ARTIGO DE REVISÃO　　**REVIEW ARTICLE**

Peripheral arterial disease:
exclusion criteria for exercise training?

Doença arterial periférica:
critério de exclusão na reabilitação ao exercício?

Silvia Magalhães[1] ▮ Afonso Rocha[2] ▮ Ana Isabel Silva[2] ▮ Fernando Parada[3]

Resumo

Introdução: A Doença Arterial Periférica está fortemente associada a um risco cardiovascular aumentado e limita a capacidade para a marcha, contribuindo ainda mais para a diminuição da atividade física, descondicionamento cardiopulmonar e muscular periférico, um perfil cardiovascular mais adverso e agravamento do prognóstico da cardiomiopatia isquémica.

Objectivo: Determinar a prevalência da claudicação vascular no contexto da reabilitação cardíaca em ambiente hospitalar, e avaliar a sua influência nos resultados da reabilitação cardíaca, incluindo aspectos funcionais, psicossociais e de qualidade de vida.

População e Métodos: Estudo intervencional longitudinal dos doentes que completaram um programa de 2 meses de reabilitação cardíaca fase II, recrutados entre outubro de 2008 e março de 2010. Dados sociodemográficos, clínicos, laboratoriais, ecocardiográficos e da capacidade funcional foram colhidos nos processos clínicos. A qualidade de vida e a limitação da marcha foram avaliados pelo *Short-Form* 36 (SF-36) version 2 e *Walking Impairment Questionnaire* (WIQ), respectivamente. Os autores sumarizaram a capacidade de marcha usando um valor médio dos três componentes da WIQ e posteriormente categorizaram em 2 grupos: claudicantes (<80%) e não-claudicantes (≥80%).

Resultados: Um total de 126 doentes foi analisado, incluindo 47 (40,8%) com claudicação clínica. Excepto no género, com maior proporção de claudicantes no sexo masculino (p<0,05), não havia diferenças entre grupos na idade, nível educacional e estado profissional. A prevalência de hipertensão, diabetes, tabagismo, excesso de peso e obesidade abdominal foi maior no grupo claudicante. A incapacidade na marcha associou-se a maiores níveis de ansiedade, a sintomas depressivos, a diminuição da capacidade funcional e funcionalidade das componentes mentais e físicas da qualidade de vida associada à saúde, no início e no fim do programa. Ambos os grupos mostraram melhorias semelhantes nos parâmetros antropométricos, funcionais e de qualidade de vida.

Conclusões: Um programa de RC individualizado permite ganhos significativos na capacidade funcional e qualidade de vida associada à saúde, mesmo nos mais incapacitados pela DAP. O ajuste da intensidade e frequência das sessões de treino permitirá melhorias significativas e a adesão às recomendações da prevenção secundária da doença coronária neste subgrupo de doentes com patologia coronária.

Palavras-chave: Doença Arterial Periférica; Reabilitação Cardíaca.

Abstract

Background: Peripheral arterial disease (PAD) is strongly associated with increased cardiovascular risk and limits walking ability, further contributing to physical inactivity, cardiopulmonary and peripheral muscle deconditioning, worsened cardiovascular risk factor profile further compromising prognosis of ischemic cardiomiopathy.

(1) Resident of PMR; Alcoitão Rehabilitation Medicine Centre, Portugal.
(2) Clinical Assistant of PMR; Cardiac Rehabilitation Unit - Department of Physical Medicine and Rehabilitation, São João Hospital, Portugal.
(3) Director of Department of PMR, São João Hospital, Portugal.
E-mail: magalhaessilvia@gmail.com

Objective: Establish prevalence of vascular claudication in a hospital-based cardiac rehabilitation (CR) setting, and assess its influence on cardiac rehabilitation outcomes, including functional, psychosocial and quality of life aspects.

Methods and Subjects: Longitudinal interventional study of patients who completed a two-month phase II CR program, recruited between October 2008 and March 2010. Data on sociodemographic, clinical, laboratorial, echocardiographic and functional capacity was collected from clinical files. Quality of life and walking limitation were assessed by Short-Form 36 (SF-36) version 2 and the Walking Impairment Questionnaire (WIQ), respectively. The authors summarized walking ability using a mean value of the three components of the WIQ, and further categorized patients in two groups: claudicating (<80%) and non-claudicating (≥80%).

Results: A total of 126 patients were analyzed, including 47 (40,8%) with clinical claudication. Except for gender, with higher proportion of claudication in males (p<0,05), there were no difference between groups in age, level of education or professional status. Prevalence of hypertension, diabetes, tobacco consumption, overweight and abdominal obesity was higher in the claudicating group. Walking impairment was associated with higher levels of anxiety, depressive symptoms, lower functional capacity and functional impairment in both physical and mental dimensions of health-related quality of life, both at program entry and completion. Both groups showed similar improvements in anthropometric, functional and quality of life measures.

Conclusions: An individually tailored CRP allows for significant gains in functional capacity and health-related quality of life, even in those severely impaired by their peripheral arteriopathy. Adjustments in both intensity and volume of exercise training sessions will allow for significant improvements and compliance with recommendations for secondary prevention in coronary heart disease in this subset of the coronary heart disease patients.

Keywords: Peripheral Arterial Disease; Cardiac Rehabilitation.

Introduction

Peripheral arterial disease is a major component of a more systemic affection named atherosclerosis [1]. Due to the coexistence of coronary and cerebrovascular disease, there is also an increased risk of myocardial infarction, stroke and cardiovascular death in patients with peripheral arterial disease [2]. Although frequently asymptomatic, it can cause severe calf pain during progressively shorter walks alleviating only with rest (intermittent claudication), further contributing to a sedentary lifestyle and aggravating the general unfavorable cardiovascular risk profile [1,3]. Due to the walking impairment, claudicating patients develop progressive difficulties on daily life activities, resulting in reduced quality of life [4].

Besides general lifestyle measures and medical therapy, exercise has recently received increase attention as an effective therapeutic measure, acting through several physiological metabolic, vascular and skeletal muscle such as collateral vessels formation, vasodilatation by nitric oxide activity increase, oxidative metabolism improvement, among others [5]. Exercise has been shown to improve distance to both initial claudication and maximal pain, thereby improving pain free walking ability and absolute walking ability [6]. Supervised exercise training and the alternative model of exercise of "test in-train out" have greater impact than non-supervised exercise [1,7]. Associated to the physical gains, there are important achievements in performance of daily activities, not only in symptomatic patients, but also in asymptomatic ones [8]. The benefits of a supervised program extend beyond the duration of the program and should be followed by an individually tailored home exercise program in all patients [1].

Methods

A longitudinal prospective cohort study involving 126 patients referred to the Cardiac Rehabilitation Unit within three months after suffering an acute coronary event and who completed a phase II cardiac rehabilitation program. Recruitment period was between October 2008 and March 2010. This program included an average of 16 biweekly, 60 minute duration exercise training sessions consisting of 45 minutes of aerobic training, with an intensity targeting 50-70% heart rate reserve (based on the admission cardiac stress test according to the Karvonen method [9]) and a Borg effort perception of 11-13/20, followed by 10-15 minutes strength training involving 2 sets of 10-15 repetitions (50-70% of 1 RM), including major muscle groups of upper (pectoris major, latissimus dorsi, deltoid, biceps and triceps) and lower (quadriceps, hamstrings) limbs. Whenever patients could not achieve the desired intensity goals due to significant claudication we followed the general guidelines with 20-35 minutes of intermittent walking (exercise-rest-exercise) in treadmill with initial

speed set to elicit claudication symptoms within 3-5 minutes and maintained until moderate to severe claudication occurred (analogic visual scale: ≥7/10cm), followed by decrease in speed or full stop until symptoms resolve [5].

Additionally patients were offered psycho-educational and behavioral intervention including six group educational sessions with a trained psychologist dealing with cardiovascular risk factors, nutrition, coping strategies, stress management, tobacco cessation and sexual function. Individualized counseling and intervention was also available for active smokers willing to quite.

Data on sociodemographic, clinical, laboratorial, echocardiographic and functional capacity was collected from clinical files. Quality of life and walking limitation were assessed by Short-Form 36 (SF-36) version 2 and the Walking Impairment Questionnaire (WIQ), respectively. The authors summarized walking ability using a mean value of the three components of the WIQ, and further categorized patients in two groups: claudicating (<80%) and non-claudicating (≥80%). Statistical analysis was made with SPSS (Statistical Package for the Social Sciences).

Results

A total of 126 patients were evaluated, consisting mostly of men 115(91,3%) submitted to percutaneous revascularization procedures 106 (84,1%). Clinical claudication was present in 47(40,8%) patients. No between-group differences were detected in sociodemographic characteristics (Table 1).

Claudicating patients showed an overall worse cardiovascular risk profile, including higher proportions of dyslipidemia, diabetes, excessive weight, hypertension and active smoking (Table 1). No differences in acute coronary syndrome severity, as assessed by levels of myocardial necrosis markers (Table 1), or angiographic extent of coronary artery disease were detected (Table 2). The majority of the

Table 1 - Sociodemographic, cardiovascular risk factors and biochemical data analysis.

	Total sample (n=126)	Claudicating patients (n=56)	Non-claudicating patients (n=70)	*p*
Sociodemographic Data				
Male gender, n (%)	115 (91,3)	47 (40,8)	68 (59,1)	0,01
Age (years), mean (SD)	53,3 (±9,0)	53,9 (±9,0)	52,7 (±9,1)	0,45
Level education (years), P50(P25-P75)	6 (4-11)	4 (4-9)	6 (4-11,5)	0,28
CDV Risk Factors				
Previous history of CHD, n (%)	22 (17,5)	11 (19,6)	11 (15,7)	0,64
Family history of CHD, n (%)	35 (27,8)	17 (30,4)	18 (25,7)	0,69
Dyslipidemia, n (%)	82 (65,1)	39 (69,6)	43 (61,4)	0,35
Hypertension, n (%)	52 (41,3)	28 (50,0)	24 (34,3)	0,10
Diabetes mellitus, n (%)	21 (16,7)	14 (25,0)	7 (10,0)	0,03
Overweight (BMI≥ 25Kg/m^2), n (%)	86 (68,2)	41 (73,2)	45 (64,3)	0,19
Active smokers, n (%)	76 (60,3)	36 (64)	40 (57,1)	> 0,2
Biochemical Data				
Maximum Troponin I (pg/L), mean (SD)	37,0 (± 69,8)	44,9 (± 98,5)	29,4 (±38,9)	0,98
Maximum BNP (pg/mL), mean (SD)	168,9 (± 177,4)	178,9 (±206,8)	156,4 (±155,5)	0,87
Mioglobin (pg/L), mean (SD)	551,1 (± 1009,8)	528,9 (± 1169,6)	504,3 (± 902,1)	0,98

Table 2 - Angiographic characterization of coronary artery disease extension.

| Coronariograph	Total sample (n=126)	Claudicating patients (n=56)	Non-claudicating patients (n=70)	*p*
Vessel obstruction < 60%, n (%)	4 (3,3)	1 (1,9)	3 (4,3)	
1-vessel disease, n (%)	70 (56,9)	33 (62,3)	37 (52,9)	0,4
2-vessels disease, n (%)	34 (27,6)	15 (28,3)	19 (27,1)	
3-vessels disease, n (%)	15 (12,2)	4 (7,5)	11 (15,7)	

Table 3 - Rehabilitation effects on anxious and depressive symptoms.

	Non-claudicating			Claudicating		
	Baseline [P50(P25-P75)]	Mean difference [mean(SD)]	p*	Baseline [P50(P25-P75)]	Mean difference [mean(SD)]	p*
HADS-anxiety	5,5 (2,0 – 12,0)	-0,7 (5,1)	0,36	4,0 (1,0-7,0)	-1,25 (0,5)	<0,05
HADS-depression	6,5 (2,7-10,2)	+0,2 (4,8)	0,73	4,0 (1,0-7,0)	-0,47 (3,0)	0,44

NOTE: HADS scale was available: at baseline (N=93; 42 non-claudicating and 31 claudicating patients) and at program completion (N=74; 51 non-claudicating and 43 claudicating patients)

Table 4 - Functional capacity and physical activity evolution with a CR program.

Functional capacity and physical activity	Claudicating patients (n=56)		Non-claudicating patients (n=70)	
	Baseline-post difference	p	Baseline-post difference	p
METS (max), mean (SD)	3,3 (±1,5)	< 0,001	4,1 (±1,6)	< 0,001
IPAQ (METS-min/week), mean (SD)	377 (±1709)	0,12	826,4 (±1810)	0,001
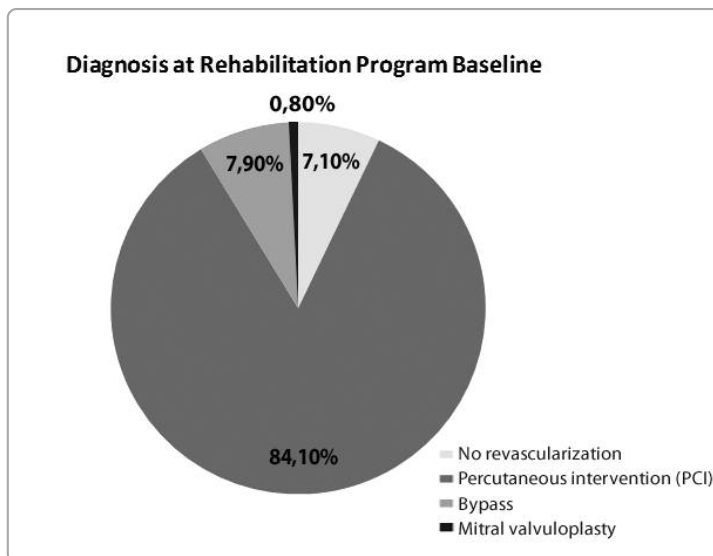
Graphic 1 - Diagnosis at rehabilitation program admission

126 patients was submitted to percutaneous intervention - Graphic 1.

Patients completed a mean of 15,2 (4,6) exercise sessions and 4,7 (2,1) educational sessions. Claudicating group showed important improvement in anxiety symptoms (Table 3).

Claudicating patients showed worse overall quality of life than their non-claudicating counterparts, both at program initiation and completion (Table 4). Cardiac rehabilitation resulted in significant improvements in physical and mental domains of quality of health perception in either group (Table 5), with higher relative improvement in those more severely impaired (claudicating).

Discussion

Significant peripheral arterial disease may become clinically relevant, impacting on functional, psychosocial and quality of life dimensions. The inability to maintain walking due to intermittent claudication results in decrease in global physical activity, cardiopulmonary and muscular deconditioning and worsening of cardiovascular risk factor profile. All patients might benefit from secondary prevention measures adopted in a cardiac rehabilitation setting, and exercise training individually tailored to patient's characteristics, is an adjunct tool to the global improvement in cardiovascular risk factor burden and functional capacity.

Concomitant peripheral vascular disease is a marker for more advanced atherosclerotic involvement of the vascular bed, and its presence and severity directly correlate with baseline risk factor profile. We did confirm these findings and also showed that there were no significant differences in the degree of angiographic coronary vessel disease or severity of index coronary event. The higher proportion of ST-segment elevation myocardial infarction, with more extensive myocardial damage and higher levels of

Table 5 - Characterization of SF-36 domains at admission and after CR program completion.

SF-36 Domains	Claudicating patients (n=56)			Non-claudicating patients (n=70)		
	Baseline	PostCRP-baseline MD	p	Baseline	PostCRP-baseline MD	p
Physical functioning, mean (SD)	42,2 (± 9,7)	+4,9 (± 7,9)	< 0,01	48,8 (± 6,6)	+3,9 (± 5,0)	< 0,01
Role-physical, mean (SD)	38,3 (± 11,1)	+6,1 (± 10,8)	< 0,01	45,0 (± 11,5)	+2,9 (± 10,9)	0,03
Bodily pain, mean (SD)	43,0 (±12,5)	+6,3 (± 13,9)	0,001	51,4 (± 11,8)	+3,2 (± 10,5)	0,01
General health, mean (SD)	40,9 (± 9,6)	+0,08 (± 8,9)	0,94	44,9 (± 7,8)	+1,9 (± 6,5)	0,02
Vitality, mean (SD)	42,9 (± 12,4)	+6,3 (± 11,3)	< 0,01	52,0 (± 12,4)	+3,6 (± 10,5)	< 0,01
Social functioning, mean (SD)	38,3 (±12,5)	+5,9 (± 13,1)	0,001	47,3 (± 10,5)	+1,7 (± 9,3)	0,13
Role-emotional, mean (SD)	37,2 (± 15,1)	+3,5 (± 11,7)	0,03	46,0 (± 11,3)	+0,8 (± 14,1)	0,60
Mental health, mean (SD)	39,9 (± 15,3)	+2,6 (± 10,9)	0,08	47,1 (±12,7)	+3,6 (± 13,4)	0,03
Summary physical domain, mean (SD)	42,7 (± 8,0)	+5,2 (± 7,9)	< 0,01	48,2 (± 7,2)	+3,4 (± 6,0)	< 0,01
Summary mental domain, mean (SD)	39,0 (± 14,6)	+3,2 (± 10,7)	0,03	48,0 (± 10,5)	+1,3 (± 10,5)	0,30

myocardial necrosis biomarkers, in younger patients with less-advanced atherosclerotic disease, might explain the lack of association between claudication and extent of coronary disease.

Claudication strongly impacts both physical and emotional dimensions of quality of life, interfering with patients self-perception, self-esteem and social participation [10]. Despite lower levels of quality of life at the beginning and completion of an exercise-based cardiac rehabilitation program, claudicating patients showed similar relative improvements to non-claudicating patients, advocating that this should not be regarded as an exclusion criterion for the exercise program. Furthermore, progression in physical capacity allowed claudicating patients to increase their maintenance physical activity, improving cardiometabolic risk factor control.

This study has several limitations. Firstly, our definition of claudication relied only in subjective questionnaire of walking ability with no confirmation or quantification of the degree of peripheral vascular disease through objective measurements such as ankle-brachial index or Doppler echocardiography. Hence, there is a high possibility for differential mis-classification (considering claudication when limitation is of non-vascular origin), affecting internal validity of our findings. Since more severe claudication is often regarded as an exclusion criterion for exercise programs and no randomization was performed, selection bias is probable and therefore our results should be interpreted cautiously and not generalized to other population groups.

Furthermore, we did not quantify the amount of physical activity performed outside the training sessions (both leisure and exercise intended) and, although we did not find significant differences in beta-blocker use between the two groups, other pharmacological options were not considered in this analysis.

Conclusion

Peripheral arterial disease is a major component of the atherosclerotic syndrome and has a high implication in the functional and mental status of patients. An individually tailored CRP allows for significant gains in functional capacity and health-related quality of life, even in those severely impaired by their peripheral arteriopathy, and should not be considered an exclusion criteria for exercise training. Adjustments in both intensity and volume of exercise training sessions will allow for significant improvements and compliance with recommendations for secondary prevention in coronary heart disease.

Referências / *References*:

1. Salameh MJ, Ratchford EV. Update on peripheral arterial disease andclaudication rehabilitation. Phys Med Rehabil Clin N Am. 2009, 20: 627-656

2. Albuquerque RR. A doença arterial periférica no idoso. Geriatria. 2007, 3(15): 5-12

3. White C. Intermitent claudication. N Engl J Med. 2007, 356; (12): 1241-50

4. Crowther RG, Spinks WL, Leicht AS, Sangla K, Quigley F, Golledge J. Effects of a long-term exercise program on lower limb mobility, physiological responses, walking performance and physical activity levels in patients with peripheral arterial disease. J Vasc Surg. 2008; 47:303-9

5. Stewart KJ, Hiatt WR, Regensteiner JG, Hirsch AT. Exercise training for claudication. N Engl J Med. 2002, 347 (24): 1941-51

6. Menard JR, Smith HE, Riebe D, Braun C, Blissmer B, Patterson RB. Long-term results of peripheral arterial disease rehabilitation. J Vasc Surg. 2004; 39:1186-92

7. Manfredini F, Malagoni AM, Mascoli F, Mandini S, Taddia MC, Basaglia N, et al. Training rather than walking – The Test In- Train Out program for home-based rehabilitation in peripheral arteriopathy. Circ J. 2008; 72: 946-952

8. Mcdermott MM, Ades P, Guralnik JM, Dyer A, Ferrucci L, Liu K, et al. Treadmill exercise and resistance training in patients with peripheral arterial disease with and without intermittent claudication. JAMA. 2009; 301(2):165-174

9. Braddom R, Buschbacher R, Chan L, Kowalske KJ, Laskowski ER, Matthews DJ, editors. Physical Medicine & Rehabilitation. New York: Elsevier; 2007

10. Menard JR, Smith HE, Riebe D, Braun CM, Blissmer B, Patterson RB. Long-term results of peripheral arterial disease rehabilitation. J Vasc Surg. 2004; 39:1186-92