

Carotid morphofunctional responses to maximal aerobic exercise in patients with coronary artery disease

Respostas morfofuncionais da carótida ao exercício aeróbico máximo em pacientes com doença arterial coronariana

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ABSTRACT

Objective: To evaluate the acute effects of maximal aerobic exercise on carotid morphofunctional markers in patients with coronary artery disease (CAD) and healthy individuals. **Methods:** Patients with CAD (n = 8; 62.3 ± 4.3 years; 27.1 ± 3.1 kg/m²) who had completed phase II of a cardiac rehabilitation program (CRP) and healthy individuals (CONT; n = 5; 61.6 ± 3.5 years; 27.3 ± 3.2 kg/m²) were evaluated for carotid morphofunctional markers by ultrasonography before and after a cardiopulmonary exercise test (CPET). **Results:** Maximal oxygen uptake was lower in the CAD group compared with CONT (16.7 ± 3.5 vs. 24.0 ± 5.2 mL/kg/min; P = 0.01). Before CPET, no differences were observed between groups for systolic diameter (CAD: 6.05 ± 0.65 vs. CONT: 6.23 ± 0.20 mm; P = 0.6), diastolic diameter (CAD: 5.41 ± 0.73 vs. CONT: 5.73 ± 0.15 mm; P = 0.4), peak systolic velocity (CAD: 66.27 ± 12.24 vs. CONT: 61.33 ± 15.67 cm.s⁻¹; P = 0.4), or end-diastolic velocity (CAD: 20.63 ± 4.15 vs. CONT: 21.07 ± 3.97 cm.s⁻¹; P = 0.4). Carotid intima-media thickness (cIMT) was borderline higher in the CAD group (0.93 ± 0.23 vs. 0.71 ± 0.10 mm; P = 0.07). After CPET, both groups showed increases in systolic diameter (CAD: +0.26; CONT: +0.16 mm; P < 0.001), diastolic diameter (CAD: +0.31; CONT: +0.17 mm; P = 0.03), and peak systolic velocity (CAD: + 9.80; CONT: + 8.66 cm.s⁻¹; P = 0.04). End-diastolic velocity (CAD: + 0.60; CONT: -3.75 cm.s⁻¹; P = 0.4) and cIMT (CAD: -0.02; CONT: -0.01 mm; P = 0.1) did not change significantly in either group (P > 0.05). No between-group differences were observed in CPET-induced changes. **Conclusion:** Patients with CAD who had completed phase II of a cardiac rehabilitation program exhibited preserved vascular responses to maximal exercise

Keywords: physical exercise; coronary artery disease; atherosclerosis; endothelial dysfunction.

RESUMO

Objetivo: Avaliar os efeitos agudos do exercício aeróbico máximo sobre marcadores morfofuncionais da carótida em pacientes com doença arterial coronariana (DAC) e indivíduos saudáveis. **Métodos:** Pacientes com DAC (n = 8; 62,3 ± 4,3 anos; 27,1 ± 3,1 kg/m²), que completaram a fase II de um programa de reabilitação cardíaca (PRC), e indivíduos saudáveis (CONT; n = 5; 61,6 ± 3,5 anos; 27,3 ± 3,2 kg/m²) foram avaliados quanto aos marcadores morfofuncionais da carótida por ultrassonografia antes e após um teste cardiopulmonar de exercício (TCPE). **Resultados:** O consumo máximo de oxigênio foi menor em DAC em comparação com CONT (16,7 ± 3,5 vs. 24,0 ± 5,2 ml/kg/min; P = 0,01). Antes do TCPE, não foram observadas diferenças entre os grupos para diâmetro sistólico (DAC: 6,05 ± 0,65 vs. CONT: 6,23 ± 0,20 mm; P = 0,6), diâmetro diastólico (DAC: 5,41 ± 0,73 vs. CONT: 5,73 ± 0,15 mm; P = 0,4), velocidade de pico sistólico (DAC: 66,27 ± 12,24 vs. CONT: 61,33 ± 15,67 cm.s⁻¹; P = 0,4) e velocidade diastólica final (DAC: 20,63 ± 4,15 vs. CONT: 21,07 ± 3,97 cm.s⁻¹; P = 0,4). A espessura íntima-média carotídea (cIMT) apresentou valor limítrofe mais elevado em DAC (0,93 ± 0,23 vs. 0,71 ± 0,10 mm; P = 0,07). Após o TCPE, ambos os grupos aumentaram o diâmetro sistólico (DAC: +0,26; CONT: + 0,16 mm; P < 0,001), diâmetro diastólico (DAC: + 0,31; CONT: + 0,17 mm; P = 0,03) e velocidade de pico sistólico (DAC: + 9,80; CONT: + 8,66 cm.s⁻¹; P = 0,01). A velocidade diastólica final (DAC: -0,02; CONT: -3,75 cm.s⁻¹; P = 0,5) e a cIMT (DAC: -0,02; CONT: -0,01 mm; P = 0,1) não se alteraram significativamente em nenhum grupo (P > 0,05). Não foram observadas diferenças entre os grupos nas alterações induzidas pelo TCPE. **Conclusão:** Pacientes com DAC que concluíram a fase II do PRC apresentaram respostas vasculares preservadas ao exercício máximo.

Palavras-chave: exercício físico; doença arterial coronariana; aterosclerose; disfunção endotelial

Introduction

Coronary artery disease (CAD) is one of the leading causes of morbidity and mortality worldwide among cardiovascular diseases [1]. Traditional risk factors, such as diabetes, hypertension, dyslipidemia, and physical inactivity, significantly contribute to its development [2]. The CAD is the main clinical manifestation of atherosclerosis, a condition characterized by the progressive accumulation of lipid plaques in the walls of medium and large-sized arteries, impairing blood flow and potentially leading to severe cardiovascular events [3,4].

In addition to arterial obstruction, the chronic inflammatory process inherent to atherosclerosis and the resulting impairment of endothelial function are associated with systemic vascular dysfunction, including morphofunctional alterations of the carotid artery. Among these alterations, increases in carotid intima-media thickness (cIMT) stand out, along with changes in systolic and diastolic diameters, peak systolic velocity, and end-diastolic velocity [4–6].

These markers are widely used to assess arterial structure, blood flow, and hemodynamic changes, as well as to identify atherosclerotic plaques and significant stenosis. The cIMT is considered a subclinical biomarker of atherosclerosis, whereas peak systolic velocity is frequently used to detect hemodynamically relevant stenosis. These hemodynamic characteristics can be assessed using B-mode ultrasound with Doppler, and alterations in these markers are recognized as independent predictors of cardiovascular risk [7].

Evidence indicates that regular practice of multimodal physical exercise, including aerobic, resistance, and flexibility exercises, reduces the risk of cardiovascular complications [8]. In particular, aerobic training may induce vascular adaptations, with studies demonstrating benefits on cIMT in different populations, including healthy individuals [9,10].

Maximal aerobic exercise can be assessed during cardiopulmonary exercise testing (CPET), which allows the determination of maximal oxygen uptake ($\text{VO}_{2\text{max}}$), an important indicator of cardiorespiratory fitness. The CPET consists of a progressive, individualized protocol that gradually increases workload until maximal effort is reached, enabling the integrated analysis of cardiovascular, respiratory, and metabolic responses to exercise. Changes in vascular function, such as those observed in atherosclerosis, may be associated with reduced CPET performance and lower $\text{VO}_{2\text{max}}$ [11,12]. Despite the recognized benefits of physical training, studies investigating the acute responses of carotid morphofunctional markers to maximal aerobic exercise in patients with CAD are still scarce, especially following structured cardiac rehabilitation programs. Therefore, the aim of the present study was to evaluate the impact of maximal aerobic exercise on carotid morphofunctional markers in patients with CAD participating in a cardiac rehabilitation program and in healthy individuals, considering that maximal exercise induced by CPET may reveal relevant vascular responses in this population.

Methods

Participants

Eight patients with CAD were recruited from the Hospital Universitário Pedro Ernesto (HUPE), and five healthy volunteers without evidence of CAD (CONT) were randomly recruited. Both groups included individuals of both sexes aged 50-70 years with a body mass index (BMI) $< 30 \text{ kg/m}^2$. Due to the exploratory nature of the study and the availability of eligible patients during the data collection period, no formal sample size calculation was performed.

Patients with CAD were considered eligible if they had completed phase II of the HUPE cardiac rehabilitation program, which included individualized physical exercise, including both aerobic and resistance training, varying according to the patient's capacity, generally between 50% and 60% of maximum heart rate. CAD was defined as the presence of acute coronary syndrome (myocardial infarction with or without ST-segment elevation or unstable angina) or obstructive CAD, diagnosed by coronary angiography, in patients with stable angina.

Exclusion criteria for the CAD group included: a) diagnosis of heart failure, pulmonary disease, Chagas disease, or tuberculosis; b) regular physical exercise practice (≥ 3 days/week for 30 min) in the last 6 months; c) malnutrition (BMI $< 18.5 \text{ kg/m}^2$); d) smoking; and e) obesity (BMI $\geq 30 \text{ kg/m}^2$). Individuals in the CONT group were also excluded if they had a previous or current diagnosis of hypertension, ischemic disease, and/or diabetes mellitus, in addition to having a pacemaker or using antidepressant medication.

All participants received oral and written instructions regarding the risks and benefits of the study and signed an informed consent form. The study was registered at ClinicalTrials.gov (NCT06579807), approved by the HUPE Research Ethics Committee (CAAE 81718324.3.0000.5259), and conducted in accordance with the SPIRIT 2013 recommendations (Standard Protocol Items: Recommendations for Interventional Trials) [13].

Study design

This is an observational study with repeated measures, with assessments performed before and immediately after maximal exercise. The evaluations were conducted during a single visit to the Laboratory of Physical Activity and Health Promotion of the State University of Rio de Janeiro, always in the morning (8:00–11:00 a.m.), in a room with controlled temperature between 22–24°C and relative humidity between 60–70%. Participants were instructed to avoid physical activity, alcohol, and stimulants for 48 hours prior to the assessments.

Initially, medical history was assessed. After 20 minutes of rest in the supine position, a carotid ultrasound evaluation was performed. Subsequently, blood pressure (BP) was measured using an automatic digital device (Omron™, Matsusaka, Japan), along with resting heart rate (HR), prior to CPET. Thereafter, CPET was per-

med, and within 5 minutes after its completion, carotid ultrasound evaluation was repeated. Figure 1 illustrates the study's experimental design.

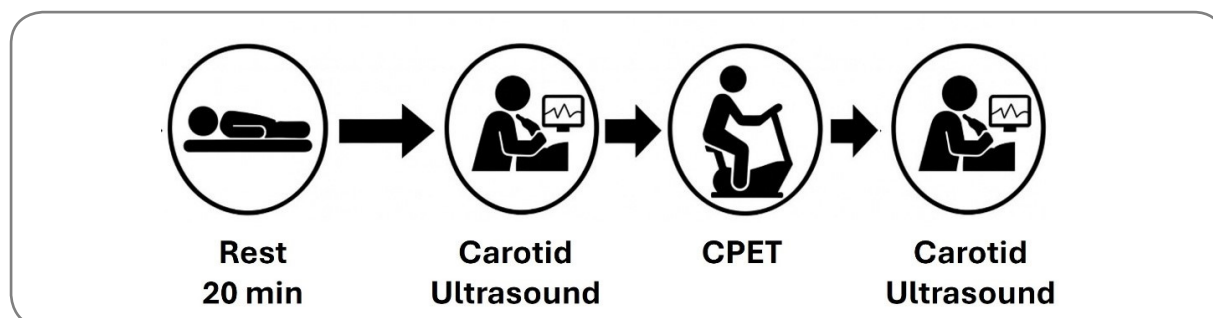


Figure 1 - Experimental design. CPET: cardiopulmonary exercise testing

Carotid artery morphofunctional assessment

Carotid intima-media thickness (cIMT) of the right common carotid artery was assessed with the participant in the supine position, with the head turned to the side (45°), using a portable ultrasound device (GE LOGIQ, General Electric Healthcare, Chicago, IL, USA) equipped with a 12L-RS linear probe (38 mm) operating at a frequency of 10 MHz.

Real-time B-mode ultrasound enabled longitudinal carotid artery imaging to confirm cIMT measurements. All measurements were performed by a trained technician and were taken 10 to 20 mm proximal to the carotid bifurcation (carotid bulb), focusing on the far wall, which provides better definition [7]. The cIMT values were manually measured as the mean of three measurements using ImageJ (NIH, USA).

B-mode Doppler ultrasound also allowed assessment of the systolic (SD) and diastolic (DD) diameters of the carotid artery. From Doppler analysis, peak systolic velocity (PSV) and end-diastolic velocity (EDV) were obtained using the Triplex ultrasound technique, which combines B-mode imaging with color Doppler and pulsed-wave Doppler spectral analysis. To improve velocity measurement accuracy, the insonation angle was set between 30° and 60° [7].

Cardiopulmonary exercise testing

The test was performed on an electromagnetically braked cycle ergometer (Inbramed®, Porto Alegre, Brazil) connected to a computer, using an individualized ramp protocol. The protocol was developed based on estimated $\text{VO}_{2\text{max}}$ values using a non-exercise model [14]. The cardiorespiratory fitness model was designed for individuals aged 18 to 80 years and can be applied to both men and women. Based on these values, the initial and final workload rates and the workload increment rates were calculated [15] using the metabolic equations proposed by the American College of Sports Medicine [16] to ensure the test duration ranged from 8 to 12 minutes.

During the CPET, gas exchange and ventilatory variables (VO_2 , VCO_2 , and VE) were collected breath-by-breath using a silicone mask (Hans Rudolph®, Shawnee, USA) connected to an Ultima Cardio₂ metabolic cart (Medical Graphics®, Saint Louis,

USA) [17]. Gas analyzers were calibrated before each test according to the manufacturer's instructions, using a certified standard gas mixture containing oxygen (17.01%) and carbon dioxide (5.00%), balanced with nitrogen (AGAR, Rio de Janeiro, RJ, Brazil). The accuracy of flow and volume measurements obtained by the pneumotachograph was verified using a 3-L calibration syringe (Hans Rudolph®, Kansas, USA).

Data were averaged over 30-s intervals, and $\text{VO}_{2\text{max}}$ was defined as the highest 30-s average obtained during the test. For the test to be considered maximal, participants were required to meet at least three of the following criteria [18]: a) volitional exhaustion; b) achievement of 90% of age-predicted maximal heart rate (HR) estimated by the equation $220 - \text{age}$ or absence of HR increase with increasing workload; c) presence of a VO_2 plateau (variation $< 2.1 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ between two consecutive workloads); d) respiratory exchange ratio (R) > 1.1 ; and e) Borg scale rating ≥ 17 .

Statistical analysis

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Results

Clinical and cardiorespiratory characteristics of the participants are presented in Table I. No significant differences were observed between the CAD and CONT groups regarding sex distribution, age, body mass index, resting systolic and diastolic blood pressure, or resting heart rate. In contrast, $\text{VO}_{2\text{max}}$ was significantly lower in the CAD group compared to the CONT group ($P = 0.01$). Patients in the CAD group were using statins (87.5%), antiplatelet agents (75%), beta-blockers (62.5%), and renin-angiotensin-aldosterone system inhibitors (75%). In the CONT group, only 20% of the volunteers were using statins, with no use of medications from other classes.

The carotid artery ultrasonographic variables assessed before and immediately after CPET are described in Table II. At pre-CPET, no differences were observed between groups in systolic and diastolic diameters, peak systolic velocity, or end-diastolic velocity. The cIMT was borderline higher in the CAD group than in the CONT group ($P = 0.07$).

After CPET, a similar increase was observed in both groups for carotid systolic and diastolic diameters, peak systolic velocity, and heart rate, with no differences between groups. End-diastolic velocity and cIMT did not show significant changes after CPET in either group.

Table I - Clinical characteristics of the CAD and CONT groups

	CAD (n = 8)	CONT (n = 5)	P
Men (n, %)	6 (75%)	3 (60%)	0.9
Age (years)	62.3 ± 4.3	61.6 ± 3.5	0.7
BMI (Kg/m ²)	27.1 ± 3.1	27.3 ± 3.2	0.9
VO _{2max} (ml/kg/min)	16.7 ± 3.5	24.0 ± 5.2	0.01
Resting SBP	122.7 ± 17.6	123.2 ± 11.5	0.9
Resting DBP	76.8 ± 9.9	76.2 ± 6.9	0.8
Resting HR	64.3 ± 17.1	63.0 ± 6.5	0.8

CAD = coronary artery disease patients; CONT = healthy individuals; VO_{2max} = maximal oxygen uptake; SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate

Table II - Mean (standard deviation) of carotid ultrasonographic variables pre- and post-CPET in patients with coronary artery disease (CAD) and healthy individuals (CONT)

		Pre- CPET	Post- CPET	P groups	P time
Systolic diameter (mm)					
	CAD	6.05±0.65	6.31±0.54	0.62	<0.001
	CONT	6.23±0.20	6.39±0.17		
Diastolic diameter (mm)					
	CAD	5.41±0.73	5.72±0.69	0.45	0.03
	CONT	5.73±0.15	5.90±0.38		
Peak systolic velocity (cm.s ⁻¹)					
	CAD	66.27±12.24	71.39±12.60	0.69	0.01
	CONT	61.33±15.67	69.99±10.96		
End-diastolic velocity (cm.s ⁻¹)					
	CAD	20.63±4.15	18.57±9.54	0.53	0.53
	CONT	21.07±3.97	17.32±2.54		
cIMT (mm)					
	CAD	0.93±0.23	0.91±0.22	0.07	0.13
	CONT	0.71±0.10	0.70±0.09		
Heart rate (bpm)					
	CAD	58.68±11.13	69.88±11.49	0.45	<0.001
	CONT	61.09±3.08	74.81±8.52		

CPET = cardiopulmonary exercise testing; cIMT = carotid intima-media thickness

Absolute changes (post-pre-CPET) in carotid ultrasonographic variables are presented in Figure 2. No significant differences were observed between the CAD and CONT groups in maximal exercise-induced responses for any of the evaluated variables.

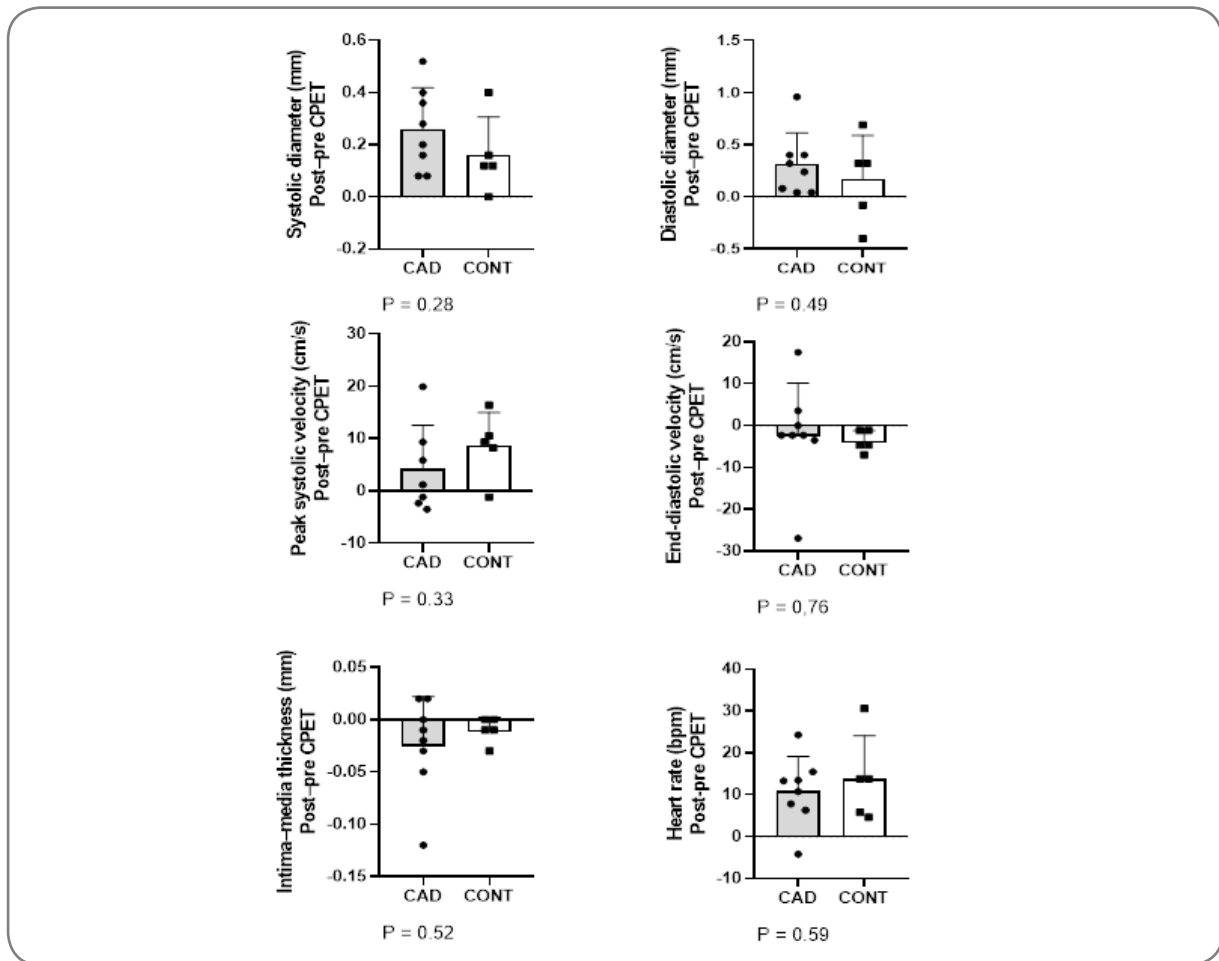


Figure 2 - Changes in carotid ultrasonographic variables with maximal aerobic exercise

Discussion

The main finding of the present study was that patients with CAD, after phase II of a cardiac rehabilitation program, exhibited carotid artery morphofunctional responses similar to those observed in healthy individuals during maximal aerobic exercise. Despite the lower VO_{2max} observed in the CAD group, the acute changes induced by CPET, characterized by increases in systolic and diastolic diameters and peak systolic velocity, occurred similarly between groups, suggesting preserved vascular responsiveness in this population.

The lower cardiorespiratory fitness observed in patients with CAD is consistent with previous evidence associating cardiovascular impairment and atherosclerosis with reduced VO_{2max} [12]. Studies have shown that structural and functional alterations of the cardiovascular system, including endothelial dysfunction and increased arterial stiffness, are associated with poorer cardiorespiratory performance [19,20]. However, our findings indicate that, despite overall functional impairment, the carotid artery's acute response to maximal exercise may be preserved in clinically stable patients participating in cardiac rehabilitation programs.

The cIMT showed borderline higher values in the CAD group than in the CONT group, although this difference was not statistically significant. The absence

of changes in cIMT after CPET was expected, as this marker reflects chronic structural adaptations of the arterial wall and is not readily influenced by acute changes induced by a single exercise session. Consistent evidence indicates that significant reductions in cIMT occur predominantly after long-term exercise interventions [9], generally exceeding six months, especially in individuals with elevated baseline values or atherosclerotic plaques [10]. Thus, the absence of cIMT changes in the present study does not negate the beneficial effects of exercise but reinforces the distinction between acute vascular adaptations and long-term structural remodeling.

On the other hand, the increases observed in carotid systolic and diastolic diameters, as well as in peak systolic velocity after the CPET, reflect acute hemodynamic adaptations to maximal exercise. These responses are associated with increases in cardiac output, pulse pressure, and arterial wall shear stress, which stimulate endothelium-dependent vasodilation mechanisms, as described in the literature [21,22]. The preservation of these responses in the CAD group suggests maintenance of vascular accommodation capacity during transient increases in hemodynamic demand, possibly favored by prior participation in a structured cardiac rehabilitation program.

Although parameters such as flow velocity and arterial diameter are widely used to assess vascular function, there are few studies specifically investigating their acute responses to maximal aerobic exercise in patients with CAD.

Previous studies in healthy individuals have shown that acute exercise may temporarily increase arterial stiffness and modify carotid hemodynamic parameters. Liu et al. [23] observed acute increases in elastic modulus and arterial diameter immediately after cycling exercise, with progressive attenuation of these responses over weeks of training. Similarly, Yuan et al. [24] reported a transient increase in carotid stiffness and elevation of the oscillatory shear index after high-intensity interval exercise. These changes are mainly attributed to abrupt increases in systolic blood pressure, heart rate, and pulsatile flow, which elevate shear stress and circumferential wall tension. In the present study, although arterial stiffness indices were not directly assessed, the increases observed in systolic and diastolic diameters and peak systolic velocity are consistent with an acute hemodynamic response to increased cardiac output and pulse pressure, as described in healthy individuals. Thus, the findings of the present study help fill this gap, indicating that maximal exercise is well tolerated by clinically stable patients after phase II of cardiac rehabilitation and can elicit vascular responses comparable to those observed in individuals without cardiovascular disease.

Some limitations should be considered. The main limitation is the small sample size, which limits the generalizability of the findings and prevents stratified analyses, such as comparisons between patients with and without atherosclerotic plaques. The absence of significant differences between groups should be interpreted with caution, considering the small sample size and the consequent low statistical power. In addition, ultrasonographic assessment was restricted to the right common carotid artery, without bilateral analysis or evaluation of other vascular territories.

Although the common carotid artery is widely used as a representative site for central vascular alterations, this approach limits broader inferences about systemic circulation and may mask heterogeneous responses across vascular beds. Future studies, including bilateral carotid assessment, larger samples, and stratification by degree of carotid atherosclerosis, are needed to further elucidate vascular responses to exercise in this population.

Conclusion

Maximal aerobic exercise increased carotid diameter and peak systolic velocity similarly in both patients with CAD and healthy individuals, with no changes in cIMT or end-diastolic velocity after CPET. Overall, the results suggest that, in patients with stable CAD after phase II of cardiac rehabilitation, the acute carotid vascular response to maximal exercise is preserved compared with healthy individuals, despite lower cardiorespiratory fitness.

Author affiliations

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Conflict of interests

The authors declare no conflict of interest.

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Author contributions

Concept and study design: Paz GA, Souza MGC, Borges JP; Data acquisition: Paz GA, Soares ALC, Santos TR, Costa CLF; Data analysis and interpretation: Paz GA, Soares ALC, Borges JP; Statistical analysis: Paz GA, Borges JP; Funding acquisition: Souza MGC, Borges JP; Manuscript writing: Paz GA, Souza MGC, Borges JP; Critical revision of the manuscript for important intellectual content: Paz GA, Soares ALC, Santos TR, Costa CLF, Meirelles CM, Gomes PSC, Souza MGC, Borges JP.

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