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Brazilian Journal of Exercise Physiology

Systematic review

Comparison of moderate-intensity continuous exercise with highintensity interval exercise in the variables of the cardiopulmonary test in patients with coronary artery disease: a meta-analysis

Comparação do exercício de moderada intensidade contínuo com exercício intervalado de alta intensidade nas variáveis do teste cardiopulmonar em pacientes com doença arterial coronariana: uma metanálise

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ABSTRACT

Background: The objective of Cardiovascular rehabilitation is reducing the risks of mortality with two training modalities: high intensity interval training (HIIT) and moderate continuous intensity training (MIT). The exercise prescription is performed by cardiopulmonary exercise test. There are differences about which one is the best training for this patient. AIM: To compare the effects of HIIT and moderate continuous training on the variables on the CPX test in patients with Coronary Artery Disease. Method: It is a systematic review of randomized clinical trials on Coronary Artery Disease. This study was registred on PROSPERO. The search was executed on the data base: MEDLINE, Scielo, LILACS e PEDro. The selection of studies was made in two phases: Reading of title and abstract and reading of full article. The data extraction was performed by the transcription of information. The methodological quality was evaluated by the PEDro scale and the risk of bias scale. The statistical analyses was made by the software Rstudio by the random effect model and was aplied the Q-Cochran test for evaluate the heterogenity statistical. Results: Was included 10 clinical trial. The methodological quality evaluated by PEDro scale generated the score four through nine and the risk bias scale found low risk of bias. For the variables: $VO_{2 peak}$ (p=0,04), Anaero-bic Threshold (p=0,05), HR _{max} (p=0,01), SBP _{max} (p=0,02), the HIIT show be better. There's no difference between the modalities for the others variables. **Conclusion**: The HIIT showed the best modality of training for the incrasse of VO_{2 max}, Ventilatory Threshold, SBP max e HR max.

Keywords: Coronary heart disease, High Intensity Interval Training, Exercise.

RESUMO

Fundamento: a reabilitação cardiovascular tem o objetivo de reduzir os riscos de mortalidade e dentro dessa intervenção há duas modalidades de treino: hiit e o mit, a prescrição de exercício é realizado pelo teste cardiopulmonar. Há divergência, sobre qual a melhor modalidade de exercício para este paciente. **Objetivo:** comparar os efeitos do hiit com os do exercício contínuo nos parâmetros do teste cardiopulmonar em pacientes com doença arterial coronariana. **Método:** Trata-se de uma revisão sistemática de ensaios clínicos randomizados em coronariopatas. Registrou-se o estudo na PROSPERO. Foram realizadas as buscas nas bases de dados MEDLINE, Scielo, LILACS e PEDro. A seleção de estudos foi realizada em duas etapas: leitura de título e resumo e leitura do artigo na integra. A extra40

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ção dos dados foi realizada pela transcrição das informações. A qualidade metodológica foi avaliada pela escala PEDro e escala risco de viés. A análise estatística foi feita com o programa Rstudio pelo modelo randômico e foram aplicados o teste Q-Cochran para avaliar a heterogeneidade estatística. **Resultados:** foram incluídos 10 ensaios clínicos. A qualidade metodológica avaliada pela PEDro gerou notas de quatro a nove, e a escala risco de viés detectou baixo risco de viés. Para as variáveis: VO_{2 pico} (p=0,04), limiar ventilatório (p=0,05), FC_{máx} (p=0,01), PAS_{máx} (p=0,02), o HIIT mostrou ser mais eficaz. As demais variáveis não apresentaram diferença entre as duas modalidades. **Conclusão:** o hiit mostrou ser a modalidade treinamento mais eficaz para o incremento do VO_{2 máx}, limiar ventilatório, PAS_{máx} e FC_{máx}.

Palavras-chave: Doença Arterial Coronariana, Treinamento Intervalado de Alta Intensidade, Exercício.

Introduction

The Coronary Artery Disease (CAD) is one of the leading causes of death in the world [1,2]. Currently in the Brazilian scenario, there has been an increase in the number of deaths from cardiovascular diseases (CVD) in recent years; in 2017 alone, an estimated 383,961 deaths were caused by the disease [3]. The increase in the number of deaths in the last five years directly affected the country's economy with the increase in the number of surgical hospitalization, consultations with the cardiologists, costs with medicine and social security. In this context were created strategies for reduction of those costs [4].

The cardiovascular rehabilitation has the aim to increase the functional capacity and quality of life beyond reducing the risk of morbidity and mortality and hospitalization [5-7]. The cardiopulmonary exercise test (CPX test) is the gold standard method for functional evaluation and to determine the CD severity. In addition, data extracted from the test are useful to guide the clinical prescription of exercise in cardiovascular rehabilitation. Among the most relevant are Heart Rate Maximum (HR max), Maximum oxygen consumption (VO₂ max) and Ventilatory Threshold (VT) [8-12].

Among the types of aerobic training in the cardiac rehabilitation program the high intensity interval training (HIIT) and moderate continuous intensity training (MIT) are used. The interval training is executed with periods of high intensity (70% of VO_{2 max}) interleaved by periods of moderate or low intensity (25% a 40% do VO_{2 max}) [13]. The continuous training consists in a constant effort and is executed with moderate intensity in stable state [14-16].

The professionals have divergent opinions on which is the best modality of exercise for the treatment of CAD, and there is a gap about the effect of HIIT and MIT in the other variables evaluated on the cardiopulmonary exercise test. Based on this fact, it is necessary to synthesize the existing results in the literature to allow its extrapolation to other populations and encourage new clinical research. Thus, the aim of this study is to compare the effects of HIIT and moderate continuous training on the variables of the CPX test in patients with coronary artery disease.

Methods

This is a systematic review with meta-analysis and Guideline PRISMA guidelines will be followed [17]. This study was registered in the database PROSPERO with the code: CRD42017069574.

Eligibility criteria

This review included randomized clinical trials carried out in patients with coronary artery disease, whom performed the cardiopulmonary exercise test and compared the effects between HIIT and moderate continuous exercise performed in clinical environment (Phase II). It excluded study protocol and research about rehabilitation in patients with CAD associated to other diseases like stroke and peripheral arterial obstructive disease.

Search strategy

The search was initially performed by two blind researchers, with the same strategy and then the articles selected were evaluated together. When there was disagreement between the two researchers, a third researcher was called for definition. We searched the databases Medline (Accessed via Pubmed), Scielo, Pedro and Lilacs, through the strategy PICOS. MeSH Thesaurus and DeCS were used to find the descriptors and their synonyms.

There are the descriptors included on the search strategy: coronary artery diseases) OR disease, coronary artery) OR diseases, coronary artery) OR coronary arteriosclerosis) OR arteriosclerosis, coronary) OR coronary arteriosclerosis) OR atherosclerosis, coronary) OR atherosclerosis, coronary) OR coronary atherosclerosis) OR coronary atherosclerosis) OR arteriosclerosis, coronary) OR coronary diseases) OR coronary heart disease) OR disease, coronary) OR diseases, coronary) OR coronary heart diseases) OR diseases, coronary heart) OR heart disease, coronary) OR heart diseases, coronary)) AND ((((((((((((((((((((()) interval training) OR high-intensity interval trainings) OR interval training, high-intensity) OR interval trainings, high-intensity) OR training, high-intensity interval) OR trainings, high-intensity interval) OR high-intensity intermittent exercise) OR exercise, high-intensity intermittent) OR exercises, high-intensity intermittent) OR high-intensity intermittent exercises) OR sprint interval training) OR sprint interval trainings) OR hiit) OR intermittent training) OR aerobic interval training)) AND (((((((moderate continuous intensive exercise) OR continuous training at moderate intensity) OR aerobic continuous training) OR moderate continuous training) OR continuous training) OR moderate-intensity continuous training) OR continuous moderate exercise). The search was filtered with the filter: Clinical trial without restriction of year and language.

Data collect

The selection of the studies was performed in two moments. In the first moment: reading the title and summary of the article and in the second moment: reading the complete article. The data was extracted through transcription of the information and a file was created, containing the identification of the article (author and year), methodology and results. To obtain additional information, we consulted a researcher experienced in the area and searched the references of the articles collected.

The methodological quality of the studies was independently assessed using the PEDro scale and the bias risk scale [18,19]. The items evaluated were: randomization technique; blinding technique; intention-to-treat analysis; and reporting losses or exclusions.

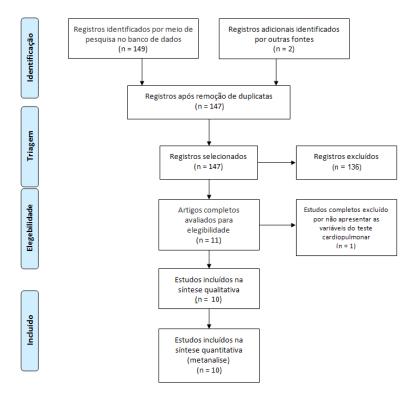
Statistical analyses

The dependents variables are: Maximum Oxygen Consumption $(VO_2 max)$, Ventilatory Threshold (VT), Oxygen Pulse, Inclination of the ventilatory equivalent of carbon dioxide $(VE/VCO_2 slope)$, respiratory exchange ratio (VO_2/VCO_2) , Workload, Maximum Blood Pressure and Maximum Heart Rate; and the independent variables are exercise intensity, training modality, number of participants, age, sex BMI, ejection fraction.

The program RStudio version 1.0.143 for Windows was used for elaboration, data analysis and construction of the Forest Plot chart. Statistical heterogeneity was assessed by visual inspection of the confidence interval and by the Q-Cochran test and chi-square test (X²). Data was analyzed using the random effect model.

Results

Ten studies were included in this meta-analysis, see Flow diagram 1. Among the samples collected, there were a total of 678 patients with a diagnosis of stable CAD, according to the eligibility criteria of the clinical trials. Participants exercised at least three times a week for 45 minutes for a period of 12 weeks. The researchers used different methods for the prescription of physical exercise, the variables used were: the percentage of VO_{2 max}, VO₂ relative to the anaerobic threshold, percentage of HR max and peak power of work. See Table I and II.



Flow diagram 1. Search strategy results.

The methodological quality of the studies was evaluated by the PEDro scale and by the risk of bias scale. In the PEDro scale, the lowest score was: 4 and the highest score was: 9. The risk of bias was assessed by the bias risk scale. The results of the scale detected low risk of bias among the studies included in the review.

Author/year	Score of PEDro
Rognmo et al 2004	9
Warbuton et al 2005	4
Currie et al 2013	5
Curre et al 2014	5
Keteyan et al 2014	9
Cardozo et al 2015	5
Conraads et al 2016	6
Jaureguazar et al 2016	7
Prado et al 2016	5
Pattyn et al 2017	5

Table III. Evaluation of the methodological quality of the studies included in the meta-analysis.

The cut-off point adopted by the authors to consider the study of high methodological quality was \geq 7 [19]

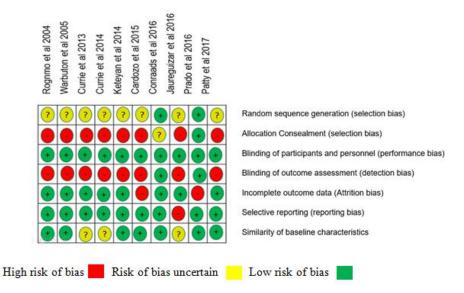
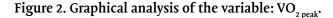


Figure 1. Evaluation of the risk of bias through the risk of bias scale of the studies included in the meta-analysis.

Submitted below are the results of the quantitative synthesis through the graphical analysis.

		HIIT			MIT	2		Mean Difference	Mean Difference
Study	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Rognmo et al 2004	37.8	12.4	8	34.8	5.7	9	1.7%	3.00 [-6.36; 12.36]	
currie et al 2013	24.5	4.5	11	22.3	6.1	11	6.1%	2.20 [-2.28; 6.68]	
Currie et al 2015	27.2	6.0	9	24.2	7.4	10	3.7%	3.00 [-3.03; 9.03]	
Cardozo et al 2015	24.4	5.0	23	21.8	6.1	24	10.0%	2.60 [-0.58; 5.78]	
Jaureguizar et al 2016	24.0	4.8	36	22.8	6.5	36	12.6%	1.20 [-1.44; 3.84]	
Conraads et al 2016	28.6	6.9	89	26.8	6.7	85	16.4%	1.80 [-0.22; 3.82]	
Ketevian et al 2014	26.0	5.9	15	23.5	4.6	13	7.6%	2.50 [-1.39; 6.39]	
Prado et al 2016	22.3	1.1	18	23.0	1.3	17	25.5%	-0.70 [-1.50; 0.10]	
Pattyn et al 2017	28.6	6.9	85	26.8	6.7	89	16.3%	1.80 [-0.22; 3.82]	-
Total (95% CI)			294			294	100.0%	1.31 [0.06; 2.56]	•
Heterogeneity: Tau ² = 1.	438: Ch	$u^2 = 1$	5.66. d	= 8 (P	= 0.0	(5); r ² =	49%	•	
Test for overall effect: Z					1.10	- 10 -	12120		-10 -5 0 5
									Favor [MIT] Favor[HIT]



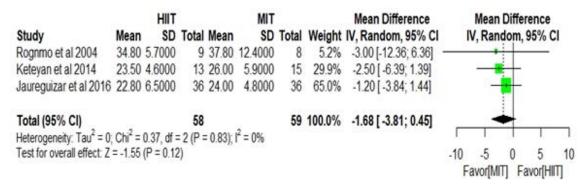


Figure 3. Graphical analysis of the variable: VO_{2 peak} only with the articles of high methodological quality.

	HI	т		MIT			Mean Difference	Mean Difference
Study	Mean S) Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Currie et al 2013	17.7 3.	0 11	15.3	3.3	11	10.3%	2.40 [-0.24; 5.04]	
Cardozo et al 2015	15.6 4.	6 23	13.4	2.7	24	12.9%	2.20 [0.03; 4.37]	
Jaureguizar et al 2016	14.5 2	7 36	14.4	3.5	36	18.3%	0.10 [-1.34; 1.54]	-
Warburton et al 2005	29.0 8.	0 7	23.0	2.0	7	2.8%	6.00 [-0.11; 12.11]	
Keteyian et al 2014	17.1 4.	3 15	14.9	2.7	13	10.4%	2.20 [-0.42; 4.82]	
Prado et al 2016	15.3 0.	7 18	14.0	0.7	17	26.1%	1.30 [0.84; 1.76]	
Pattyn et al 2017	14.3 4	2 85	15.3	4.8	89	19.2%	-1.00 [-2.34; 0.34]	
Total (95% CI)		195			197	100.0%	1.09 [0.02; 2.17]	•
Heterogeneity: Tau ² = 1	.094; Chi ² :	17.08	df = 6 (F	><0	01); I ²	= 65%		
Test for overall effect: Z					0			-10 -5 0 5 10
								Favor [MIT] Favor[HIIT]

Figure 4. Graphical analysis of the variable: Ventilatory threshold

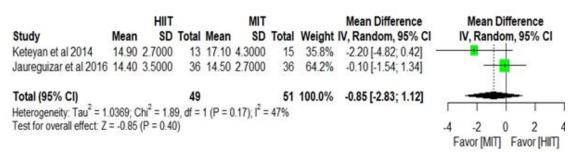


Figure 5. Graphical analysis of the variable: ventilatory threshold, only with the articles of high methodological quality.

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		HIIT			MIT			Mean Difference	Mean Difference
Study	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Rognmo et al 2004	151	19.0	8	155	13.0	9	5.9%	-4.00 [-19.67; 11.67]	
Currie et al 2013	139	15.0	11	123	16.0	11	8.3%	16.00 [3.04; 28.96]	
Currie et al 2015	146	16.0	9	128	29.0	10	3.5%	18.00 [-2.79; 38.79]	
Cardozo et al 2015	133	24.0	24	129	19.0	23	9.1%	4.00 [-8.35; 16.35]	
Jaureguizar et al 2016	126	14.0	36	119	21.0	36	17.5%	7.00 [-1.24; 15.24]	
Keteyian et al 2014	131	17.0	15	135	26.0	13	5.4%	-4.00 [-20.55; 12.55]	
Prado et al 2016	131	4.7	18	122	4.1	17	50,4%	9.00 [6.08; 11.92]	
Total (95% CI)			121				100.0%	7.63 [3.64; 11.62]	+
Heterogeneity: Tau ² = 6				= 6 (P =	0.28)	1 = 20	0%		
Test for overall effect: Z	= 3.75 (P < 0.	01)						-30 -20 -10 0 10 20 3
									Favor [MIT] Favor [HIIT]

Figure 6. Graphical analysis of the variable: maximum heart rate (HR max).

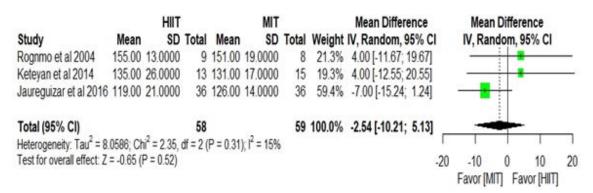


Figure 7. Graphic analysis of the variable: maximum heart rate, only with the articles of high methodological quality.

Discussion

This meta-analysis is unique in comparing the effects of HIIT and continuous moderate intensity exercise (MIT) on the various variables evaluated in the cardiopulmonary test. In the design of the clinical trials after the interventions, a comparison was made between the parameters evaluated in ergospirometry before and after the exercise. This study found that in subjects with CAD, there was a superiority of HIIT over MIT for the following parameters: $VO_{2 \text{ peak}}$, Ventilatory Threshold (VT), and HR may.

Ventilatory Threshold (VT), and HR max. The VO_{2 peak} is considered the main variable in the cardiopulmonary test, because it has a strong correlation with survival, quality of life and the evaluation of the functional capacity. This same result was found in other studies conducted in patients with CAD, acute myocardial infarction (AMI) and heart failure (HF) [30,31]. With these results, the social and cultural paradigm that cardiopathy patients can only perform low-intensity aerobic exercises is undone.

The first ventilatory threshold, also called anaerobic threshold or aerobic threshold is a very important variable obtained in CP. This point is defined as the first ventilation tipping point for carbon dioxide (CO_2) elimination due to lactate buffering by sodium bicarbonate. The earlier this point occurs during an incremental test, the lower an individual's ability to perform sustained aerobic activities [32-34], which corroborates the results of the present study.

The representative variables representative of cardiac function as HR max were increased for individuals who underwent HIIT [9,33,34]. However, a

meta-analysis published in 2017 comparing HIIT with MIT in cardiac patients did not find any difference between the exercise modalities for maximal heart rate and blood pressure. This result was justified by the short time of intervention and the comprehensive number of the cardiopathic population [34].

Of the studies included in the sample only three showed to be of high quality, and, when performing a secondary analysis only with these clinical trials, a change was contacted in the results contained in the general quantitative synthesis, because there was no difference between the modalities of exercise for variables: $VO_{2 peak}$, VT, HR max. This phenomenon can be explained by the reduced sample size between the studies, which suffered a variation of 8 to 36 participants and by the protocol chosen to perform the test, which used two distinct instruments: the cycler and the treadmill and few studies were included in this secondary analysis. The largest deficits found in the other seven studies contemplated in this research were the non-description of randomization techniques, absence of the technique of blinding and loss of participants above 15%.

Thus, it is necessary to carry out better studies, and a deficit of research with the Brazilian population of heart patients is pointed in the literature. This review presents as probable limitation the time bias and information bias due to the methodological quality of the studies, and the strengths of this study are: systematic methodology, comprehensive search in the literature, presence of meta-analysis, evaluation of methodological quality of clinical trials and explicit and reproducible eligibility criteria.

Conclusion

High Intensity Interval Training (HIIT) proved to be the most effective training modality for increment of $VO_{2 max}$, ventilatory threshold and maximum heart rate in patients with coronary artery disease.

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