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Vascular function and structure in veteran athletes following myocardial infarction

Short title: vasculature in post-MI athletes

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Abstract

Purpose. Despite athletes demonstrate a lower cardiovascular risk and superior vascular function compared to sedentary peers, they are not exempted from cardiac events (*i.e.*, myocardial infarction [MI]). The presence of a MI is associated with increased cardiovascular risk and impaired vascular function. We tested the hypothesis that lifelong exercise training in post-MI athletes, similar as in healthy controls, is associated with a superior peripheral vascular function and structure compared to a sedentary lifestyle in post-MI individuals.

Methods. We included 18 veteran (>20 years) athletes (ATH) and 18 sedentary controls (SED). To understand the impact of lifelong exercise training following MI, we included 20 veteran post-MI athletes (ATH+MI) and 19 sedentary post-MI controls (SED+MI). Participants underwent comprehensive assessment using vascular ultrasound (vascular stiffness, intima-media thickness (IMT), and endothelium (in)dependent mediated dilation). Lifetime Risk Score was calculated for a 30-year risk prediction of cardiovascular disease mortality of the participants.

Results. ATH demonstrated a lower vascular stiffness, and smaller femoral IMT compared to SED. Vascular function and structure did not differ between ATH+MI and SED+MI. ATH (4.0%±5.1) and ATH+MI (6.1%±3.7) had a significantly better lifetime risk score compared to their sedentary peers (SED: 6.9%±3.7 and SED+MI: 9.3%±4.8). ATH+MI had no secondary events *versus* two recurrent MI and six elective percutaneous coronary interventions within SED+MI ($P<0.05$).

Conclusion. Although veteran post-MI athletes did not have a superior peripheral vascular function and structure compared to their sedentary post-MI peers, benefits of lifelong exercise training in veteran post-MI athletes relate to a better cardiovascular risk profile and lower occurrence of secondary events.

Key Words: physical activity; endothelial function; cardiovascular risk; secondary prevention; lifelong exercise training

INTRODUCTION

Exercise training is an effective strategy to lower the risk for cardiovascular diseases (21, 32, 36). The marked cardio-protective effects of exercise are in part explained via traditional risk factors, such as a lower cholesterol level, blood pressure, and body mass index (19, 24). Additional benefits of regular exercise training may relate to a direct effect on the arterial wall, leading to remodeling of the arteries and improvement of endothelial function (35). For example, exercise training exerts its benefits on the artery wall through repeated elevation in blood flow and vascular laminar shear stress, which results in increased nitric oxide bioavailability, promotion of an antioxidant state, and improvement in vascular function and structure (8, 18).

Previous studies comparing athletes and sedentary controls consistently found that athletes have higher vascular compliance and better vascular wall structure compared to sedentary controls (33, 35). Younger athletes also typically demonstrate outward remodelling, as evidenced by larger conduit artery diameters and a larger resistance artery vascular bed (17). Some controversy is present around the effects of regular exercise training on endothelial function of conduit arteries measured with the flow-mediated dilation (FMD) (6, 15, 16, 27, 40). Variation in FMD between these studies may, at least partly, relate to structural remodelling in athletes (*i.e.*, larger diameter in athletes), that may contribute to a lower FMD (16). Exercise training is a widely accepted powerful strategy to lower risk for future cardiovascular events, which is at least partly related to improved vascular function (12).

Despite the vascular health benefits and reduction of cardiovascular risk with regular exercise (19, 24, 32, 36), veteran athletes are not exempted from acute coronary syndromes or myocardial infarction (22, 38). Previous work demonstrated that post-myocardial infarction (post-MI) patients have an impaired vascular function and structure compared to healthy peers (1, 10). Whether lifelong exercise training in post-MI patients may be associated with a preserved vascular function and structure is currently unknown. Therefore, we tested the hypothesis that lifelong exercise training in post-MI athletes, similar as in healthy controls, is associated with a superior peripheral vascular function and structure compared to a sedentary lifestyle in post-MI individuals.

METHODS

Participants

In total, we included 75 middle-aged men. We included 36 healthy, asymptomatic men who were divided over two groups: a) 18 veteran (>20 years) athletes (ATH) and b) 18 sedentary controls (SED). To understand the role of a MI on the impact of lifelong exercise, we included 39 participants who were divided into: a) 20 veteran (>20 years) post-MI athletes (ATH+MI) and b) 19 sedentary post-MI controls (SED+MI). Athletes performed regular moderate or vigorous endurance exercise training (*e.g.*, running or cycling) for ≥3.5 hours per week for ≥20 years. Sedentary individuals performed habitual physical activities for ≤2 hours per week for ≥20 years. Smokers, participants with diabetes mellitus type 1 or 2, and those not able to perform an incremental maximal cycling test were excluded from participation in our study. The Local Committee on Research Involving Human Subjects of the region Arnhem and Nijmegen approved the study and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. All participants gave their written informed consent.

Lifelong exercise history

We asked the participants about their lifelong exercise history over five age-periods: I) 20-29 years, II) 30-39 years, III) 40-49 years, IV) 50-59 years, and V) >60 years. Three queries were asked per period: 1) type of activity (*e.g.*, running, cycling, etc., or nothing), 2) exercise time (hours) per activity per week, and (3) self-perceived exercise intensity (light, moderate, or vigorous) per activity. Based on Ainsworth’s compendium of physical activities (2), we determined the corresponding metabolic equivalent of task (MET) score per activity. Based on the ACSM position stand (13), we defined moderate intensity activities between 3 and 5.9 MET, and vigorous intensity activities as ≥6 MET. Weekly exercise time was defined as the amount of time (in hours) spent on moderate and/or vigorous intensity exercise activities per week. The average weekly exercise time and intensity (*i.e.*, percentage of time spent on light, moderate, and vigorous intensity) were calculated over the last 20 years before study participation.

Experimental design

Participants visited our laboratory on two separate days during this cross-sectional study. On Day 1, participants were medically screened for eligibility, followed by an incremental maximal cycling test. On Day 2, participants underwent a comprehensive assessment of vascular function and structure using non-invasive echo-Doppler ultrasound techniques.

Experimental measures

Day 1: Screening + Incremental maximal cycling test

Screening. A physician medically screened participants by taking a detailed medical history, physical examination, and 12-lead electrocardiogram. Cardiac medical history of the post-MI participants was retrieved from their medical history reports, which encompassed the clinical diagnosis of the MI, details of the size and location of the MI, and treatment strategy. To gain insight in the cardiovascular risk profile of the participants, we calculated the Lifetime Risk Score (LRS) for a 30-year risk prediction of cardiovascular disease mortality (4). Parameters taken into account for the LRS were age, systolic blood pressure, total cholesterol, physical fitness level, and body mass index.

Incremental maximal cycling test. Peak oxygen uptake (VO_2peak, mLO_2/min/kg) of the participants was determined via an incremental maximal cycling test. Heart rate was continuously measured via a 12 lead-electrocardiogram. Oxygen uptake (VO_2 [ml/min]), carbon dioxide output (VCO_2

[ml/min]), and respiratory exchange ratio (RER) were measured via a gas analyser (CPET, Cosmed v9.1b, Rome, Italy). Lactate concentration (mmol/L) was measured via a capillary blood sample taken one-and-a-half minute after cessation of the test with the *Lactate Pro™ 2 (Arkray,* type LT-1730, Kyoto, Japan).

Day 2: Vascular function and structure

All measurements were performed according to recent guidelines for vascular assessment and in a temperature-controlled room (34) using a T3000 ultrasound system (Terason Teratech Corporation, Boston, United States) equipped with a 10-MHz 12L5 linear transducer. Continuous Doppler velocity was obtained using a position insonification angle of <60° (6). Participants followed a ≥6h fasting period, ≥18h abstinence from caffeine, alcohol, vitamin supplements, and performed no vigorous physical activity at least 24h before the test. Measurements began after a resting period in the supine position for at least 15 minutes (34). Subsequently, heart rate and blood pressure were manually assessed using a sphygmomanometer. Blood samples were obtained after the vascular measurements from the antecubital vein for the analysis of blood glucose, and traditional cardiovascular risk markers (cholesterol, HDL, LDL, triglycerides, and glycated hemoglobin [HbA1c]).

Brachial artery endothelium-dependent flow-mediated dilatation (FMD). The FMD (an index of endothelial function) of the brachial artery was measured by positioning the Echo-Doppler probe on the brachial artery. A pneumatic cuff (E20 rapid cuff inflator, Hokanson, Bellevue, United States) was placed on the right forearm, distally from the imaged artery. Diameter and flow velocity were recorded at the baseline during one-minute, followed by 5 minutes of ischemia by inflating the pneumatic cuff at 220 mmHg. Diameter and blood velocity recordings resumed 30 seconds before deflating the cuff and continued for 3 minutes thereafter, during the reperfusion (34).

Brachial artery conduit artery vasodilatory capacity (CADC). After a 20-minute resting period, the CADC (an index of arterial structure) was measured using the same equipment. The pneumatic cuff was inflated to 220 mmHg on the right upper arm, proximal from the imaged artery, for 5 minutes. Participants performed handgrip exercise from minute one until minute four (one-second contraction/one-second relaxation) at ~30 newton during the ischemic period. Diameter and blood velocity recordings resumed 30 seconds before deflating the cuff and continued for 3 minutes thereafter, to detect peak flow and peak diameter (26).

Brachial artery endothelium-independent dilatation. After another 20-minute rest, the vasodilator response to glyceryl trinitrate mediated vasodilatation (GTN; an index of vascular smooth muscle function) was measured. After recording baseline brachial artery diameter across 1-min, a single dose (400 µg) sublingual GTN (nitric oxide donor) was administered. Recording of diameter and blood velocity of the artery continuous 8 minute thereafter (14).

FMD, CADC, and GTN dilation were analyzed by custom-designed edge-detection and wall tracking software written in LabVIEW (LabVIEW 6.02, National Instruments, Austin, United States) as described elsewhere (5). Briefly, from B-mode a region of interest (ROI) was drawn to calibrate the artery diameter. Within this ROI a pixel-density algorithm automatically identified the vessel wall. For the calibration of the blood flow velocity another ROI was drawn around the Doppler waveform. Baseline diameter was calculated as the mean of data acquired during one-minute baseline recording, preceding cuff inflation. Peak diameter and peak of blood flow velocity was detected during three minutes of reperfusion. Brachial artery FMD, CADC, and GTN response were calculated as the relative difference in peak diameter and baseline diameter.

Pulse wave velocity: vascular stiffness

As an index for vascular stiffness, central and peripheral pulse wave velocity were measured using a three-lead electrocardiogram and an Echo-Doppler ultrasound machine (Waki Doppler, Atys Medical, Soucieu en Jarrest, France) at the left carotid artery, right common femoral artery, and radial artery. The distances were measured between sternal notch and site of measurement for the carotid artery and between radial artery and common femoral artery via the umbilicus (20). At least 10 cardiac cycles were recorded for analyses. Based on the interval between the R-wave on the electrocardiogram and onset of the Doppler waveform, central and peripheral pulse wave velocities were calculated in Matlab (MATLAB and Statistics Toolbox Release R2014, The MathWorks, Inc., Natick, United States).

Conduit artery intima-media thickness

Intima-media thickness (IMT) of the left common carotid, brachial, and superficial femoral artery were recorded using the same ultrasound machine. Image sequences of ≥10 seconds were recorded 1.5 to 2.5 cm distally of the bifurcation of the common carotid and superficial artery, while having the vessel in a longitudinal imaging plane. Diameter and wall thickness were collected from two distinct angles. Analysis was performed using custom-designed off-line edge-detection and wall-tracking software written in LabVIEW (LabVIEW 6.02, National Instruments, Austin, United States). This DICOM-based software is largely independent of investigator bias and has been previously described in detail (28, 29). Briefly, each recording was converted to a DICOM file at a frame rate of 30 Hz. Detection of the far wall media-adventitia interface was performed on every frame selected. The mean diameter and wall thickness were calculated by using the formula: (1/3 x systolic diameter or wall thickness) + (2/3 x diastolic diameter or wall thickness). Additionally, to correct for differences in vascular tone between measurements wall:lumen-ratio was calculated. All files were analyzed blinded by an independent researcher.

Power calculation and statistical analysis

Based on anticipated difference in %FMD between study groups of 3.5% with a SD of 2.4 (6, 10), a power of 90% and alpha 5% significance level, we calculated that 18 subjects per group should be included. To correct for possible drop-out, we included 20 subjects per study group.

Characteristics of the participants and vascular function and vascular structure were summarized with means and standard deviations or median and interquartile range (IQR), when appropriate. Categorical data were analysed using the *Fisher's exact* test. Parameters were checked for normality using a *Shapiro-Wilk* test. Non-normal data were Ln-transformed before the statistical analysis. Data that could not be transformed into Gaussian distribution were analysed using nonparametric tests. For aim 1 and 2, differences between veteran athletes and sedentary peers, either with or without a history of MI, were assessed using an independent *Student's t* or *Mann-Whitney U* test, when appropriate. All statistical analyses were performed using SPSS 21.0 software (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.). Statistical significance was assumed at $p<0.05$ (two-sided).

RESULTS

Veteran athletes *vs.* sedentary controls

ATH had a lower body weight and body mass index compared to SED, whilst no differences were present for age, height, and mean arterial pressure (Table 1). ATH performed significantly more exercise per week compared to SED (7.1 hours/weeks [5.8-11.9] *vs*. 0.5 hours/weeks [0.0-1.4], $P<0.01$), respectively. ATH performed most of their activities at a moderate intensity (66%), followed by vigorous (33%) and light intensity (1%). ATH reached a higher VO_2peak and power output during the incremental exercise test compared to SED (Table 1). ATH showed higher HDL and lower LDL and triglyceride levels compared to SED, whilst no differences were found for HbA1c and cholesterol (Table 1). As a consequence of these differences, ATH demonstrated a lower lifetime risk score compared to SED (Table 1). Participants with a positive family history of cardiovascular diseases did not differ between ATH (n=8, 44%) and SED (n=6, 33%), P=0.73.

Vascular function + structure. Whilst ATH and SED did not differ in brachial diameter and SR_{AUC}, the FMD was lower in ATH compared to SED (Table 2). We found no differences between ATH and SED for CADC or GTN response, whereas FMD/GTN ratio was significantly lower in ATH compared to SED (Table 2). ATH demonstrated a lower central and peripheral pulse wave velocity (*i.e.,* higher vascular compliance) compared to SED (Figure 1). No differences between groups were found for IMT, diameter, and wall:lumen-ratio of the carotid and brachial artery, whilst femoral artery IMT and wall:-lumen-ratio was smaller in ATH compared to SED (Table 2).

Veteran post-MI athletes *vs.* sedentary post-MI controls

ATH+MI had a lower body weight and body mass index compared to SED+MI (Table 3). ATH+MI performed significantly more exercise per week compared to SED+MI (5.7 hours/week [4.9-9.4] *vs*. 0.2 hours/week [0.0-1.2], P<0.01), respectively. ATH+MI performed most of their activities at a moderate intensity (63%), followed by vigorous (34%) and light intensity (3%). Intensity patterns did not differ between ATH and ATH+MI. ATH+MI reached a higher VO_2peak and power output during the incremental exercise test compared to SED+MI (Table 3). Cholesterol, HDL, and LDL levels did not differ between ATH+MI and SED+MI, but ATH+MI had lower triglyceride levels compared to SED+MI (Table 3). ATH+MI demonstrated a lower lifetime risk score compared to SED+MI (Table 3). Participants with a positive family history of cardiovascular diseases did not differ between ATH+MI (n=15, 75%) and SED+MI (n=15, 79%), P=1.00.

No differences were observed in extent and location of the MI between groups (Table 4). Treatment strategy (surgical and rehabilitation) did not differ between groups (Table 4). Six SED+MI needed an elective percutaneous coronary intervention (PCI) and two reported a recurrent MI, whereas none of the ATH+MI needed an elective PCI or reported a recurrent MI. The use of anticoagulants, lipid lowering and antihypertensive agents did not differ between groups, whilst fewer ATH+MI used ACE-inhibitors (Table 4).

Vascular function + structure. We found no significant differences between ATH+MI and SED+MI for brachial artery diameter, FMD, CADC, GTN, or GTN/FMD ratio (Table 5). We also found no differences between groups for central or peripheral pulse wave velocity (Figure 1). We found no significant differences in carotid, brachial and femoral artery IMT, diameter and wall:lumen-ratio between groups.

DISCUSSION

We present the following findings. First, in line with our hypothesis, some markers of vascular function (*i.e.*, pulse wave velocity) and structure (*i.e.*, femoral IMT and wall:lumen-ratio) were significantly better in asymptomatic veteran athletes compared to their sedentary peers, potentially contributing to the benefits of lifelong exercise. Second, in contrast with our hypothesis, we found no differences in vascular function or structure between veteran post-MI athletes and sedentary post-MI controls, which may be a consequence of pharmaceutical strategies. Third, veteran athletes with or without a history of MI had a significantly better cardiovascular risk profile compared to their sedentary peers. Furthermore, veteran post-MI athletes reported no secondary events, which contrasts the 8 events that occurred in the sedentary post-MI controls. Taken together, our findings indicate that veteran post-MI athletes do not have a superior vascular function and structure compared to their sedentary peers, whilst benefits of lifelong exercise relate to better cardiovascular risk profile and a lower occurrence in secondary events.

Impact of lifelong exercise on vascular function and structure: asymptomatic individuals

Our results support the hypothesis that benefits of lifelong exercise training go beyond traditional risk factors (19) and improves functional and structural aspects of the vascular system. For example, femoral IMT was significantly smaller in veteran athletes compared to sedentary controls, which is in line with previous studies that report that regular exercise training is associated with a smaller conduit artery wall thickness (25, 30). Related to functional characteristics of the vasculature, we found that veteran athletes have a higher central and peripheral vascular compliance compared to sedentary controls. This observation confirms previous studies which demonstrated that exercise training improves arterial compliance (3, 33).

Somewhat conflicting with the observations related to central and peripheral compliance, we observed a significantly lower FMD in veteran athletes compared to their sedentary peers. A previous study demonstrated that young healthy athletes had a lower FMD compared to their sedentary peers (5.1% *vs.* 6.0% respectively) (16). The authors suggested that the lower FMD in young athletes might relate to inherent structural changes in the artery and the interaction between artery structure and function (16). In the present study, however, baseline diameter did not differ between athletes and sedentary controls. It is therefore unlikely that structural differences explain the lower FMD responses among athletes. Also differences in smooth muscle cell sensitivity for nitric oxide cannot explain our results, since the GTN response did not differ between groups (ATH: 17.1%±6.7 *vs.* SED: 15.1±5.4, P=0.33). Alternatively, an interaction between vasodilator mechanisms and the autonomic sympathetic nervous system may contribute to a lower FMD in athletes (16). Athletes typically exhibit altered autonomic balance, which may contribute to attenuated conduit artery endothelium-dependent responses to elevation in shear (16). However, future studies are necessary to explore this hypothesis. Our findings indicate that endothelial flow-mediated vasodilation is lower in veteran athletes compared to their sedentary peers, whereas differences are not simply related to structural differences or smooth muscle sensitivity between groups.

Impact of lifelong exercise on vascular function and structure: post-MI individuals

Although a history of MI is associated with impairment in cardiovascular risk and vascular function, regular exercise training is known to improve cardiovascular risk and vascular function. However, in the present study no differences in vascular function and structure were found between veteran post-MI athletes and sedentary post-MI peers. A possible explanation for these unexpected observations may relate to the extent of the MI. However, we observed no differences in cardiac enzyme markers, location of the MI and duration since MI between ATH-MI and SED-MI. Alternatively, previous studies that revealed an impaired endothelial function in post-MI patients observed these effects within 1-12 months following MI (1, 10), whereas we measured the endothelial function after 7±5 years following MI. Since the endothelium recovers during the first months post-MI (39), our results may be partly explained by the long time since MI and/or bias in selecting ‘healthy’ post-MI patients given the long time since MI. Finally, prescription of medication after MI may contribute to our observations, especially since several cardiac medications directly improve endothelial function (23, 41). Antihypertensive agents most likely decrease in oxidative stress and increase nitric oxide bioavailability (23), whereas statins are associated with an improvement in endothelial function and FMD (41). Therefore, the combination of the prolonged post-MI period and use of cardiac medications may ameliorate endothelial function and structure in both post-MI groups. This might explain absence of differences in vascular function and structure between post-MI athletes and sedentary peers.

Despite the absence of differences in vascular function and marginal differences in cardiovascular risk factors, veteran post-MI athletes showed a better cardiovascular lifetime risk score compared to their sedentary post-MI peers. The higher cardiorespiratory fitness in athletes was the major contributor to the better risk score among athletes. Cardiorespiratory fitness is strongly related with reduced risk for morbidity and mortality as well it mitigates the risk of a second cardiac event (7, 9). Although, our study was not powered to investigate the relation between lifelong exercise and secondary events following MI, our results indicated that post-MI athletes reported fewer complications (elective PCI or recurrent MI) after the MI compared to their sedentary post-MI peers. Alternative benefits of regular exercise training may relate to an improvement in circulating hormones, endothelial progenitor cells, and/or (exercise) preconditioning of the vasculature (11, 31, 37). Future research is warranted to elucidate benefits of exercise training in more detail to close the ‘risk factor gap’ in cardiovascular disease (19).

LIMITATIONS

This study was inherent to some limitations. First, the cross-sectional design of our study makes it difficult to give detailed view of the development of vascular function and structure across time and study the impact of a MI. Second, post-MI participants were allowed to take their medication before the measurements due to ethical considerations. Medication usage might influence the results of the vasculature. However, since both post-MI groups took their medication, we believe it likely that the medication effect on the vasculature did not influenced our major observations regarding the comparison between post-MI groups. Finally, most of our veteran athletes performed primarily lower limb endurance exercises, such as running and cycling. Therefore, it is difficult to translate our results to other types of exercise training, especially since resistance exercise training may be of special interest in older populations.

CONCLUSION

The present study indicates that some markers of vascular function (*i.e.*, compliance) and structure (*i.e.,* femoral IMT and wall:lumen-ratio) were significantly better in asymptomatic veteran athletes compared to their sedentary peers. Whilst these observations are in line with previous reports and emphasise the benefits of regular exercise, we unexpectedly found no differences in vascular function and structure between veteran post-MI athletes and sedentary post-MI controls. Whilst medication use may contribute to these findings, regular exercise training in veteran post-MI athletes was still associated with significantly better cardiovascular risk profile and lower occurrence of secondary events compared to sedentary post-MI controls.

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Conflicts of Interest and Source of Funding

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The results of the present study do not constitute endorsement by ACSM. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

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FIGURES

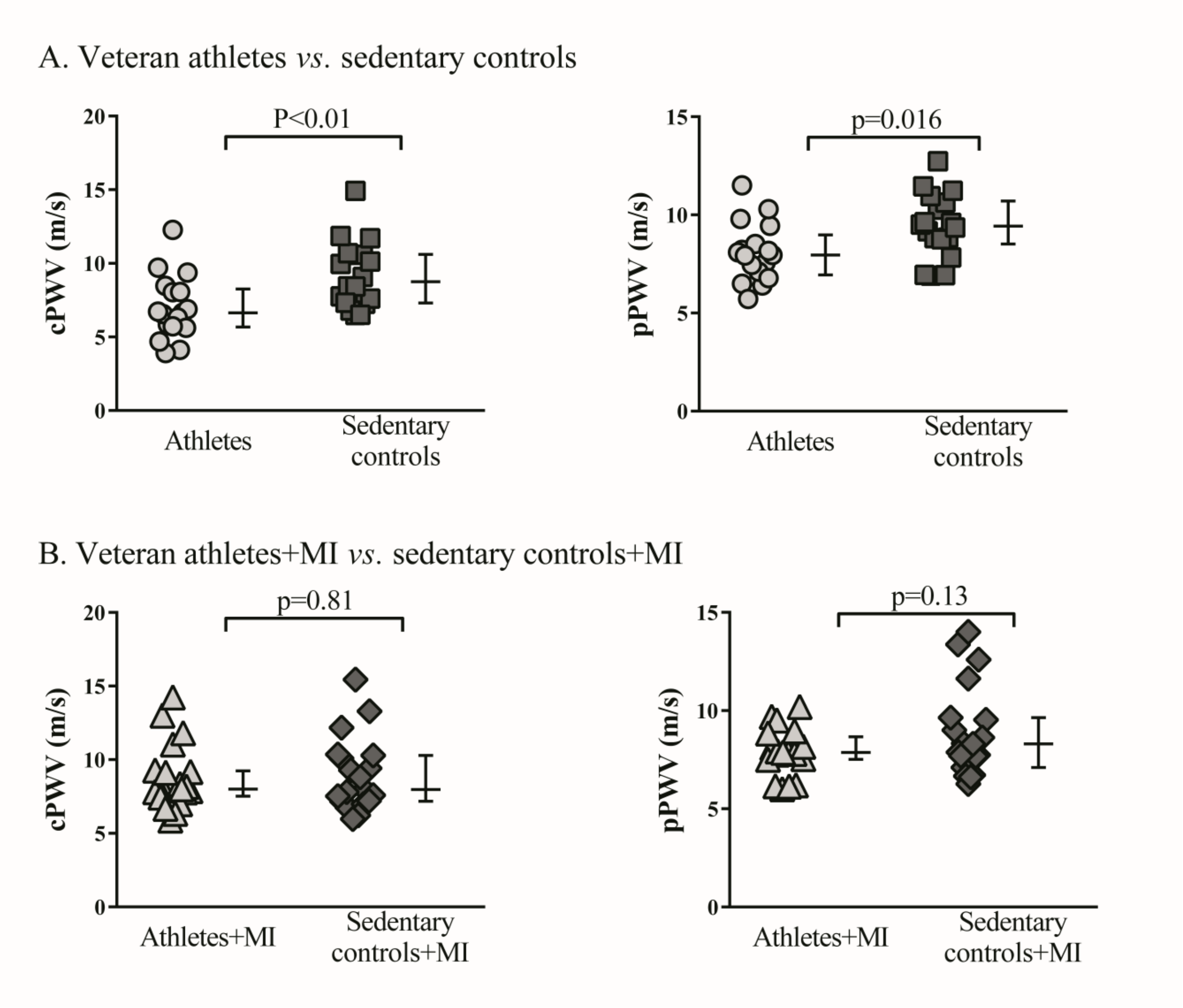

Figure 1. Arterial stiffness of (A) athletes (circles) vs. sedentary controls (squares) and (B) athletes+MI (triangles) and sedentary controls+MI (diamonds) of the central pulse wave velocity and peripheral pulse wave velocity. Athletes had lower central and peripheral pulse wave velocity, indicating that athletes had decreased vascular stiffness (*i.e.*, higher vascular compliance) compared to sedentary controls. No differences were observed in vascular stiffness between post-MI groups. Data is presented as median and interquartile range.

cPWV: central pulse wave velocity, pPWV: peripheral pulse wave velocity

Table 1. Characteristics of the athletes (ATH) *vs.* sedentary (SED) controls. Data is presented as mean and standard deviation or median and interquartile range. P-value refers to an *independent Student's t* test or *Mann-Whitney U* test.

	ATH *n*=18	SED *n*=18	***p* value**
CHARACTERISTICS			
Age (years)	61±7	58±7	0.29
Height (cm)	179±8	181±6	0.31
Weight (kg)	74±8	87±10	<0.01
Body Mass Index (kg/m^2)	23.6 (21.1-24.9)	26.7 (25.0-27.4)	<0.01
Mean arterial pressure (mmHg)	98 (90-106)	103 (93-107)	0.70
Systolic Blood Pressure (mmHg)	134 (122-142)	136 (124-146)	0.53
Diastolic Blood Pressure (mmHg)	84±10	84±10	0.92
Resting Heart Rate (beats/min)	52±6	64±11	<0.01
Exercise time (hours/week)	7.1 (5.8-11.9)	0.5 (0.0-1.4)	<0.01
INCREMENTAL EXERCISE TEST			
VO_2peak (mL/min/kg)	48.0±8.5	32.8±5.2	<0.01
Maximal heart rate (beats/min)	165±13	171±15	0.29
RER (ratio: VCO_2 / VO_2)	1.13 (1.06-1.17)	1.08 (1.05-1.14)	0.020
Lactate (mmol/L)	8.9 (11.6-12.3)	11.1 (9.4-12.8)	0.77
Power Output (W)	319±58	209±46	<0.01
CARDIOVASCULAR RISK PROFILE			
Lifetime risk score	4.0 (1.7-7.0)	6.9 (4.4-10.2)	<0.05
Glucose (mmol/L)	4.6 (4.4-5.0)	4.7 (4.4-4.9)	0.66
HbA1c (mmol/mol)	35.5 (34.4-38.3)	35.5 (35.5-38.3)	0.53
Cholesterol (mmol/L)	5.4±0.8	5.9±0.9	0.07
HDL (mmol/L)	1.8±0.3	1.4±0.3	<0.01
LDL (mmol/L)	3.3±0.8	4.0±0.8	<0.05
Triglycerides (mmol/L)	0.8 (0.7-1.2)	1.3 (1.0-2.4)	<0.01

RER: Respiratory Exchange Ratio; HbA1c: Glycated haemoglobin; HDL: High-density lipoprotein; LDL: low-density lipoprotein.

Table 2. Vascular function and structure of the athletes (ATH) and sedentary (SED) controls. Data is presented as mean and standard deviation or median and interquartile range (IQR). P-value refers to an *independent Student's t* test or *Mann-Whitney U* test.

	ATH *n*=18	SED *n*=18	***p* value**
VASCULAR FUNCTION			
FLOW MEDIATED DILATION			
Baseline diameter (mm)	4.3 (3.9-4.9)	4.4 (4.3-4.5)	0.65
Peak dilation (%)	3.8±1.7	6.4±2.8	<0.01
Shear Rate (AUC)	21177 (14041-31869)	18251 (12830-23160)	0.34
CONDUIT ARTERY VASODILATORY CAPACITY			
Baseline diameter (mm)	4.4±0.6	4.3±0.6	0.84
Peak dilation (%)	16.0±4.9	15.2±8.9	0.75
Shear Rate (AUC)	32380±10375	34566±13973	0.61
GLYCERYL TRINITRATE DILATATION			
Baseline diameter (mm)	4.2±0.6	4.4±0.8	0.43
Peak dilation (%)	17.1±6.7	15.1±5.4	0.33
FMD / GTN ratio	0.23 (0.15-0.30)	0.40 (0.25-0.69)	<0.01
VASCULAR STRUCTURE			
CAROTID ARTERY			
IMT (mm)	0.69 (0.58-0.81)	0.71 (0.65-0.86)	0.16
Diameter (mm)	6.4 (5.8-6.7)	6.8 (6.4-7.3)	0.07
wall:lumen-ratio	0.11 (0.09-0.13)	0.11 (0.10-0.12)	0.79
BRACHIAL ARTERY			
IMT (mm)	0.44±0.11	0.47±0.11	0.41
Diameter (mm)	4.0 (3.8-4.3)	4.4 (3.8-4.8)	0.13
wall:lumen-ratio	0.11 (0.09-0.13)	0.10 (0.09-0.11)	0.84
FEMORAL ARTERY			
IMT (mm)	0.59 (0.52-0.65)	0.64 (0.58-0.71)	<0.05
Diameter (mm)	7.3±1.4	6.9±0.7	0.23
wall:lumen-ratio	0.08 (0.06-0.09)	0.09 (0.08-0.11)	0.01

AUC: area under the curve; IMT: Intima-media thickness

Table 3. Characteristics of the post-MI athletes (ATH+MI) *vs.* sedentary post-MI (SED+MI) controls. Data is presented as mean and standard deviation or median and interquartile range. P-value refers to an *independent Student's t* test, *Mann-Whitney U* test, or *Fisher's exact* test.

	ATH+MI *n*=20	SED+MI *n*=19	***p* value**
CHARACTERISTICS			
Age (years)	60±6	61±5	0.44
Height (cm)	176±5	176±6	0.72
Weight (kg)	77±7	84±13	<0.05
Body Mass Index (kg/m^2)	24.5 (23.9-26.0)	26.8 (24.3-28.6)	<0.05
Mean arterial pressure (mmHg)	95 (93-100)	92 (88-101)	0.17
Systolic Blood Pressure (mmHg)	131 (126-142)	124 (114-136)	0.051
Diastolic Blood Pressure (mmHg)	79±9	77±11	0.49
Resting Heart rate (beats/min)	57±7	60±9	0.26
Exercise time (hours/week)	5.7 (4.9-9.4)	0.2 (0.0-1.2)	<0.01
Post-MI time before study participation (years)	5 (3-10)	7 (4-10)	0.73
INCREMENTAL EXERCISE TEST			
VO_2peak (mL/min/kg)	40.9±5.5	29.7±6.0	<0.01
Maximal heart rate (beats/min)	164±15	146±18	<0.01
RER (ratio: VCO_2 / VO_2)	1.10 (1.07-1.15)	1.08 (1.05-1.14)	0.31
Lactate (mmol/L)	10.5 (9.2-11.2)	11.5 (9.4-12.4)	0.19
Power Output (W)	274±40	190±49	<0.01
CARDIOVASCULAR RISK PROFILE			
Lifetime risk score	5.4 (3.3-8.6)	8.6 (6.2-12.8)	<0.05
Glucose (mmol/L)	4.6 (4.5-5.0)	4.8 (4.4-5.0)	0.95
HbA1c (mmol/mol)	36.6 (35.5-37.7)	37.7 (37.4-40.2)	<0.01
Cholesterol (mmol/L)	4.5±0.9	4.2±0.9	0.25
HDL (mmol/L)	1.6±0.4	1.4±0.3	0.08
LDL (mmol/L)	2.6±0.8	2.3±0.7	0.22
Triglycerides (mmol/L)	0.9 (0.8-1.1)	1.2 (1.0-2.0)	<0.05

RER: Respiratory Exchange Ratio; HbA1c: Glycated haemoglobin; HDL: High-density lipoprotein; LDL: low-density lipoprotein.

Table 4. Cardiac medical history data of post-MI athletes (ATH+MI) *vs.* sedentary post-MI (SED+MI) controls. P-value refers to an independent *Student's t, Mann-Whitney U, or Fisher's exact test* (two-sided). Data is presented as mean and standard deviation or median and interquartile range.

		ATH+MI		**SED+MI**	***p*-value**
Post-MI time before study participation (years)		5 (3-10)		7 (4-10)	0.73
ENZYME MARKERS*					
CK (u/L)	*n*=17	775 (251-2029)	*n*=17	871 (422-2467)	0.45
CREAT (umol/L)	*n*=14	87 (78-103)	*n*=16	89 (77-93)	0.70
AST (u/L)	*n*=14	38 (26-135)	*n*=15	84 (36-208)	0.22
LDH (u/L)	*n*=13	407 (335-638)	*n*=14	422 (178-537)	0.52
INFARCT LOCATION					
Anterior (n)		7 (35%)		10 (53%)	0.34
Inferior (n)		7 (35%)		8 (42%)	0.75
Non-STEMI (n)		6 (30%)		1 (5%)	0.09
TREATMENT*					
PCI (n [%])		18 (95%)		16 (94%)	1.00
Thrombolytic therapy (n [%])		1 (5%)		1 (6%)	
CARDIAC REHABILITATION					
Cardiac rehabilitation (n [%])		13 (65%)		11 (79%)	0.47
SECONDARY EVENTS					
Elective PCI (n)		0 (0%)		6 (32%)	<0.01
Recurrent MI (n)		0 (0%)		2 (11%)	0.23
MEDICATION					
Anticoagulant (n)		19 (95%)		19 (100%)	1.00
Anti-platelet (n)		18 (90%)		17 (89%)	1.00
Vitamin K antagonist (n)		1 (5%)		2 (11%)	0.61
Antihypertensive agents (n)		14 (70%)		18 (95%)	0.09
ACE-inhibitor (n)		5 (25%)		14 (74%)	<0.01
AT1-antagonist (n)		3 (15%)		3 (16%)	1.00
Beta-blocker (n)		8 (40%)		14 (74%)	0.05
Diuretic (n)		1 (5%)		4 (21%)	0.18
Calcium channel blockers (n)		1 (5%)		0 (0%)	1.00
Lipid lowering agents (n)		16 (80%)		19 (100%)	0.11
Statins (n)		16 (80%)		18 (95%)	0.34

*Based on a sub sample; hospital data not available

MI: myocardial infarction; PCI: Percutaneous coronary intervention; CK: Creatine kinase; CREAT: Creatinine; ASAT: Aspartate transaminase; LDH: Lactate dehydrogenase; Non-STEMI: non-ST elevation acute coronary syndrome; ACE: angiotensin converting enzyme; AT: angiotensin.

Table 5. Vascular function and structure of the post-MI athletes (ATH+MI) and sedentary post-MI (SED+MI) controls. Data is presented as mean and standard deviation or median and interquartile range (IQR). P-value refers to an *independent Student's t* test or *Mann-Whitney U* test.

	ATH+MI *n*=20	SED+MI *n*=19	***p* value**
VASCULAR FUNCTION			
FLOW MEDIATED DILATION			
Baseline diameter (mm)	4.5 (4.1-4.8)	4.2 (3.7-4.6)	0.42
Peak dilation (%)	4.0±1.9	5.3±3.3	0.16
Shear Rate (AUC)	16646 (9987-23701)	16837 (12395-19196)	0.89
CONDUIT ARTERY VASODILATORY CAPACITY			
Baseline diameter (mm)	4.4±0.5	4.3±0.6	0.77
Peak dilation (%)	14.0±6.2	13.1±5.2	0.65
Shear Rate (AUC)	31593±9054	31394±9546	0.95
GLYCERYL TRINITRATE DILATATION			
Baseline diameter (mm)	4.3±0.6	4.4±0.6	0.82
Peak dilation (%)	16.0±6.2	13.8±4.8	0.23
FMD / GTN ratio	0.23 (0.18-0.41)	0.35 (0.19-0.49)	0.19
VASCULAR STRUCTURE			
CAROTID ARTERY			
IMT (mm)	0.79 (0.64-0.86)	0.77 (0.69-0.80)	0.64
Diameter (mm)	6.9 (6.5-7.2)	6.5 (6.2-7.1)	0.17
wall:lumen-ratio	0.11 (0.09-0.13)	0.12 (0.10-0.13)	0.26
BRACHIAL ARTERY			
IMT (mm)	0.48±0.1	0.46±0.11	0.47
Diameter (mm)	4.2 (3.6-5.1)	4.2 (3.8-4.6)	0.69
wall:lumen-ratio	0.11 (0.10-0.12)	0.11 (0.10-0.12)	0.71
FEMORAL ARTERY			
IMT (mm)	0.70 (0.65-0.82)	0.65 (0.56-0.71)	0.05
Diameter (mm)	7.4±0.8	6.9±0.9	0.10
wall:lumen-ratio	0.10 (0.09-0.11)	0.10 (0.08-0.11)	0.60

AUC: area under the curve; IMT: Intima-media thickness