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Systematic review

Acute inflammatory responses to high-intensity versus moderate-intensity exercise in young men: a systematic review

Respostas inflamatórias agudas ao exercício de alta intensidade versus exercício de intensidade moderada em homens jovens: uma revisão sistemática

Carlos José Nogueira[1,2], Josiana Kely Rodrigues Moreira da Silva[1,3,6], Viviane Monteiro Dias[1,4], Paula Paraguassu Brandão[1,4,6], Estélio Henrique Martin Dantas[1,5]

1. Universidade Federal do Estado do Rio de Janeiro (UNIRIO), Rio de Janeiro, RJ, Brazil
2. Força Aérea Brasileira (FAB) / Escola Preparatória de Cadetes do Ar (EPCAR), Barbacena, MG, Brazil
3. Universidade do Estado do Pará, Belém PA, Brazil
4. Universidade Celso Lisboa (UCL), Rio de Janeiro, RJ, Brazil
5. Universidade Tiradentes (UNIT), Aracajú, SE, Brazil
6. Universidade Estácio de Sá, Brazil

ABSTRACT

Background: Physical exercise has considerable effects on inflammation markers. **Objective:** The aim of this review was to compare the acute effects of high-intensity exercise and moderate-intensity exercise on inflammation in young men. **Methods:** A search was conducted in the Medline/Pubmed, Embase, Cochrane Library, Lilacs/BVS and Web of Science databases and completed in July 2021. Studies were eligible if they met the predefined inclusion criteria: a) randomized clinical trials and quasi-experimental studies; b) conducted on active young men (15 to 24 years old); c) written in Portuguese, English or Spanish; d) applying intense and/or moderate physical exercise protocols. The search strategy was built with the following descriptors: "young adult", "exercise", "high-intensity interval training", and "inflammation". The specific components examined included circulating levels of cytokines IL-6, IL-10, IL-1β, and TNF-α. The risk-of-bias in the results of the studies was assessed with the tools Rob 2 and ROBINS-I. **Results:** From the 1417 records identified, 5 studies were selected for analysis (n = 96). Most studies showed a high risk-of-bias. **Conclusion:** The results suggested an increase in the acute inflammatory response, regardless of exercise intensity. It is assumed that the inflammatory response may also have been influenced by the duration and type of exercise. Further research is needed to examine the impact of exercise intensity on inflammation.

Keywords: exercise; inflammation; cytokines; high intensity interval training; tumor necrosis factor alpha.

RESUMO

Introdução: O exercício físico tem efeitos consideráveis nos marcadores de inflamação. **Objetivo:** O objetivo desta revisão foi comparar os efeitos agudos do exercício de alta intensidade e do exercício de intensidade moderada na inflamação em homens jovens. **Métodos:** Uma busca foi realizada nas bases de dados Medline/PubMed, Embase, Cochrane Library, Lilacs/BVS e Web of Science e concluída em julho de 2021. Os estudos eram elegíveis se atendessem aos critérios de inclusão predefinidos: a) ensaios clínicos randomizados e quase-experimentais; b) realizado em homens jovens ativos (15 a 24 anos); c) escritos em português, inglês ou espanhol; d) aplicação de protocolos de exercícios físicos intensos e/ou moderados. A estratégia de busca foi construída com os seguintes descritores: "adulto jovem", "exercício", "treinamento intervalado de alta intensidade" e "inflamação". Os componentes específicos examinados incluíram níveis circulantes de citocinas IL-6, IL-10, IL-1β e TNF-α. O risco de viés nos resultados dos estudos foi avaliado com as ferramentas Rob 2 e ROBINS-I. **Resultados:** Dos 1.417 registros identificados, 5 estudos foram selecionados para análise (n = 96). A maioria dos estudos mostrou um alto risco de viés. **Conclusão:** Os resultados sugeriram um aumento da resposta inflamatória aguda, independente da intensidade do exercício. Supõe-se que a resposta inflamatória também pode ter sido influenciada pela duração e tipo de exercício. Mais pesquisas são necessárias para examinar o impacto da intensidade do exercício na inflamação.

Palavras-chave: exercício; inflamação; citocinas; treinamento intervalado de alta intensidade; fator de necrose tumoral alfa.

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Correspondence: Carlos José Nogueira, Universidade Federal do Estado do Rio de Janeiro – UNIRIO, Laboratório de Biociências da Motricidade Humana (LABIMH), Rua Dr Xavier Sigaud, 290/301, Praia Vermelha, Rio de Janeiro RJ. carlosjn29@yahoo.com.br

Introduction

Inflammation is described as a defense response of the body against an aggressor agent to promote healing/repair [1]. The extent of this process is regulated by pro- and anti-inflammatory factors [2].

Physical exercise leads to a robust inflammatory response determined by the recruitment of leukocytes and increase in the level of circulating inflammatory markers produced by immune cells and directly from active muscle tissue [3].

Exercise-induced changes in inflammation can be divided into acute effects (changes during and immediately after exercising) and chronic effects (changes in resting or baseline levels when the acute effects induced by exercise are washed away) [3,4].

Overload during exercise causes microtraumas of different levels in striated skeletal muscle tissue, connective tissue, and bone tissue resulting in an acute inflammatory response, orchestrated, among others, by neutrophils and macrophages whose function is to clean, repair and restore previously damaged tissues [5]. The pro-inflammatory response promotes the release of interleukin-1 beta (IL-1β) and tumor necrosis factor alpha (TNF-α), which are expressed in the skeletal muscle, followed by the expression of the anti-inflammatory cytokines interleukin-6 (IL-6), interleukin 1 receptor antagonist protein (IL-1ra), soluble TNF-α receptors and interleukin-10 (IL -10) [6].

Previous studies found different results when comparing the acute and chronic effects of high-intensity intermittent training (HIIT) and moderate-intensity training on the metabolic profile and inflammatory response in adult men [7,2].

Cabral-Santos *et al*. [2] concluded that when the volume of both exercise protocols equals, both promote similar inflammatory responses, leading to an anti-inflammatory state. In contrast, the findings of Lira *et al*. [7] showed that HIIT had a greater impact on the acute response of IL-6 regardless of the training period, and an acute increase in the post-exercise TNF-α levels, regardless of the intensity and the training period. IL-10 increased immediately after acute exercise, regardless of the training period and intensity.

Evidence from a recent systematic review [3] points to an acute inflammatory response after training. TNF-α and IL-10 increased only after intense exercise, and a greater increase in the levels of IL-6 and IL-1β after intense exercise compared to moderate exercise. However, it is noteworthy that the participants of the studies analyzed in the review were moderately or highly trained adults and athletes.

Because of the scarcity of studies comparing these training protocols in a younger population, the present study aimed to analyze and summarize the available scientific evidence on the acute effects of high-intensity versus moderate-intensity physical exercise on inflammatory markers in young men.

Methods

This review was prepared in accordance with the Cochrane Handbook for Systematic Reviews of Interventions [8] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses PRISMA Statement 2020 [9]. It was based on the methodological instructions for the preparation of a systematic review and meta-analysis proposed by Martimbianco [10]. The review protocol was registered with PROSPERO (International Prospective Register of Systematic Reviews), nº CRD42021259733.

Search strategy

A sensitive search was performed in the databases: Medical Literature Analysis and Retrieval System Online (Medline, via Pubmed), Embase, Cochrane Library, Latin American and Caribbean Health Sciences Literature (Lilacs) via VHL Regional Portal and Web of Science. We conducted a handsearch in reference lists of included studies, after analysis of the full text, to retrieve potentially relevant studies that had not appeared in the initial search. Searches were conducted in July 2021.

We used Boolean operators in the research protocol, requiring the title, abstract, or keywords to include the following Descriptors in Health Sciences (DeCS) and Medical Subject Headings (MeSH): "young adult", "exercise", "high-intensity interval training", and "inflammation". Similar terms or synonyms were used to ensure a more inclusive initial search and avoid an overly narrow scope of the studies analyzed. The search strategies used are presented along with the search strategy used in Medline via Pubmed adapted to other databases (Chart I).

Research question

The research question and the search strategy were constructed using the Population, Intervention, Comparison, and Outcome (PICO) model, common in the Evidence-Based Practice and recommended for the development of systematic reviews [11].

From the foregoing, young men (15 to 24 years old) [12] doing regular physical activity (at least 1 year) were selected as "Population"; studies with intense physical exercise were considered for "Intervention"; studies involving moderate-intensity physical exercise were considered for "Control"; and the primary and/or secondary outcomes that assessed acute inflammatory responses were considered as "Outcome". Thus, the following PICO question was constructed: Does high-intensity physical exercise induce greater acute inflammatory responses than does moderate-intensity exercise in young men?

Chart I- Strategies used for electronic searches

Database	Search strategy
Medline/ Pubmed	((“Young Adult”[Mesh] OR “Adult, Young” OR “Adults, Young” OR “Young Adults”) AND ((“Exercise”[Mesh] OR “Activities, Physical” OR “Activity, Physical” OR “Acute Exercise” OR “Acute Exercises” OR “Aerobic Exercise” OR “Aerobic Exercises” OR “Exercise Training” OR “Exercise Trainings” OR “Exercise, Acute” OR “Exercise, Aerobic” OR “Exercise, Isometric” OR “Exercise, Physical” OR “Exercises” OR “Exercises, Acute” OR “Exercises, Aerobic” OR “Exercises, Isometric” OR “Exercises, Physical” OR “Isometric Exercise” OR “Isometric Exercises” OR “Physical Activities” OR “Physical Activity” OR “Physical Exercise” OR “Physical Exercises” OR “Training, Exercise”) OR (“High-Intensity Interval Training”[Mesh] OR “Exercise, High-Intensity Intermittent” OR “High Intensity Interval Training” OR “High-Intensity Intermittent Exercise” OR “High-Intensity Intermittent Exercises” OR “High-Intensity Interval Trainings” OR “Interval Training, High-Intensity” OR “Sprint Interval Training” OR “Sprint Interval Trainings” OR “Training, High-Intensity Interval”))) AND (((((“Inflammation”[Mesh] OR “Inflammations” OR “Innate Inflammatory Response” OR “Inflammatory Response, Innate” OR “Innate Inflammatory Responses”)
Embase	(‘young adult’/exp OR ‘adult, young’ OR ‘prime adult’ OR ‘prime adults’ OR ‘young adult’ OR ‘young adults’) AND (‘exercise’/exp OR ‘exercise’ OR ‘exercise performance’ OR ‘exercise training’ OR ‘fitness training’ OR ‘physical conditioning, human’ OR ‘physical effort’ OR ‘physical exercise’ OR ‘physical exertion’ OR ‘high intensity interval training’/exp OR ‘high intensity interval training’ OR ‘high-intensity intermittent exercise’ OR ‘high-intensity intermittent training’ OR ‘high-intensity interval exercise’ OR ‘high-intensity interval training’) AND (‘inflammation’/exp OR ‘acute inflammation’ OR ‘inflammation’ OR ‘inflammation response’ OR ‘inflammatory response’ OR ‘response, inflammatory’
Cochrane	#1 “Young Adult” OR “Adult, Young” OR “Adults, Young” OR “Young Adults” #2 “Exercise” OR “Activities, Physical” OR “Activity, Physical” OR “Acute Exercise” OR “Acute Exercises” OR “Aerobic Exercise” OR “Aerobic Exercises” OR “Exercise Training” OR “Exercise Trainings” OR “Exercise, Acute” OR “Exercise, Aerobic” OR “Exercise, Isometric” OR “Exercise, Physical” OR “Exercises” OR “Exercises, Acute” OR “Exercises, Aerobic” OR “Exercises, Isometric” OR “Exercises, Physical” OR “Isometric Exercise” OR “Isometric Exercises” OR “Physical Activities” OR “Physical Activity” OR “Physical Exercise” OR “Physical Exercises” OR “Training, Exercise” #3 “High Intensity Interval Training” OR “Exercise, High Intensity Intermittent” OR “High Intensity Interval Training” OR “High Intensity Intermittent Exercise” OR “High Intensity Intermittent Exercises” OR “High Intensity Interval Trainings” OR “Interval Training, High Intensity” OR “Sprint Interval Training” OR “Sprint Interval Trainings” OR “Training, High Intensity Interval” #4 = #2 OR #3 #5 “Inflammation” OR “Inflammations” OR “Innate Inflammatory Response” OR “Inflammatory Response, Innate” OR “Innate Inflammatory Responses” #6 = #1 AND #4 AND #5
Web of Science	#1 TS=(“Young Adult” OR “Adult, Young” OR “Adults, Young” OR “Young Adults”) #2 TS=(“Exercise” OR “Activities, Physical” OR “Activity, Physical” OR “Acute Exercise” OR “Acute Exercises” OR “Aerobic Exercise” OR “Aerobic Exercises” OR “Exercise Training” OR “Exercise Trainings” OR “Exercise, Acute” OR “Exercise, Aerobic” OR “Exercise, Isometric” OR “Exercise, Physical” OR “Exercises” OR “Exercises, Acute” OR “Exercises, Aerobic” OR “Exercises, Isometric” OR “Exercises, Physical” OR “Isometric Exercise” OR “Isometric Exercises” OR “Physical Activities” OR “Physical Activity” OR “Physical Exercise” OR “Physical Exercises” OR “Training, Exercise”) #3 TS=(“High-Intensity Interval Training” OR “Exercise, High-Intensity Intermittent” OR “High Intensity Interval Training” OR “High-Intensity Intermittent Exercise” OR “High-Intensity Intermittent Exercises” OR “High-Intensity Interval Trainings” OR “Interval Training, High-Intensity” OR “Sprint Interval Training” OR “Sprint Interval Trainings” OR “Training, High-Intensity Interval”) #4 = #2 OR #3 #5 TS=(“Inflammation” OR “Inflammations” OR “Innate Inflammatory Response” OR “Inflammatory Response, Innate” OR “Innate Inflammatory Responses”) #6 = #1 AND #4 AND #5
Lilacs/BVS	((“young adult” OR “adulto joven” OR “adulto jovem”) OR (“adultos jovens” OR “jovem adulto” OR “jovem” OR “jovens” OR “juventude”)) AND ((“exercise” OR “ejercicio físico” OR “exercício físico”) OR (“high-intensity interval training” OR “entrenamiento de intervalos de alta intensidad” OR “treinamento intervalado de alta intensidade”)) AND ((“inflammation” OR “inflamación” OR “inflamação”)

Eligibility criteria

Randomized clinical trials and quasi-experimental (non-randomized) studies published in English, Spanish and Portuguese were included. There was no restriction on publication date or duration of studies. The following exclusion criteria were stipulated: studies other than randomized and nonrandomized clinical trials; studies carried out with adults (≥ 25 years), older adults, children, disabled young people, people with chronic diseases or other limitations; studies with high performance athletes and studies with animal models.

Study selection

Two review authors independently screened the studies, and disagreements were resolved by consensus or deliberation with a third reviewer. The selection of studies was carried out in two stages. At the first stage, titles and abstracts of records retrieved in the initial search were examined, and potentially eligible studies were pre-selected. At the second stage, the full text of the pre-selected studies was evaluated to confirm eligibility. The screening process was carried out using the Rayyan web application (https://rayyan.qcri.org) [13]. The entire study screening process followed the steps proposed by the PRISMA 2020 [9] Flowchart, as illustrated in Figure 1.

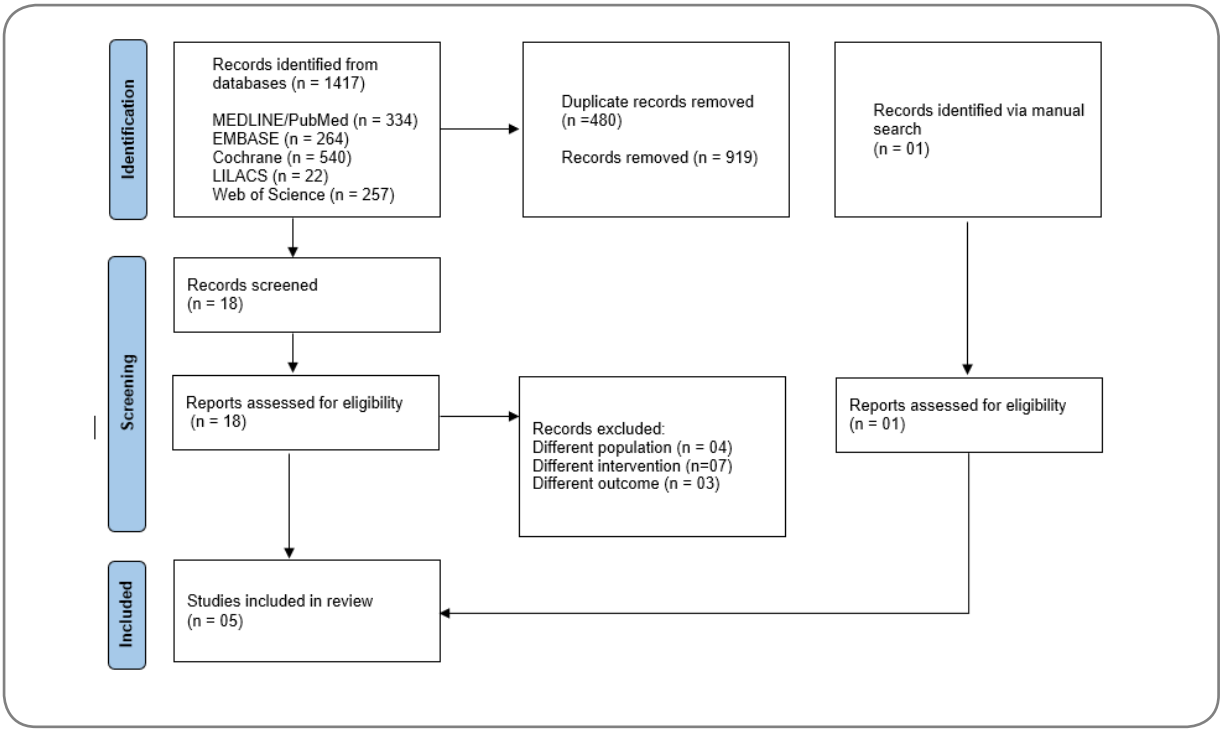

Figure 1 - Flow diagram of article selection. Adapted from: Page *et al.* [9]

Data extraction

At this step, we used standardized data extraction forms. Two reviewers independently conducted the extraction of data regarding the methodological characteristics of the studies, interventions and outcomes. Disagreements were resolved by consensus. Data on exercise type, exercise intensity and duration, and exercise-indu-

ced changes in inflammation markers were identified and evaluated. The effects of exercise intensities on inflammatory markers were examined in blood samples collected pre- and post-exercise and up to 72h post-exercise.

Risk-of-bias assessment

The risk of bias was assessed independently by two reviewers using suitable tools for each study design. The Cochrane [14] risk-of-bias tool for randomized trials (RoB 2) has five domains, as follows: 1) bias arising from the randomization process; 2) bias due to deviations from intended interventions; 3) bias due to missing outcome data; 4) bias in measurement of the outcome; and 5) bias in selection of the reported result. For non-randomized or quasi-randomized studies, the ROBINS-I [15] tool has seven domains for assessment of bias: 1) bias due to confounding; 2) bias in the selection of participants into the study; 3) bias in the classification of interventions; 4) bias due to deviations from the intended interventions; 5) bias due to missing data; 6) bias in measurement of outcomes; and 7) bias in the selection of the reported result. The risk-of-bias assessment of randomized clinical trials is summarized in Figure 2, and the risk of bias of non-randomized or quasi-experimental studies is summarized in Figure 3.

Results

The initial search identified 1417 records in the databases. After excluding 480 duplicates, 937 studies were examined (reading of title and abstract) and 18 studies were pre-selected for full text reading and eligibility assessment. Fourteen studies were excluded for presenting different populations, interventions and outcomes. One study was identified and included through handsearching in the reference lists of the eligible studies. Finally, 05 studies were selected for the qualitative synthesis (n = 96) (Figure 1).

Study characteristics

The studies were categorized according to design, exercise protocol and inflammatory markers measured. Two studies used a randomized clinical trial design with experimental group(s) and a control group [16,17]. The others used a non-randomized or quasi-experimental design [18-20], while two studies [18,20] presented a crossover model.

The studies applied the following exercise protocols: upper limb resistance training [16,17]; walking [18] and running on a treadmill [20]; interval and continuous exercises on the cycle ergometer [19].

The inflammatory marker interleukin-6 was evaluated in all studies [16-20], TNF-α in three studies [16-18] and IL-10 [20] and IL-1β [17] in one study.

Most studies collected blood samples prior to exercise, immediately post exercise, and at different times up to 24 hours post exercise. However, some markers were

evaluated up to 48 hours (IL-6 and TNF-α) [18] and 72 hours after exercise (IL-6, TNF-α and IL-1β) [17].

Because the studies presented distinct characteristics of interventions such as different protocols and measurement times of inflammatory markers, it was not possible to carry out a quantitative synthesis among the set of studies. Therefore, a qualitative approach was more appropriate. Chart II shows the characteristics of the study.

Chart II - Characteristics of the studies

Study	Design	Participants	Intervention protocol/ control	Inflammatory markers/time of evaluation	Results
Brunelli *et al.* (2014) [16]	RCT	18 trained young men (22.0 ± 1.8 years)	EG (n = 9): acute tri-set RT protocol using two combinations of three exercises for the same muscle group; 6 to 8 repetitions at 75% of 1MR per exercise CG (n = 9): did not perform RT	IL-6 e TNF-**α** (prior, 15 min and 24 h post)	↔ TNF-**α**, IL-6 over measured times
Uchida *et al.* (2009) [17]	RCT	35 young soldiers trained (19.1 +1.8 years)	EG: TR (50%1-RM, 75% 1-MR, 90% 1-RM, 110% 1-MR CG: did not perform RT	IL-6, TNF-**α**, IL-1 **β** (prior, 24, 48 and 72 h post)	↔ IL-6, TNF-**α**, IL-1 **β**
Brown *et al.* (2018) [18]	QRCT	17 healthy young men (22.6 ± 4.6 years)	HIIW: 3 × 5 min a 80% VO_{2max} separated by 3 × 5 min at 30% VO_{2max} CMW: 60% VO_{2max} for 30 min	IL-6 and TNF-**α** (prior, post, 2h, 4h, 24h, 48h post)	↔ HIIW vs CMW IL-6 and TNF-**α** (peak immediately post-exercise) IL-6 and TNF-**α** remained elevated up to 4 h post-exercise
Leggate *et al.* (2010) [19]	QRCT	11 healthy young men (22.3 ± 4.0 years)	HIIE: 10 x 4 min on cycle ergometer at 85 to 90% $VO2_{max}$, 2 min rest MICE: 60% VO_{2max} for 59 min on cycle ergometer	IL-6 (prior, post, 1,5, 6 and 23 h post)	↑ IL-6 during HIIE compared to MICE
Neves *et al.* (2014) [20]	QRCT	15 physically active young men (21.0 ± 1.9 years)	HIAE: 80% VO_{2max} LIAE: 40% VO_{2max}	IL-6, IL-10 (prior, post, 2h post)	AIE: acute elevation of IL- 6 (68%); ↔ IL-10 BIE: acute reduction of IL-6 (18%), IL-10 (72%) ↔ IL-6, IL-10 2h post

↑ = significant increase ($p < 0.05$); ↓ = significant reduction ($p < 0.05$); ↔ = no changes; RCT = Randomized Clinical Trial; QRCT = Quasi-Randomized Clinical Trial; EG = Experimental Group; CG = Control group; HIIW = High Intensity Intermittent Walking; CMW = Continuous walking of moderate intensity; HIIE = High-intensity intermittent exercise, MICE = Moderate-intensity continuous exercise; HIAE = High Intensity Aerobic Exercise; LIAE = Low/moderate intensity aerobic exercise; RT = Resistance training; MR = Maximum repetition; IL-6 = Interleukin 6; IL-1β = Interleukin 1 beta; TNF-α = Tumor necrosis factor alpha

Risk of bias of individual studies

The Cochrane risk-of-bias tool for randomized trials RoB 2 [16,17] presented a high risk of overall bias (100%), taking into account the worst assessment for each study (Figure 2). Both studies had problems with randomization, that is, the authors did not report how the randomization was performed and whether the allocation sequence was adequately concealed. The studies were considered as having high risk of bias [16] and a number of concerns [17] due to deviations from the intended intervention, as participants and instructors were aware of the interventions provided to the groups of the research.

Uchida *et al.* [17] investigated plasma concentrations of IL-1β, IL-6 and TNF-α and found them not detectable for some participants even after exercise, resulting in a high risk of bias due to missing outcome data. There was a low risk of bias resulting from the measurement of outcomes and selection of reported results in the two randomized clinical trials [16,17]. This estimation derives from the use of appropriate methods of outcome measurement, with no difference between the experimental and control groups. There was no evidence of publication bias in the two studies analyzed.

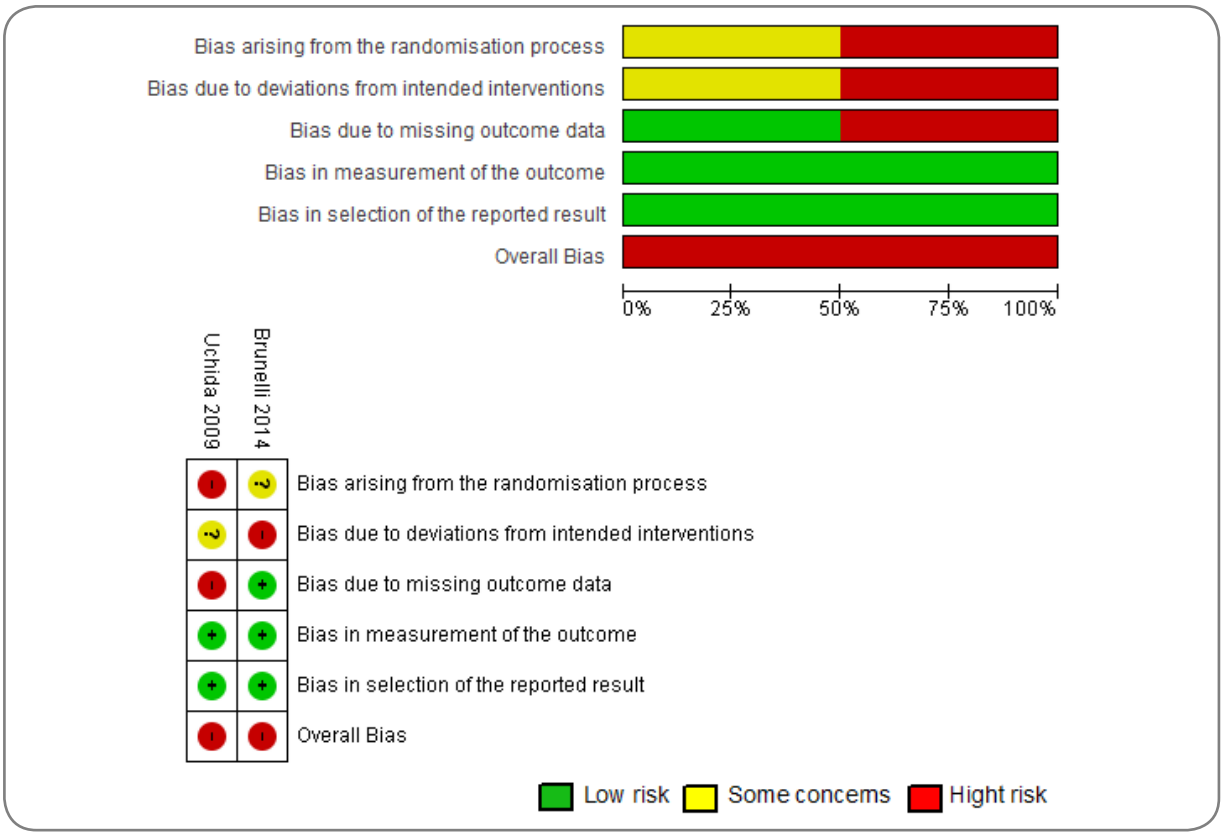

Figure 2 - Percentage distribution and risk-of-bias scenario in individual studies (Rob2) [14]

In the assessment carried out with the ROBINS-I (Figure 3), two quasi-experimental studies [18,19] had severe risk of overall bias considering the worst evaluation for each study. Both studies had no control group (rest or did not perform the compared training), which probably implied a high risk of bias on D3. However, the study

by Neves *et al.* [20] was found as having a moderate risk of bias, considering that the it presented a low or moderate risk of bias for all domains.

	D1	D2	D3	D4	D5	D6	D7	Total
Brown (2018)	-	+	X	+	+	-	+	X
Leggate (2010)	-	+	X	+	+	-	+	X
Neves (2014)	-	+	-	+	+	-	+	-

Green (+) = low risk of bias; Yellow (-) = moderate risk of bias; Red (X) = serious risk of bias; Wine-colored (!) = critical risk of bias.
Domains:

- D1: Bias related to confounding factors;
- D2: Bias related to participant selection;
- D3: Bias related to intervention classification;
- D4: Bias related to deviations from intended interventions;
- D5: Bias related to missing data;
- D6: Bias related to outcome assessment;
- D7: Selection bias in the report of results.

Figure 3 - Summary of risk of bias in non-randomized studies using the ROBINS-I [15] tool

Discussion

The analysis of individual studies with resistance training of different intensities for upper limbs showed that there were no significant changes in plasma concentrations of proinflammatory cytokines after exercise over the measurement times, regardless of intensity. IL-6 and TNF-α showed trivial to small effect sizes after high-intensity resistance training (tri-set) (75% of 1MR) compared to control [16]. There were also no significant changes in IL-6, TNF-α and IL-1β markers after bench press training at different intensities and the same volume (50% of 1MR, 75% of 1MR, 90% of 1MR and 110% of 1MR) [17].

In contrast to the findings of this analysis, the concentration of IL-6 significantly increased after high-intensity resistance training in healthy adult men [21,22] and trained and untrained men [23], with increased levels up to one hour post-exercise [21,23].

Another study showed a significant increase in the plasma concentration of TNF-α up to 2 hours after both high volume and high intensity and low volume and high intensity resistance exercises [24]. Ihalainen *et al.* [25] observed that IL-1β increased immediately after high-intensity resistance exercise (80% of 1MR) in adults. It is noteworthy that these studies evaluated different muscle groups in adult individuals with different training statuses, which may partially explain the different results.

Apparently, resistance exercise-induced inflammation does not result in large increases in pro-inflammatory cytokines such as high-intensity aerobic and intermittent exercises [7,18-20,26]. Factors other than muscle damage, including exercise duration, energy requirements, and oxidative stress are assumed to determine the size of the cytokine response [3,17].

Studies using different protocols of aerobic and intermittent exercises showed conflicting results [18-20]. Brown *et al.* [18] found significant increases in the pro-inflammatory cytokines IL-6 and TNF-α after high- and moderate-intensity walking exercises. The peak of these cytokines occurred immediately after exercise and remained elevated until at least 4 hours post-exercise. Thus, the exercise of walking, regardless of the intensity, promoted a systemic increase in the concentrations of IL-6 and TNF-α.

These results are consistent with the findings of Cyprian *et al.* [27] for the serum concentration of IL-6, which did not change significantly when comparing pre- and post-exercise values in both intervention groups (continuous vs. intermittent), as well as in the control group within at least 5 hours after rest. In another study, TNF-α increased immediately after the acute exercise session, despite the intensity of different protocols of intermittent exercise in adults [7].

However, Leggate *et al.* [19] showed that high-intensity intermittent exercise (HIIT) caused a significantly greater increase in IL-6 concentrations than continuous moderate-intensity exercise. Similar results were found in other studies [7,26].

Lira *et al.* [7] observed a significant increase in IL-6 immediately after a session of HIIT compared with the acute and chronic effects of HIIT versus continuous training of moderate intensity in physically active adults. The plasma IL-6 response to exercise was found significantly higher after high-intensity interval exercise than low-intensity exercise in adult men and women [26].

Nevertheless, Leggate *et al.* [19] obtained contrary results from the study by Cabral-Santos *et al.* [2], who demonstrated that both exercise protocols (HIIT versus moderate continuous), for a corresponding volume, promote similar inflammatory responses, leading to an anti-inflammatory state.

Neves *et al.* [20] compared aerobic exercises of different intensities and observed a greater acute response of IL-6 after the high-intensity protocol than the aerobic exercise of low to moderate intensity. The concentration of IL-10, on the other hand, showed a greater acute systemic reduction for the aerobic exercise of low to moderate intensity compared to aerobic exercise of high intensity immediately after strain [20].

These results for IL-6 are different from the findings of Pozzolo *et al.* [28], in which IL-6 showed no variation between pre- and post-exercise in the two aerobic exercise sessions with different intensities, nor in the comparison between one session and another. However, they are consistent with IL-10 concentrations, which significantly reduced in continuous low-intensity aerobic exercise [28]. It is assumed that less intense exercise protocols are associated with a lower anti-inflammatory response and that there is no change in the anti-inflammatory activity when the exercise intensity is increased [28].

The evidence, however, needs to be interpreted considering some limitations. The first is due to the small size of the total sample (n = 96) of participants in the reviewed studies, which may have affected the interpretation and reproducibility of the results. Among other factors, differences in design, experimental and control

protocols, outcome measures, and the missing outcome data in one study prevented further quantitative synthesis. The conclusions were based on data of relatively low quality and therefore high risk of bias. Important methodological issues such as lack of information on randomization and allocation sequence concealment limited the strength of the conclusions of the studies included. Finally, the results of this review cannot be extrapolated to the general population, as it analyzed only young individuals.

Conclusion

Overall, the analysis of individual studies showed an acute inflammatory response post exercise, with increase in most pro-inflammatory markers. However, the increases are independent of exercise intensity in a younger population, especially when resistance exercise protocols are used. Furthermore, we believe that the acute inflammatory response may also have been influenced by the duration and type of exercise. Therefore, due to limitations and inconsistency in the evidence found, the results must be interpreted with caution.

Future research of greater methodological quality, capable of associating intensity with volume and type of training, as well as separately clustering other age groups, may clarify the results found so far.

Conflict of interest
No conflicts of interest have been reported for this article.

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There were no external sources of funding for this study.

Authors' contributions
Conception and design of the research: Nogueira CJ; **Data collection:** Nogueira CJ, Brandão PP, Silva JKRM, Dias VM; **Data analysis and interpretation:** Nogueira CJ, Brandão PP, Silva JKRM, Dias VM; **Statistical analysis:** Not applicable; **Obtaining Financing:** Not applicable; **Manuscript writing:** Nogueira CJ, Dantas EHM; **Critical review of the manuscript:** Nogueira CJ, Brandão PP, Silva JKRM, Dias VM; **Final review of the manuscript:** Nogueira CJ, Brandão PP, Dantas EHM.

Academic link
This study is linked to the thesis of doctoral student Nogueira CJ, from the Stricto Sensu Post-Graduation Program in Nursing and Bioscience Federal University of the State of Rio de Janeiro (UNIRIO), Rio de Janeiro, Brazil.

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