in total peripheral resistance in both groups. Acute exercise induced a significant impairment in PORH and ACh-induced response in rowers, but not in sedentary, whereas the SNP-induced vasodilation was not affected by acute exercise in any group. Antioxidant capacity significantly increased only in sedentary after acute exercise.

Conclusion Single acute exercise session impaired microvascular reactivity and endothelial function in rowers but not in sedentary, possibly due to (1) more rowing grades and higher exercise intensity achieved by rowers; (2) a higher increase in arterial pressure in rowers than in sedentary men; and (3) a lower antioxidant capacity in rowers.

Keywords Acute exercise · Microvascular reactivity · Hemodynamics · Endothelium · Oxidative stress

Abbreviations

ACh	Acetylcholine
AE	Acute exercise
ApoA	Apolipoprotein A
ApoB	Apolipoprotein B
AUC	Area under the curve
BMI	Body mass index
BP	Blood pressure
CO	Cardiac output
CV	Cardiovascular
DBP	Diastolic blood pressure
ECW%	Extracellular water%
FBC	Full blood cell count
FFM%	Fat free mass%
FM%	Fat mass%
FMD	Flow-mediated dilation
FRAP	Ferric-reducing ability of plasma

Communicated by Carsten Lundby.

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HDL	High-density lipoprotein cholesterol
HR	Heart rate
hsCRP	High-sensitivity C-reactive protein
ICG	Impedance cardiography
ICW%	Intracellular water%
LDF	Laser Doppler flowmetry
LDL	Low-density lipoprotein cholesterol
MAP	Mean arterial pressure
MDA	Malondialdehyde
NO	Nitric oxide
PORH	Post-occlusive reactive hyperemia
RE	Regular exercise
RPE	Rating of perceived exertion
SBP	Systolic blood pressure
SD	Standard deviation
SNP	Sodium nitroprusside
SV	Stroke volume
TBARS	Thiobarbituric acid reactive substances
TBW%	Total body water%
TPR	Total peripheral resistance
WHR	Waist-to-hip ratio

Introduction

As endothelium is one of the main regulators of vascular tone, favorable effects of regular exercise on endothelial and vascular function may explain, at least in part, a well-established beneficiary relation between regular exercise and cardiovascular (CV) health (Joyner and Green 2009; Green et al. 2006), in both CV patients and healthy population (Lee et al. 2010; Schuler et al. 2009). Beside beneficial effect of regular exercise on traditional CV risk factors such as blood pressure and/or blood lipids (Joyner and Green 2009; Green et al. 2006), functional studies on the conductive and resistant blood vessels in CV patients have shown that regular exercise is an effective therapy for alleviating endothelial dysfunction and inflammation of the vascular wall (Hambrecht et al. 2003). Furthermore, regular exercise improves flow-mediated dilation (FMD) of large arteries and preserves endothelial function in both CV patients and healthy population (Hambrecht et al. 2003; Dawson et al. 2013), which may be explained by several mechanisms, including increased bioavailability of nitric oxide (NO), increased antioxidant defense and reduced level of pro-inflammatory cytokines originating from endothelial cells, adipose tissue, skeletal muscle, and mononuclear blood cells (Padilla et al. 2011). A key stimulus for the release of NO is shear stress exerted on the vessel wall. Thus, repeated episodic increase in blood flow and shear stress during exercise is likely to be an essential mechanism for a positive adaptation of vascular function to regular exercise training (Laughlin et al. 2008; Birk et al. 2013). Interestingly, it has been shown that different modes of exercise (e.g., cycling, leg kicking, and walking) induce different patterns of arterial shear stress (e.g., antegrade or retrograde/turbulent shear) resulting in distinct responses of vascular function (antegrade shear associated with improvements, whereas increases in retrograde and/or turbulent shear results in decreases in vascular function) (Dawson et al. 2013). Such physiological concept which states that an improvement of physiological parameters (e.g., vascular function) to a repeated stimulus (e.g., exercise training) can be induced even when this stimulus temporarily impairs the physiological system involved is known as the "hormesis" hypothesis (Dawson et al. 2013).

The effects of acute exercise on vascular function have received relatively little attention, especially when taking into account its effect on microvascular function. It is surprising, since investigating the acute exercise model allows more experimental control of both exercise (i.e., mode, intensity, duration, etc.) and confounding variables, as well as an insight into mechanisms of the exercise (acute or chronic) response (Padilla et al. 2006). A single progressive exercise session to exhaustion induces a transient but significant increment in blood pressure and vascular blood flow (Clarkson et al. 1999; Jurva et al. 2006), thus presenting a challenge to CV system. In addition, individual studies have demonstrated a reduced endothelium-dependent FMD of the brachial artery in response to acute exercise (Jurva et al. 2006; Phillips et al. 2011), while, on the contrary, others have shown an improvement in vascular reactivity of large conductance arteries following acute exercise (Hwang et al. 2012; Currie et al. 2012). In addition, while studies on the effect of acute exercise on large conductive blood vessels yielded inconsistent results, there is a paucity of data and studies that examined the effect of aerobic acute exercise on microvascular function in healthy individuals, nor sedentary nor athletes. As the earliest changes in different pathological states occur precisely at the level of microcirculation and acute exercise presents significant challenge to CV system in general, testing the impact of acute exercise on microvascular function may have important practical and clinical implications in both, active athletes and inactive individuals.

As follows, the present study aimed to investigate the effect of acute exercise on microvascular reactivity, and both endothelium-dependent and independent vasodilation of the forearm skin microcirculation in professional rowers and sedentary subjects. In addition, we sought to determine a possible involvement of potentially altered hemodynamic variables, oxidative stress level, and/or inflammation in the regulation of skin microvascular blood flow after acute exercise in these populations.

Methods

Study population

Eighteen young healthy sedentary male students (aged 21 ± 1 years) were recruited at the Faculty of Medicine University Osijek (sedentary) and 20 age-matched young healthy active professional male rowers (aged 20 ± 2 years, $P = 0.087$) were recruited at two local rowing clubs (Rowing Club Iktus Osijek and Croatian Rowing Club Vukovar) to participate in this study (rowers). Sedentary participants reported no regular physical activity or engagement in any exercise programs for 12 months prior to the study. Active rowers have been training between 5 and 12 times a week for 5 and 8 years. Five of them participated in world rowing championship. Exclusion criteria included a history of smoking, hypertension, coronary artery disease, diabetes, hyperlipidemia, renal impairment, cerebrovascular, and peripheral artery disease. None of the participants were taking any drugs that could affect the endothelium and vascular function. Written informed consent was obtained from each participant. The study protocol and procedures conformed to the standards set by the latest revision of the Declaration of Helsinki and were approved by the Ethical Committee of the Faculty of Medicine University of Osijek (Class: 602-04/14-08/06, Number: 2158-61-07-14-03). The study protocol was performed in the Laboratory for Clinical and Sports Physiology at Faculty of Medicine University of Osijek.

Study protocol

The study protocol comprised three visits to the Laboratory for Clinical and Sports Physiology at the Faculty of Medicine University of Osijek carried out in three subsequent weeks. All testing occurred in the morning after an overnight fast. Participants were instructed not to undertake any strenuous activity during 24 h preceding the visits. The timeline of the study with performed measurements at each visit point is depicted in Fig. 1. Body Mass Index (BMI), waist-to-hip ratio (WHR), body composition measurement and venous blood sampling for full blood count (FBC), plasma electrolytes, iron, transferrin, urea, creatinine, fasting lipid panels,

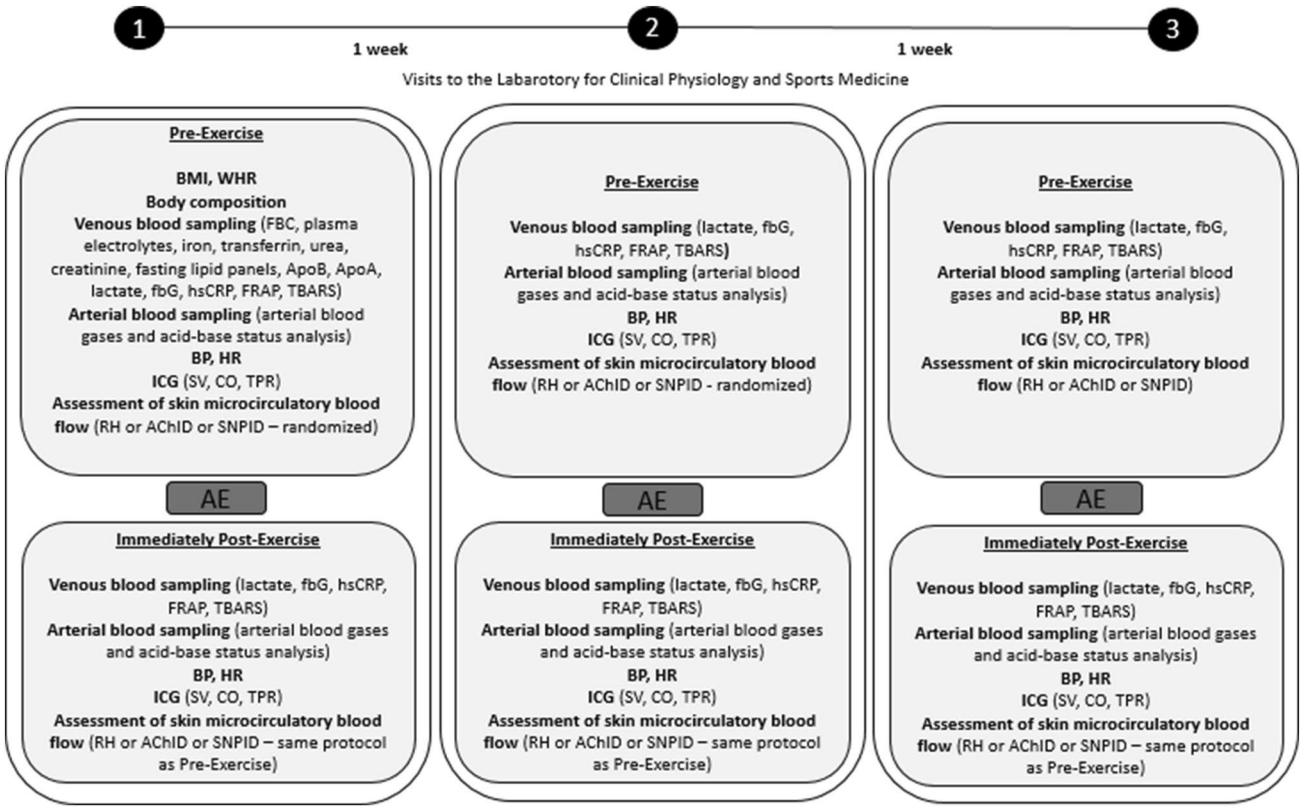

Fig. 1 Timeline of the study with performed measurements at each visit point. *BMI* body mass index, *WHR* waist-to-hip ratio, *FBC* full blood count, *ApoB* apolipoprotein B, *apoA* apolipoprotein A, *fbG* fasting blood glucose, *hsCRP* high-sensitive C-reactive protein, *FRAP* ferric-reducing ability of plasma, *TBARS* thiobarbituric acid reactive substances, *ICG* impedance cardiography, *SV* stroke volume, *CO* cardiac output, *TPR* total peripheral resistance, *RH* reactive hyperemia, *AChID* acetylcholine-induced dilation, *SNPID* sodium nitroprusside-induced dilation

and apolipoprotein B and A analysis were done at the beginning of the first study visit for each subject. At each study visit, subjects were subjected to the acute exhausting rowing session protocol. Furthermore, one protocol of assessment of skin microcirculatory blood flow (reactive hyperemia, acetylcholine, or sodium nitroprusside-induced dilation) in randomized order, venous blood sampling for lactate, fasting blood glucose and high-sensitivity C-reactive protein (hsCRP) analysis, arterial blood sampling for arterial blood gases and acid–base status analysis and blood pressure (BP), heart rate (HR), and impedance cardiography (ICG) measurements was performed before and immediately after acute exercise protocol for every subject at each study visit. All procedures were performed as described in detail bellow.

Anthropometry and body composition

BMI was calculated as body mass (kg) divided by height (m) squared, and WHR was calculated at the beginning of the first study visit. Body composition was measured with a four-terminal portable impedance analyzer (Maltron Bioscan 920-II) at the beginning of the first study visit, as well. Empirically derived formulas (the original manufacturer's software) were used to calculate the estimated BMI, fat free mass% (FFM%), fat mass% (FM%), total body water% (TBW%), extracellular water% (ECW%), and intracellular water% (ICW%).

Pre-exercise biochemical, hemodynamic, and impedance cardiography measurements

A venous blood sample was taken after 30 min of resting in supine position. Venous blood samples were analyzed for FBC, plasma electrolytes (sodium, potassium, and calcium), iron, transferrin, urea, creatinine, fasting lipid panels [total cholesterol, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), and triglycerides], apolipoprotein B (ApoB), apolipoprotein A (ApoA), lactate, fasting blood glucose, and hsCRP using the standard laboratory methods at the Department of Clinical Laboratory Diagnostics, University Hospital Osijek.

Arterial blood samples were taken from radial artery using pre-heparinized needle and syringe (sterile technique), and properly handled to minimize air exposure that could alter blood gas values. Arterial blood sampling was performed by a trained medical doctor. Arterial blood was analyzed for pH, pO_2, pCO_2, sO_2, and HCO_3^- using Techno Medica Gastat 602i Blood Gas Analyzer (Techno Medica Company, Diamond Diagnostics, MA, USA) available at the Laboratory for Clinical and Sports Physiology at Faculty of Medicine University of Osijek.

Pre-exercise BP and HR were measured at the beginning of each visit after 15 min rest in a seated position using a semi-automatic oscillometric monitor (OMRON, Osaka, Japan). The final values of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and HR were the mean of three consecutive measurements.

ICG was performed at the beginning of each study visit using the BIOPAC MP35-based measurement system (BIOPAC, Goleta, CA, USA) with non-invasive cardiac output sensor (BIOPAC SS31L) and with four disposable impedance strip electrodes (BIOPAC EL506) placed on the left side of the neck (one electrode around the base of the neck and the second one above the first one with 3 cm gap between electrodes) and in the left thorax region (the third electrode 3 cm below the thoracic xipho-sternal junction and the fourth electrode below the third one with 3 cm gap between electrodes). The ECG measurements were also recorded via the MP35 system with two spot electrodes and using the second bipolar lead. The basic principle of this methodology is that the variations in the basal thoracic impedance (Z) and the derivative of the thoracic impedance in a given beat (DZ) to an alternating high-frequency (100 KHz) and low magnitude (400 μA) current, across the thorax during cardiac ejection, result in a specific waveform that can be used to calculate stroke volume. ICG was performed after 5 min of resting in a supine position in an examination room by a trained researcher. According to the instructions of the manufacturer, the corresponding BSL 4.0.1 software was used for recording and analyzing the ICG measurements to obtain the required hemodynamic variables: stroke volume (SV) and cardiac output (CO), as previously described (Van De Water et al. 2003). Values of the hemodynamic parameters represented the mean value over the 3-min sampling period. TPR was calculated according to the formula TPR = MAP/CO.

Acute exhausting rowing session protocol

At each study visit all participants were subjected to a progressively incremental rowing protocol that was modified to comprise 5 × 4-min submaximal grades and a single maximal grade (Hahn et al. 2000). Rowing protocol was performed on the Dynamic Indoor Rower Concept 2 rowing ergometer (Concept2 Inc., Morrisville, VT, USA). All sedentary subjects were informed and instructed how to perform exercise on the rowing ergometer by a former professional rower. Submaximal grades were determined by the given load and lasted for 4 min each. All participants started with an initial workload of 150 W, with stage progression of 40 W. The submaximal grades were separated by 1-min recovery periods, with a 5-min rest before the maximal stage. Subjects were then instructed to row with a maximum power until complete exhaustion with no time limitation. BP and HR were determined before the test, during each recovery

period and immediately after maximal exercise. Rating of perceived exertion (RPE) was used for subjective quantification of individual's perception of the physical demands of the activity. In this study, a category-ratio scale (CR10), introduced by Borg (1998), and using rating ranges from 0 (nothing at all) to 10 (very very hard activity), was used, since it has shown a good reliability and validity in healthy, clinical, and athletic adult populations (Chen et al. 2002).

Post-exercise biochemical, hemodynamic, and impedance cardiography measurements

Immediately after acute exercise, venous blood sample was taken for lactate, fasting blood glucose, and hsCRP analysis. Arterial blood sample was taken for arterial blood gases and acid–base status analysis. BP, HR, and ICG measurements (SV, CO, and TPR) were performed again immediately after acute exhausting rowing session. All repeated measurements and analyzing procedures were performed as described in detail above.

Assessment of skin microcirculatory blood flow

Microcirculatory blood flow was assessed by laser Doppler flowmetry (LDF) (MoorVMS-LDF, Axminster, UK) in response to three different stimuli to test microvascular reactivity, each of the stimuli applied during one study visit. The type of the LDF protocol applied at a particular study visit was randomly chosen for each participant. LDF measurements were performed before and immediately after acute exercise session during each study visit. Measurements were performed in a temperature-controlled room (mean ± SD temperature = 23.5 ± 0.5 °C). Data collection started 30 min after resting in a supine position to acclimatize. The laser Doppler was attached to the skin of the volar forearm, 13–15 cm from the wrist, at the same place at each study visit. During the acute exercise session, the probe holder stayed attached to the skin to provide that pre- and post-exercise measurement was performed at exactly same location.

The first microvascular reactivity protocol was an induction of post-occlusive reactive hyperemia (PORH) following the release of a transient occlusion of blood flow (Crakowski et al. 2006). There are several mediators that contribute to PORH, most notably sensory nerves, and endothelium-derived vasodilator factors, including endothelium-derived hyperpolarizing factors (EDHF) and possibly prostaglandins, suggesting that PORH presents an useful tool for assessment of overall changes in microvascular function and its endothelium (Roustit and Cracowski 2012). After a 5-min baseline measurement, occlusion of the brachial artery was induced by inflating a pneumatic cuff on the upper arm to 30–50 mmHg above the SBP. Measurements were taken before, during, and after the release of 1-min occlusion. Microcirculatory blood flow in a given time was expressed in arbitrary perfusion units and determined by software calculating the area under the curve (AUC) during baseline flow, occlusion, and reperfusion. Because the flow does not reach the value of zero even when perfusion is absent, flow values were expressed as a quotient of a standard comparator—baseline flow. The final result was expressed as the difference between percentage of flow change during reperfusion and occlusion in relation with baseline (R–O% increase). The procedures for the PORH LDF measurements were done according to our previously described protocols (Cavka et al. 2013, 2015).

The second and third microvascular reactivity protocols were non-invasive tests that measure skin microvascular blood flow in response to the iontophoresis of acetylcholine (ACh), which is considered endothelium-dependent vasodilation, and to the iontophoresis of sodium nitroprusside (SNP), which is considered endothelium-independent vasodilation. Iontophoresis is a non-invasive method for the transdermal application of charged substances by means of an externally applied electrical current. Substances were placed in an iontophoretic drug-delivery electrode that was attached at the site of the LDF probe. After baseline recording for 5 min, either the positively charged vasodilator ACh (1%) was iontophorezed with anodal current applied by means of seven pulses of direct electric current of 0.1 mA for 30 s with 30 s between each dose, or negatively charged SNP (1%) was applied by means of three pulses of 0.1 mA of negative current for 30 s, followed by a four pulses of 0.2 mA for 30 s, with 90 s between each dose. The pulsed iontophoretic protocols are adapted to obtain a stable plateau of the maximal LDF response (Lenasi and Strucl 2008). Microcirculatory blood flow in this test was expressed in arbitrary perfusion units and determined by software calculating the AUC during baseline flow and during ACh or SNP administration. The final result was expressed as the percentage of ACh- or SNP-induced dilation in relation with baseline flow (ACh % increase or SNP % increase).

Oxidative stress and antioxidant capacity marker measurements

Additional venous blood samples were collected before and after exercise protocol in tubes with anticoagulant, snap frozen in liquid nitrogen, and stored in a refrigerator at − 80 °C until the oxidative stress analysis experiments were performed. Spectrophotometric method was used for the measurement of oxidative stress and antioxidant capacity markers. The Thiobarbituric Acid Reactive Substance (TBARS) assessment is a method which measures the products of lipid peroxidation from serum samples. Since the method is non-specific, because other substances bind to

thiobarbituric acid (including proteins), trichloroacetic acid was added to the sample to precipitate the proteins and after that the supernatant used was for further measurement. The absorbance of the sample was measured by Nanophotometer P300 UV/VIS, IMPLEN at 572 and 532 nm with malondialdehyde (MDA) used as a standard (µM MDA) (Oakes and Van Der Kraak 2003). The ferric-reducing ability of plasma (FRAP) method was used for measuring antioxidant capacity of blood samples. Fe^{3+}-TPTZ (2,4,6-tris(2-pyridyl)-s-triazine) is reduced to Fe^{2+}-TPTZ in the presence of antioxidants and a blue discoloration occurs. The absorbance of the sample was measured by Nanophotometer P300 UV/VIS, IMPLEN at 593 nm with as standard (mM/L Trolox) (Benzie and Strain 1996). The general procedures for oxidative stress and antioxidant capacity marker measurements were done according to our previously described protocol (Cosic et al. 2016).

Statistical analysis

All results are reported as the mean ± standard deviation (SD). The sample size required to show a potentially significant effect is calculated based on preliminary data in ten subjects. To show an expected difference in LDF-measured microvascular blood flow change before and after study protocol with alpha = 0.05 and a statistical power of 80% for paired *t* test, the needed sample size is 12 subjects per group. Clinical characteristics and all parameters measured before and after acute exercise session were compared using a paired Student *t* test. The normality of data distribution was assessed by the Kolmogorov–Smirnov normality test. The Wilcoxon rank-sum test was used when variables were not normally distributed. When more than two repeated measures were analyzed, a one-way repeated measures ANOVA test was used. For the posttest multiple comparison analyses, the Holm–Sidak method was used. Student's *t* test was used to compare parameters between the experimental groups. When variables were not normally distributed, the Mann–Whitney rank-sum test was used. The correlations between microvascular reactivity (PORH) and corresponding parameters were determined by Persons' or Sperman's correlation tests when appropriate. $P < 0.05$ was considered statistically significant. SigmaPlot, version 11.2 (Systat Software, Inc., Chicago, IL, USA) was used for statistical analysis.

Results

Subjects' profile

The subjects from both groups demonstrated similar anthropometric measures and body composition, with no differences in BMI, WHR, FFM%, Fat%, TBW%, ECW%, and ICW% between the groups (Table 1).

Baseline biochemical parameters (FBC, urea, creatinine, electrolytes, iron, and transferrin) were similar between sedentary and rowers. However, rowers had significantly lower triglycerides and higher HDL cholesterol levels compared to sedentary (Table 2). ApoB was significantly lower in rowers compared to sedentary subjects at baseline (Table 2).

Table 1 Anthropometric measures and body composition of the study population

Parameter	Sedentary	Rowers
n	18	20
BMI, kg/m^2	24.1 ± 2.9	22.9 ± 1.7
WHR	0.82 ± 0.04	0.80 ± 0.05
FFM, %	85.7 ± 3.6	87.4 ± 2
Fat, %	14.3 ± 3.6	12.6 ± 2
TBW, %	62.6 ± 3.7	65.2 ± 3.3
ECW, %	42.5 ± 1.6	43.6 ± 3.1
ICW, %	57.5 ± 1.6	56.4 ± 3.1

Results are expressed as mean ± SD. Differences in values of assessed variables between groups were not significantly different

n number of subjects, *BMI* body mass index, *WHR* waist-to-hip ratio, *FFM* fat free mass, *TBW* total body water, *ECW* extracellular water, *ICW* intracellular water

Table 2 Biochemical characteristics of the study population

Parameter	Sedentary	Rowers
n	18	20
Leukocytes, 10E9/L	6.1 ± 0.9	6.1 ± 1.9
Erythrocytes, 10E12/L	4.8 ± 0.3	5 ± 0.2
Hemoglobin, g/L	144 ± 7.3	144 ± 7.1
Thrombocytes, 10E9/L	195 ± 43	213 ± 44
Urea, mmol/L	5.8 ± 1.1	5.9 ± 1.3
Creatinine, µmol/L	84 ± 6	84 ± 10
Sodium, mmol/L	138.4 ± 1.6	138.6 ± 1.7
Potassium, mmol/L	3.9 ± 0.3	4 ± 0.3
Calcium, mmol/L	2.4 ± 0.1	2.4 ± 0.1
Iron, µmol/L	16 ± 6.7	17.7 ± 6.3
Transferrin, g/L	2.5 ± 0.3	2.5 ± 0.3
Cholesterol, mmol/L	4 ± 0.6	3.8 ± 0.8
Triglycerides, mmol/L	1 ± 0.4	0.8 ± 0.3*
HDL cholesterol, mmol/L	1.2 ± 0.3	1.4 ± 0.2*
LDL cholesterol, mmol/L	2.6 ± 0.4	2.2 ± 0.6
Apolipoprotein B, g/L	0.74 ± 0.11	0.56 ± 0.19*
Apolipoprotein A, g/L	1.53 ± 0.21	1.59 ± 0.24

Results are expressed as mean ± SD

n number of subjects

*$P < 0.05$ sedentary vs. rowers

Hemodynamic parameters of the study population

All participants were normotensive pre-exercise. At baseline, rowers had significantly lower DBP and MAP than sedentary, while SBP was not significantly different between groups (Table 4). HR was significantly lower and SV significantly higher in rowers compared to sedentary. At baseline, CO and TPR did not differ between the groups (Table 4).

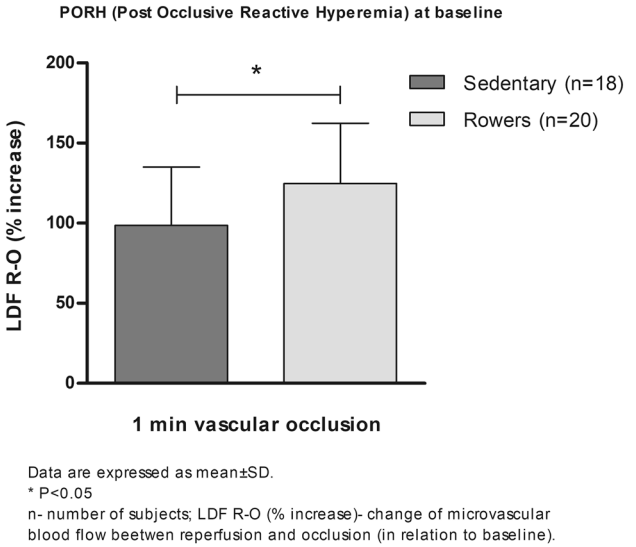

Fig. 2 Effect of regular exercise (RE) on forearm skin microvascular response to a transient brachial artery occlusion—post-occlusive reactive hyperemia (PORH), assessed by laser Doppler flowmetry (LDF) in young healthy men. Rowers exhibited significantly higher PORH following 1-min vascular occlusion than sedentary men at baseline

Baseline laser Doppler flowmetry assessment of skin microcirculatory blood flow

At baseline, rowers had significantly higher PORH after 1 min of vascular occlusion than sedentary subjects (R–O% 1-min sedentary 99 ± 37 vs. rowers 125 ± 38, $P = 0.017$) (Fig. 2). Rowers had significantly higher LDF response to ACh than sedentary at baseline (ACh % increase sedentary 795 ± 200 vs. rowers 1133 ± 384, $P = 0.039$) (Fig. 3 Panel 3A), while there was no difference in SNP-induced increase in LDF at baseline between two groups (SNP % increase sedentary 952 ± 308 vs. rowers 1117 ± 280, $P = 0.725$) (Fig. 3 Panel 3B).

The effect of acute exercise on serum lactate, glucose, high-sensitivity C-reactive protein level, and arterial blood status in sedentary and rowers

Serum lactate, glucose, and hsCRP significantly increased after acute exercise in both sedentary and rowers (Table 3). The results of arterial blood gases and acid–base status analysis have shown that metabolic acidosis occurred after acute exercise in both sedentary and rowers (Table 3). These data indicate that acute exercise protocol was conducted consistently and that acute rowing session protocol led to complete exhaustion in all subjects from both experimental groups, what was in accordance with the RPE which was ten in all subjects (Table 4).

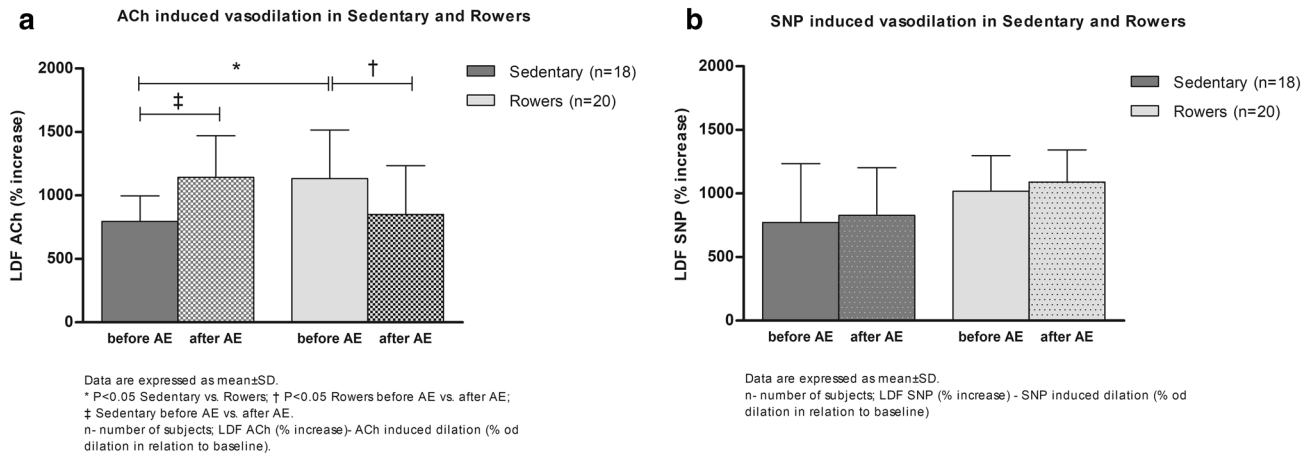

Fig. 3 Effect of regular exercise (RE) and acute exercise (AE) on forearm skin microvascular endothelium-dependent and independent vasodilation, assessed by laser Doppler flowmetry (LDF) in young healthy men. Rowers had a significantly higher Ach-induced vasodilation than sedentary at baseline (**a**), while there was no difference in SNP-induced vasodilation at baseline between two groups (**b**). The vasodilation in response to ACh was significantly impaired after AE in rowers, and significantly increased in sedentary subjects (**a**). SNP did not significantly change after AE in both sedentary and rowers (**b**)

Table 3 Biochemical parameters before and after acute exercise (AE)

Parameter	Sedentary		Rowers	
	Before AE	After AE	Before AE	After AE
n	18		20	
Glucose, mmol/L	4.8 ± 0.8	6.1 ± 1.5*	4.5 ± 0.9	6.9 ± 1†
hsCRP, mg/L	1.05 ± 0.85	1.18 ± 0.91*	0.84 ± 0.7	0.95 ± 0.73†
Lactate, mmol/L	1.32 ± 0.82	19.91 ± 2.47*	1.49 ± 0.56	16.02 ± 4.64†
pH	7.379 ± 0.021	7.215 ± 0.071*	7.392 ± 0.036	7.248 ± 0.066†
pCO_2, kPa	5.83 ± 0.25	4.55 ± 0.86*	5.86 ± 0.86	4.47 ± 0.44†
pO_2, kPa	12.86 ± 3.96	12.12 ± 4.68	12.32 ± 3.6	14.04 ± 1.99
sO_2	95.3 ± 5	91.7 ± 6.6	97.7 ± 0.5	96.5 ± 1.7†
BASE, mmol/L	0.26 ± 1.5	13.4 ± 5.5*	2.1 ± 1.5	11.2 ± 5.3†
$HCO3^-$, mmol/L	24.6 ± 1.2	14.6 ± 3.5*	25.6 ± 1.1	15.2 ± 2.8†

Results are expressed as mean ± SD

n number of subjects

*$P < 0.05$ before AE vs. after AE in sedentary

†$P < 0.05$ before AE vs. After AE in rowers

The effect of acute exercise on hemodynamic parameters in sedentary and rowers

Rowers completed more rowing grades than sedentary subjects (Table 4). All subjects reported RPE 10 on Borg scale (very very hard activity) after the final maximal rowing stage (Table 4). SBP, DBP, and MAP significantly increased during acute exercise in both groups, but SBP and MAP increased significantly more in rowers than in sedentary subjects (Table 4). HR was significantly increased during acute exercise in both groups as well (Table 4). SV and CO significantly increased during acute exercise in both groups, but significantly more in rowers than in sedentary. Finally, TPR significantly decreased after AE in both experimental groups, significantly more in rowers than in sedentary (Table 4).

The effect of acute exercise on skin microvascular reactivity in sedentary and rowers

Acute exercise did not significantly affect PORH in sedentary subjects (R–O% 1-min before AE 99 ± 37 vs. after AE 103 ± 29, $P = 0.732$) (Fig. 4a). PORH following 1 min of vascular occlusion was significantly impaired after AE compared to pre-AE measurement in rowers (R–O% 1-min before AE 125 ± 38 vs. after AE 86 ± 22, $P < 0.001$) (Fig. 4b).

Acute exercise significantly increased the ACh-induced dilation in sedentary subjects (ACh % increase before AE 795 ± 200 vs. after AE 1142 ± 328, $P = 0.05$) (Fig. 3a). Consistent with the PORH results, the ACh-induced dilation was significantly impaired after acute exercise when compared to pre- acute exercise measurement in rowers (ACh % increase before acute exercise 1133 ± 384 vs. after AE 851 ± 384, $P = 0.009$) (Fig. 3b). The SNP-induced dilation did not significantly change after acute exercise and was similar to pre-acute exercise measurement in both sedentary (SNP % increase before acute exercise 772 ± 462 vs. after acute exercise 828 ± 374, $P = 0.725$) and rowers (SNP % increase before acute exercise 1017 ± 280 vs. after acute exercise 1089 ± 253, $P = 0.132$) (Fig. 3 Panel 3B).

Oxidative stress and antioxidant capacity markers in sedentary and rowers

There were no significant differences in TBARS and FRAP levels between sedentary and rowers at baseline (Table 5). TBARS was not significantly changed after acute exercise in both sedentary and rowers (Table 5). On the other hand, the FRAP level significantly increased after acute exercise compared to pre-acute exercise measurement in sedentary, while it remained unchanged after acute exercise in rowers (Table 5).

The association between acute exercise-induced skin microvascular reactivity and blood pressure/oxidative stress changes in study population

There was significantly negative correlation between SBP increase and PORH change ($r = -0.334$, $P = 0.05$), as well as between SBP increase and ACh-induced dilation change ($r = -0.527$, $P = 0.0242$) in study population. On the other hand, we did not find significant correlation between FRAP change and SBP increase ($r = -0.432$, $P = 0.168$), as well as between FRAP and PORH change ($r = 0.460$, $P = 0.141$) or FRAP and ACh-induced dilation change ($r = -0.0167$, $P = 0.948$) following acute exercise in study population.

Table 4 Effect of AE on hemodynamic parameters in sedentary and rowers

Parameter	Sedentary	Rowers
n	18	20
Number of rowing grades	3 ± 1	4 ± 1*
RPE	10	10
SBP, mmHg		
Before AE	135 ± 12	128 ± 13
After AE	167 ± 17†	192 ± 16*,†
Δ	35 ± 14	63 ± 8*
DBP, mmHg		
Before AE	83 ± 4	78 ± 7*
After AE	88 ± 7†	87 ± 9†
Δ	15 ± 9	16 ± 6
MAP, mmHg		
Before AE	100 ± 5	95 ± 7*
After AE	111 ± 11†	119 ± 11*,†
Δ	14 ± 10	24 ± 8*
HR, bpm		
Before AE	79 ± 9	65 ± 6*
After AE	129 ± 9†	103 ± 20*,†
Δ	50 ± 13	37 ± 22
SV, mL		
Before AE	63 ± 13	77 ± 10*
After AE	70 ± 18†	126 ± 8*,†
Δ	7 ± 6	49 ± 17*
CO, L/min		
Before AE	4.97 ± 1.11	5 ± 0.65
After AE	9.02 ± 2.53†	12.79 ± 2.16*,†
Δ	4.05 ± 1.68	7.79 ± 1.57*
TPR, mmHg·min/L		
Before AE	19.16 ± 5.23	18.5 ± 2.91
After AE	13.02 ± 3.09†	9.35 ± 1.72*,†
Δ	6.15 ± 4.03	9.15 ± 1.81

n number of subjects, *AE* acute exercise, Δ difference between before and after AE, *RPE* rating of perceived exertion, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *MAP* mean arterial pressure, *HR* heart rate, *SV* stroke volume, *CO* cardiac output, *TPR* total peripheral resistance

*$P < 0.05$ sedentary vs. rowers

†$P < 0.05$ before AE vs. after AE, within group

Discussion

The effects of regular exercise on lipid profile, body composition, and hemodynamic variables

The salient finding of the present study is that regular exercise activity has a beneficial effect on vascular health and skin microvascular endothelial function even in young healthy subjects, since professional rowers exhibited lower BP level and HR, lower triglycerides, lower serum ApoB and higher HDL cholesterol level, as well as a higher reactive vascular response of skin microvascular PORH and endothelium-dependent vasodilation at baseline than age-matched lean sedentary men (Table 2), which is in concordance with earlier studies (Gordon et al. 2014; Kraus et al. 2002).

The results of our study in regard of lipid profile and hemodynamic variables are in agreement with several meta-analyses. For example, a large meta-analysis by Cornelissen and Smart (2013), which included total of 5223 healthy participants (3401 exercising and 1822 sedentary controls), demonstrated that regular exercise training lowers both SBP and DBP (Table 4). Furthermore, regular physical activity and consequent weight loss may improve serum lipid status in healthy and overweight subjects (Gordon et al. 2014; Kraus et al. 2002; Kodama et al. 2007). Moreover, a large meta-analysis combining 25 studies and a total of 1404 participants has shown that regular exercise lasting for an average of 27 weeks 3–5 times a week induced HDL cholesterol increase independent of body weight change in healthy individuals (Kodama et al. 2007).

In regards to hemodynamic adaptations to regular exercise in our study, rowers exhibited higher SV and lower HR than sedentary, as expected. There were no differences in CO and TPR between the groups at baseline (Table 4), which is in accordance with earlier studies. In trained athletes, increased SV occurs due to physiologic cardiac adaptations to the hemodynamic load associated with chronic exercise trainings (Warburton et al. 2002).

In the present study, no significant differences were found in FFM%, Fat%, TBW%, ECW%, and ICW% between rowers and sedentary (Table 1). This is in agreement with the study by Gurd and Klentrou (2003), but contrasts to Grund et al. (2001) who have shown that strength- and endurance-trained men had less FM and greater TBW% compared to untrained men. Possible reason for that difference was that endurance-trained men had decreased BMI compared to untrained men, what we did not observe in the present study.

The effects of regular exercise on microvascular and endothelial function

Regular exercise for a period of weeks to months improves microvascular reactivity in skin microcirculation by increasing endothelium-dependent vasodilation, such as response to ACh (Padilla et al. 2011; Lenasi and Strucl 2004; Wang 2005), and is even more pronounced in elite athletes compared to subjects who performed regular physical activity (Kvernmo et al. 1998; Lenasi and Strucl 2004). Similarly, Roche et al. (2010) demonstrated an enhanced response to local heating in physically active compared to sedentary children. Moreover, detraining for

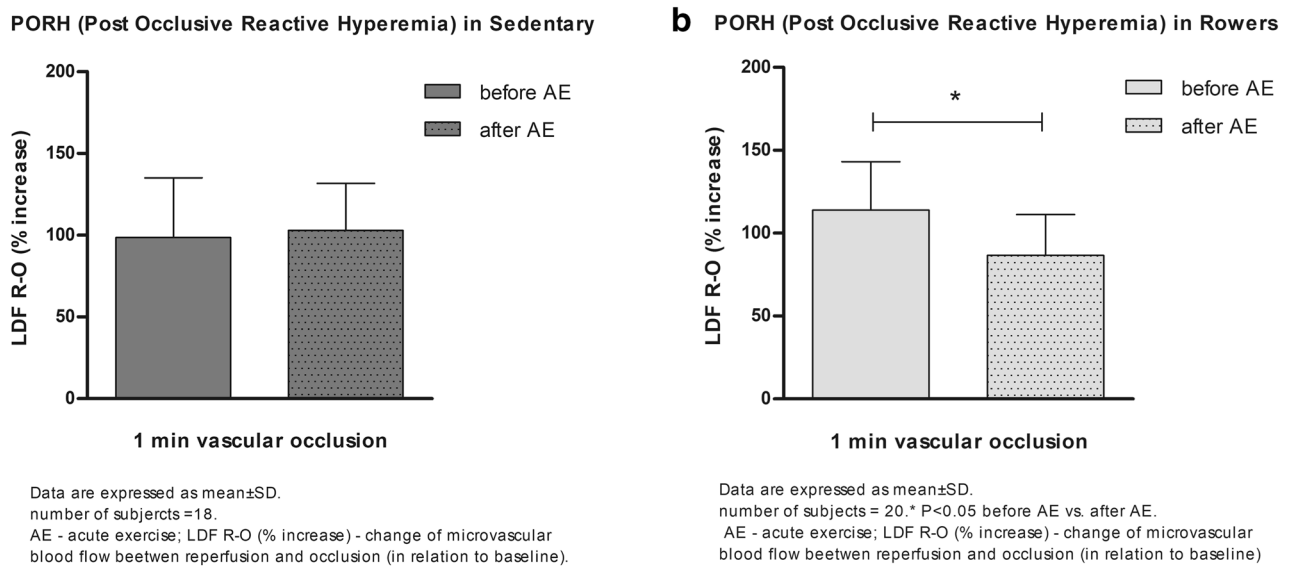

Fig. 4 Effect of acute exercise (AE) on forearm skin microvascular response to transient brachial artery occlusion—post-occlusive reactive hyperemia (PORH), assessed by laser Doppler flowmetry (LDF) in rowers and age-matched lean sedentary men. AE did not have any significant effect on PORH in sedentary (**a**), while PORH following 1 min vascular occlusion was significantly impaired after AE in rowers (**b**)

Table 5 Oxidative stress and antioxidant capacity markers before and after acute exercise (AE) in sedentary and rowers

Parameter	Sedentary		Rowers	
	Before AE	After AE	Before AE	After AE
n	18		20	
TBARS, μM MDA	0.922 ± 0.512	0.723 ± 0.330	0.664 ± 0.059	0.676 ± 0.045
FRAP, mM/L Trolox	0.515 ± 0.098	0.568 ± 0.089*	0.517 ± 0.055	0.527 ± 0.062

Results are expressed as mean ± SD

n number of subjects, *TBARS* thiobarbituric acid reactive substances, *FRAP* ferric-reducing ability of plasma

*$P < 0.05$ before AE vs. after AE in sedentary

8 weeks abolished training-induced improved endothelium-dependent skin microvascular reactivity (Wang 2005).

Consistently with the previous findings, we have demonstrated significantly greater PORH of forearm skin microcirculation (Fig. 2) and endothelium-dependent vasodilation (Fig. 3a), with no differences in endothelium-independent vasodilation between rowers and sedentary at baseline (Fig. 3b). Changes in hemodynamic forces are suggested to be primary candidates responsible for improved skin microvascular reactivity due to regular physical activity (Padilla et al. 2011; Lenasi and Strucl 2004). Since a sevenfold increase in skin blood flow is not uncommon during exercise training, repeated increases in microvascular shear stress may provoke endothelial adaptation in skin microcirculation (Lenasi and Strucl 2004; Green et al. 2010).

The effects of acute exercise on microvascular and endothelial function in rowers and sedentary

There is a paucity of studies in the literature that examined the effect of acute aerobic exercise on microvascular reactivity in healthy individuals (sedentary or athletes). In addition, we did not find any study that used rowing as an acute exercise mode for examining its effect on either macro- or microvascular function. To our knowledge, our study is the first to show that acute rowing exercise caused significant impairment in the forearm microvascular response to both transient vascular occlusion (PORH) (Fig. 4b) and ACh administration (Fig. 3 Panel 3A) in rowers, while it did not significantly affect the PORH, and even improved ACh-induced dilation in sedentary (Figs. 3a, 4a). Moreover, acute rowing exercise did not alter the endothelium-independent vasodilation in any experimental group (Fig. 3b). Earlier

studies that have been focused on macrovascular function reported reduced brachial artery FMD immediately after acute cycling or handgrip session (in less than 30 min post-exercise) in healthy individuals (Birk et al. 2013; Gonzales et al. 2011; Gori et al. 2010; Goto et al. 2003; Johnson et al. 2012a, b), which could potentially mirror our findings of microcirculatory responses in rowers. However, not all studies have observed endothelial function impairment following aerobic acute exercise and some have brought conflicting results by reporting no change or even an improvement in FMD after acute cycling exercise in trained and sedentary men (Johnson et al. 2012a, b; Jones et al. 2010). In concert with these studies, we found no change in PORH and even improvement of ACh-induced vasodilation in sedentary, opposed to microvascular impairment in athletes. Since both sedentary and rowers were exposed to the same exercise modality, functional vascular studies were performed immediately after acute exercise, and acute rowing session led all subjects to complete exhaustion, possible reasons for different microvascular responses following acute exercise in rowers and sedentary subjects is yet to be identified and clarified.

The intensity and duration of acute exercise appear to significantly modify post-exercise alterations in endothelial function. For example, higher exercise intensity (80% VO_{2max} or 80% HR_{max}) typically results in a larger decrease in FMD immediately post-exercise (Birk et al. 2013; Johnson et al. 2012a, b), while most (Harris et al. 2008; Padilla et al. 2006), but not all studies of low-to-moderate intensity exercise (50% VO_{2max}) have reported an increase in FMD after exercise in healthy subjects (Phillips et al. 2011; Rooks et al. 2011). These findings suggest that exercise intensity may contribute to post-exercise vascular response, with a higher exercise intensity associated with an attenuated FMD immediately after acute exercise in healthy subjects. Along with the acute exercise intensity, another factor that may modulate post-exercise vascular response is the duration of exercise bout (Dawson et al. 2013). Interestingly, acute exercise of longer duration typically leads to a decrease of FMD, while shorter acute exercise of the same intensity may not be sufficient to induce increased vascular response (Birk et al. 2013; Johnson et al. 2012a, b). Collectively, these observations may offer a potential explanation for no changes in post-exercise skin microvascular reactivity in sedentary who accomplished exercise of lower intensity and duration compared to rowers in our study.

The effects of acute exercise on systemic hemodynamic parameters and (anti)oxidative stress markers

It is important to emphasize that at baseline, sedentary had significantly higher HR and lower SV than rowers, which resulted in almost the same CO at rest in both groups. CO significantly increased in both groups after acute exercise (in agreement with Plowman and Smith 2010), but in sedentary CO increased more prominently at the expense of increasing HR, while in rowers at the expense of predominantly increased SV, which evidently resulted in larger increase in SBP in rowers than in sedentary during acute exercise (Table 4). As expected, DBP increased slightly in both groups after acute exercise, probably because of the balance of vasodilation in active skeletal muscles and corresponding vasoconstriction in other inactive vascular beds. This is supported by significant decrease of TPR after acute exercise in both groups, which was significantly lower in rowers than in sedentary after acute exercise (Table 4). Decreased TRP reflects maximal vasodilation in active skeletal muscles according to their need for increased blood flow which accompanies maximal acute exercise (Plowman and Smith 2010). In addition, this large drop in TPR during acute exercise is important for preserving MAP and alleviating its exaggerated increase.

The described hemodynamic changes (especially BP increase) during acute exercise are important, since it has been demonstrated that decreased FMD response (for up to 2.5 h) following acute exercise (< 5 min) occurs due to experimentally induced acute hypertension (Clarkson et al. 1999; Jurva et al. 2006). Such endothelial dysfunction due to acute hypertension was observed in microcirculation, as well (Millgard and Lind 1998). This is very intriguing, since increased BP is usually associated with increased blood flow and shear stress, which are considered to be kay stimuli for the release of NO and increased expression of antiatherogenic genes (Laughlin et al. 2008; Birk et al. 2013). However, several studies have demonstrated that aerobic/endurance and even more resistance training leads to acute increases in BP that could potentially results in immediate reduction in endothelial function (Dawson et al. 2013). For example, in healthy subjects, higher BP response during handgrip exercise was related to a larger decrease in FMD after exercise, and such decrease in FMD after acute exercise was associated with BP elevations and independent of changes in mean shear stress (Gonzales et al. 2011). In addition, studies reported that increased BP could potentially result in impaired endothelial function in sedentary subjects (Dawson et al. 2013; Gonzales et al. 2011), but not in athletes (Phillips et al. 2011), suggesting that the effects of acute hypertension during acute exercise on endothelial function may be mitigated by regular exercise. Still, none of the abovementioned studies did not use rowing as the acute exercise mode, and all were focused on macrovascular function. In the present study, we have found a negative association between SBP increase and change of microvascular reactivity during acute rowing exercise. Since rowers exhibited significantly larger increase in BP during exercise

than sedentary, a more prominent acute hypertension could be one of the possible explanations for decreased microvascular reactivity in rowers and not in sedentary men following acute exercise (Table 4). These findings present a step forward to understanding whether a BP increase (acute hypertension) present an important factor in acute exercise-induced microvascular dysfunction in young healthy men.

Increased oxidative stress level leads to a reduction in synthesis and/or bioavailability of NO, a main endothelial vasodilator (Finaud et al. 2006), but could also modify production of endothelium-derived hyperpolarizing factor (EDHF); mainly balance of vasoactive prostaglandins and other metabolites of arachidonic acid which contribute to the mechanisms of endothelium-dependent responses (Zhu et al. 2006). EDHF play a major role in PORH and ACh-induced dilation in skin microcirculation (Lorenzo and Minson 2007), whereas the results are conflicting concerning the implication of prostaglandins (Binggeli et al. 2003; Dalle-Ave et al. 2004; Medow et al. 2007). It is established that regular exercise improves oxidative status by inducing antioxidative mechanisms which contribute to improved vascular and endothelial function in physically active individuals (Dawson et al. 2013; Finaud et al. 2006). On the other hand, intensive acute exercise leads to metabolic acidosis, organism exhaustion, and increased oxidative stress which is suggested to contribute to attenuated vascular and endothelial function following acute exercise. Thus, it has been suggested that the reduction in FMD immediately after an acute exercise bout could be associated with the production of oxidative stress during acute exercise. Support to this hypothesis was given by the results that higher exercise intensities are associated with a greater oxidative stress as well as with an exaggerated decrease in FMD (Goto et al. 2003; Birk et al. 2013). Still, not all studies have reported a clear relationship between oxidative stress and FMD after acute exercise. In contrast to their earlier study, Johnson et al. have reported no relationship between post-exercise FMD and TBARS after a range of exercise intensities and duration (Johnson et al. 2012a, b). These inconsistent results had been explained by authors with the inability to measure oxidative stress at the site of FMD measurement (Johnson et al. 2012a, b). Moreover, none of the abovementioned studies did not investigated the potential contribution of BP increase to the oxidative stress changes following acute exercise, as well as theirs influence on vascular function in both macro- and microcirculation. In the present study, we have observed that at baseline, either the oxidative stress (TBARS) or the antioxidant capacity (FRAP) did not differ between the groups (Table 5), what is in concordance with study by Silvestro et al. (2006). Interestingly, FRAP was significantly increased after acute exercise in sedentary, but not in rowers (Table 5), while we have observed no change in TBARS after acute exercise in both groups. These findings suggest that increased antioxidative capacity may contribute to preserved (and even improved ACh-induced dilation) microvascular reactivity after acute exercise in sedentary men. Still, we did not find significant correlation between FRAP and SBP change, as well as between FRAP and microvascular reactivity change following acute exercise in study population. However, due to limited number of subjects involved in the present study, and considering that this is the first study investigating this issue in skin microvascular bed, definite association between antioxidant capacity, BP, and microvascular function in both young sedentary subjects and athletes should be investigated in further studies.

Limitation of the study

The choice of the skin microcirculation as a representative site and a model for microvascular function assessment in exercise could be considered as potential study limitation, due to prominently neural control of blood flow in skin microcirculation in rest (Roustit and Cracowski 2012). On the other hand, according to a number of recent studies, skin is readily accessible and provides an appropriate site to assess peripheral microvascular reactivity and to investigate vascular mechanisms in healthy subjects and in a variety of pathological states (Roustit and Cracowski 2012). It should be emphasized that tests used in the present study (PORH, ACh, and SNP-induced dilation) do not specifically assess distinct pathways (common reactivity tests are complex and involve several different), but provide an overall assessment of microvascular function. Although there are known and accepted limitations when using the LDF measurement, we employed well-established parameters, in concordance with our earlier studies and the literature (Cavka et al. 2013, 2015; Lenasi and Strucl 2008). Overall, LDF coupled to reactivity tests is widespread and accepted method for functional vascular research in the field of microcirculation. Other potential limitation of this present study is the technical inability to evaluate exercise intensity by measuring the peak VO_2, since that equipment is not available in our institutions. However, to overcome the lack of peak VO_2 measurement, we have measured serum lactate, arterial blood gases, and acid–base status which have shown that acute rowing exercise protocol was conducted consistently and led to complete exhaustion in all subjects.

In conclusion, the results of our study: (1) confirmed beneficial effects of regular exercise on vascular health and CV hemodynamic parameters in young healthy men; (2) demonstrated impaired endothelium-dependent microvascular reactivity immediately after acute exercise in rowers, but not in sedentary men; (3) implied that an improvement in microvascular function to a repeated stimulus (e.g., exercise training and consequent shear stress) can be induced even if this stimulus temporarily impairs microvascular function; and (4)

gave an insight into potential mechanisms of the interactions between acute exercise and microvascular function, involving BP, oxidative stress, and antioxidative capacity.

Acknowledgements We thank to Rowing Club Iktus Osijek and Croatian Rowing Club Vukovar for engagement in this study.

Funding This study was supported by earmarked funding grant of Faculty of Medicine Josip Juraj Strossmayer University of Osijek VIF2015-MEFOS-05 "Mechanisms involved in endothelial dysfunction development by acute high salt loading and acute exhausting exercise"; and Osijek-Baranja County project (2014–2016) "Influence of exercise on cardiovascular physiological parameters".

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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