

# Effects of Aerobic Training Progression on Blood Pressure in Individuals With Hypertension: A Systematic Review With Meta-Analysis and Meta-Regression

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## Research Article

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# Abstract

**Objective:** To analyze, through a systematic review with meta-analysis, the effects of aerobic training with and without progression on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in hypertensive adults.

**Method:** The search for the studies was carried out in the PubMed, Cochrane Central, SPORTDiscus and LILACS databases. Clinical trials that analyzed the effect of aerobic training, lasting at least six weeks, on blood pressure in hypertensive individuals comparing with a control group without intervention were selected. The selection of studies and data extraction were carried out independently by two pairs of researchers.

**Results:** Of the 13028 studies found, 24 were selected and included in this review. There was a reduction in SBP after aerobic training with progression (-10.67 mmHg; 95% CI -15.421, -5.926;  $p < 0.001$ ) and without progression (-10.17 mmHg; CI -12.213, -8.120;  $p < 0.001$ ). DBP also decreased after aerobic training with progression (-5.49 mmHg; 95% CI -8.663, -2.310;  $p < 0.001$ ) and without progression (-6.51 mmHg; 95% CI -9.147, -3.868;  $p < 0.001$ ).

**Conclusion:** Aerobic training promotes a reduction in the SBP and DBP levels of adults with hypertension, regardless of whether or not the training variables progression.

## 1 Background

Hypertension is a multifactorial chronic disease that affects more than one billion adults worldwide<sup>1</sup>, and is considered an important cardiovascular risk factor, since it is strongly associated with the occurrence of several other cardiovascular diseases<sup>2</sup> and mortality<sup>3</sup>. In addition to medication measures, changes in lifestyle are essential in the treatment of hypertension and include, among other aspects, the regular practice of physical exercises<sup>4</sup>.

In this regard, aerobic training of moderate intensity is the primary modality recommended in the management of hypertension (class of recommendation I and level of evidence A) which should be complemented by dynamic resistance training<sup>5-10</sup>. Previous review studies with meta-analysis showed significant mean reductions of 6.0 to 12.3 mmHg in systolic blood pressure (SBP) and 3.4 to 6.1 mmHg in diastolic blood pressure (DBP) in response to aerobic training in hypertensive individuals<sup>11-13</sup>. However, despite including studies with different protocols, these review studies do not analyze the influence of the progression of training variables on blood pressure (BP). In addition, the main guidelines and organizations recommend the practice of aerobic exercises lasting 30 to 60 minutes a day or 150 minutes a week at moderate intensity, performed with a frequency of four to seven times a week<sup>4,5,9,10,14</sup>. Some guidelines also recommend this practice with different intensities and durations of the exercise<sup>10,14</sup> and the gradual increase of these variables during a training program focused on the treatment of hypertension<sup>8</sup>, however the direction of these recommendations are only concerned with the dosage of these variables and not with their manipulation.

Some studies that compared the effects of different levels of these variables on aerobic training have shown reductions in BP regardless of the duration or intensity applied<sup>15-18</sup>, contradicting some indications that the reductions in BP occur in greater magnitude with higher training intensities<sup>19</sup>. Considering that higher intensities lead to significant benefits resulting from greater physiological adaptations<sup>19</sup> not only in BP but in other aspects related to health<sup>17</sup>, it seems important, when planning a training program, to progress and reach higher intensities.

In addition, despite the fact that the practice of physical exercise with the recommended frequencies, durations and intensities causes beneficial effects, especially on cardiorespiratory fitness, the occurrence of a plateau in these effects interferes with the continuity of these benefits<sup>20</sup>, possibly associated with a greater state of training. The manipulation of training variables can be an important strategy for the continuity of health benefits; however, little is known about the effects of the progression of aerobic training variables in the health context, especially in the adaptations of BP in hypertensive

adults. Thus, the objective of the present study was to analyze, through a systematic review with meta-analysis, the effects of aerobic training with and without progression in SBP and DBP of adults with hypertension.

## 2 Method

This study is characterized as a systematic review with meta-analysis and meta-regression of clinical trials. The study followed the items of PRISMA<sup>21</sup> and was previously registered on the PROSPERO platform (CRD42020161767).

### 2.1 Search for articles

The PubMed, Cochrane Central, SPORTDiscus and LILACS databases were used to search for articles. The searches were carried out in December 2019 and there were no restrictions for the year of publication. The terms used for the search were “hypertension,” “exercise” and “blood pressure,” applied together. The Boolean operators “OR” and “AND” were used and the search was performed using the MeSH terms with their respective synonyms.

### 2.2 Eligibility criteria

Clinical trials published in Portuguese, Spanish and English, which included hypertensive adults ( $\geq 18$  years old), of both sexes, who participated in a supervised and structured aerobic exercise intervention for at least six weeks were considered eligible. There were no restrictions on the modality, intensity, session duration, volume and weekly frequency of aerobic training. Clinical trials should compare at least one group with aerobic exercise with a control group without exercise. Studies that contained co-interventions linked to training (e.g., nutritional counseling) were only included if such intervention was applied to both groups (exercise and control). To be eligible, studies should provide data on SBP and DBP at rest before and after the intervention, or the difference between the pre- and post-intervention means with their respective dispersion values. Only studies that provided clinical BP measurements were eligible. All studies that combined aerobic exercise with another type of physical exercise, that presented only the value of ambulatory BP or that included hypertensive individuals with severe heart disease were excluded.

### 2.3 Study selection and data extraction

In the first selection step, the titles and abstracts of the studies were read by four independent researchers (G.T.B, B.A.V, I.H and J.C.C) divided into pairs. Subsequently, the selected articles were compared between the researchers of each pair. In the next step, the texts were read in full by the peers and the studies were included or excluded according to the eligibility criteria previously established. Disagreements between the two researchers of each pair regarding the inclusion or exclusion of the studies were resolved by the fifth researcher (A.M.G).

Data extraction was performed independently by the same researchers, divided into pairs in the same way as in the previous steps. The extracted data were compared to avoid any error in the extraction process, with the disagreements resolved by the fifth researcher. For all studies, the extraction of data related to the characteristics of the sample included: sample size; sex; average age; body mass index (BMI); training status; presence of comorbidities; time of diagnosis of hypertension; nutritional co-intervention; and adverse events arising from the intervention. For the information related to the intervention, the following data were considered: time of intervention; modality; method; session duration; weekly frequency; intensity; adherence to training; and withdrawals. In addition, the number of progressions for intensity, frequency and/or duration of the sessions was extracted. Studies that clearly reported some kind of progression in the frequency, duration and/ or intensity of the session were classified as aerobic training with progression, and those that did not clearly report or did not progress in these variables were classified as aerobic training without progression. Regarding the study outcomes, the information extracted was: SBP and DBP, with mean and measure of dispersion, for the exercise and control groups, at pre- and post-intervention.

### 2.4 Analysis of risk of bias

The assessment of risk of bias was carried out independently by the same researchers, divided into pairs and the fifth reviewer was consulted to resolve the disagreements. The risk of bias was assessed according to the Cochrane Handbook

(2019)<sup>22</sup>, considering the following criteria: generation of random sequence; concealment of allocation; concealment of the assessment of outcomes; conducting analysis by intention to treat; and description of withdrawals and exclusions. The risk of bias was classified as: high risk – when methodological criteria, such as the proper generation of random sequences, were not reported or were not performed; low risk – when the methodological criteria were properly carried out; unclear risk – when there was no adequate description of the criteria, it was not possible to evaluate it as high or low risk.

## 2.5 Data analysis

The combined effect estimates were calculated using the difference between the baseline values and the end of the intervention, with their respective standard deviation values and number of participants analyzed. Studies that presented other measures of dispersion had the values converted to standard deviation. The results of the analyses are presented as mean difference with a 95% confidence interval, and the calculations were performed using the random effects model. The statistical heterogeneity of the effects was assessed using the  $I^2$  inconsistency test, considering values above 50% as high heterogeneity<sup>22</sup>.

Subgroup analyses were performed considering training progression (without progression, with progression, progression in intensity, progression in duration and progression in intensity and duration), sex, presence of comorbidities, use of medications, intervention period, training method (continuous or interval), modalities (walking / running, cycle ergometer, different modalities) and the training environment (terrestrial or aquatic). The meta-regression analysis was performed to investigate the influence of possible confounding factors on the responses of SBP and DBP, namely: mean age (years); BMI ( $\text{kg} / \text{m}^2$ ); number of users of antihypertensive drugs; SBP baseline; weekly frequency (number of sessions per week); weekly duration (minutes); and intervention period (weeks).

To represent the results, a forest plot was generated, with the average difference and 95% confidence interval. Statistical significance was considered to be  $p < 0.05$ . All analyses were performed using the OpenMeta Analyst Software, version 10.10.

## 3 Results

### 3.1 Study selection

Initially, 13028 studies were found by searching the databases. After removing duplicates, 10900 studies were selected to read titles and abstracts. At the end of the first stage, 173 studies were selected for full reading, with 149 being excluded. Thus, 24 studies were included in the final analysis, among which 12 studies were classified as progressive aerobic training<sup>23-34</sup> and 12 studies were classified as nonprogressive aerobic training<sup>35-46</sup>. In addition, 4 studies were analyzed twice for presenting two groups of aerobic training<sup>28,31,35</sup> or for performing analyses at two different moments<sup>27</sup> (Fig. 1)

### 3.2 Characteristics of the studies

Considering all studies, 1207 participants were analyzed, of which 716 were involved in aerobic training and 491 were part of the control group. Most of the studies included adults of both sexes (41.7%), six studies analyzed only male participants (25.0%), another six analyzed only female participants (25.0%) and two studies did not report this information (8.3%). Regarding the training status, 15 studies included untrained or sedentary participants (62.5%) and nine studies did not report this information (37.5%). The average age of the participants varied between 38.1 and 73.5 years and the BMI showed values between 23.3 and 34.4  $\text{kg}/\text{m}^2$ . The general information on the characteristics of the participants is shown in Table 1.

<b>Table 1.</b> Characteristics of the studies.								
<b>Study</b>	<b>Sample size (% women)</b>	<b>Average age (years)</b>	<b>BMI (kg/m<sup>2</sup>)</b>	<b>Duration of the disease (years)</b>	<b>Trainability status</b>	<b>Comorbidities</b>	<b>Co-nutritional intervention</b>	<b>Adverse events</b>
<b>Progressive aerobic training</b>								
Abdelaal and Mohamad, 2014 <sup>23</sup>	E: 20 (60%) C: 19 (53%)	52. 5	E: 34.6 ± 1.1 C: 34.1 ± 1.2	NR	Sedentary	Obesity and DM2	No	No adverse events recorded
Baghaiee et al., 2018 <sup>24</sup>	E: 20 (0%) C: 20 (0%)	38. 1	E: 26.8 ± 2.1 C: 27.2 ± 1.3	NR	Untrained	NR	No	NR
Farahani et al., 2010 <sup>25</sup>	E: 12 (0%) C: 28 (0%)	47. 7	E: 27.4 ± 4.3 C: 28.1 ± 3.5	NR	NR	No	No	NR
Hagberg et al., 1989 <sup>26</sup>	E: 10 (NR) C: NR (NR)	64. 4	NR	NR	NR	NR	No	NR
Kokkinos et al., 1995 <sup>27</sup>	E <sub>16</sub> : 18 (0%) C <sub>16</sub> : 14 (0%) E <sub>32</sub> : 20 (0%) C <sub>32</sub> : 18 (0%)	57. 5	E <sub>16</sub> : 31.0 ± 5.5 C <sub>16</sub> : 31.0 ± 5.5 E <sub>32</sub> : 31.0 ± 4.3 C <sub>32</sub> : 31.0 ± 4.3	NR	Sedentary	No	No	NR
Lamina et al., 2010 <sup>28</sup>	E <sub>CONT</sub> : 112 (0%) E <sub>INT</sub> : 140 (0%) C: 105 (0%)	58. 4	E <sub>CONT</sub> : 25.0 ± 3.9 E <sub>INT</sub> : 22.5 ± 2.9 C: 24.2 ± 4.9	> 1. 0	Sedentary	No	No	Unfavorable responses to training
Latosik et al., 2014 <sup>29</sup>	E: 15 (100%) C: 10 (100%)	NR	E: 28.2± 6.3 C: 28.2 ± 5.5	NR	NR	No	Yes	NR
Meirelles et al., 2009 <sup>30</sup>	E: 13 (61.5%)	49. 5	E: 30 ± 1	NR	Sedentary	NR	No	NR

	C: 6 (66.6%)		C: 32 ± 2						
Soltani et al., 2019 <sup>31</sup>	E <sub>SHORT</sub> : 10 (0%)  E <sub>LONG</sub> : 10 (0%)  C: 10 (0%)	47.9	E <sub>SHORT</sub> : 30.0 ± 2.3  E <sub>LONG</sub> : 27.3 ± 2.4  C: 29.3 ± 2.3	NR	Untrained	NR	No	NR	
Tanaka et al., 1997 <sup>32</sup>	E: 12 (41.7%)  C: 6 (50%)	48.0	NR	NR	Untrained	Obesity	No	NR	
Turner et al., 2000 <sup>33</sup>	E: 11 (18.2%)  C: 7 (28.6%)	66.9	E: 30.2 ± 1.8  C: 29.6 ± 1.4	E: 4.5 ± 2.7  C: 3.0 ± 1.0	Sedentary	No	No	NR	
Wong et al., 2018 <sup>34</sup>	E: 52 (100%)  C: 48 (100%)	73.5	E: 26.0 ± 2.8  C: 26.9 ± 2.9	NR	Sedentary	NR	No	No adverse events recorded	
<b>Non-progressive aerobic training</b>									
Arca et al., 2014 <sup>35</sup>	E <sub>LAND</sub> : 19 (100%)  E <sub>WATER</sub> : 19 (100%)  C: 14 (100%)	64.0	E <sub>LAND</sub> : 28.3 ± 4.2  E <sub>WATER</sub> : 27.0 ± 5.1  C: 30.9 ± 4.8	NR	Untrained	DM2 (n=5)	No	NR	
He et al., 2018 <sup>36</sup>	E: 20 (100%)  C: 22 (100%)	57.5	E: 27.4 ± 2.1  C: 27.7 ± 2.6	NR	Untrained	No	No	NR	
Hong et al., 2018 <sup>37</sup>	E: 7 (0%)  C: 7 (0%)	51.3	NR	NR	NR	No	No	NR	
Khalid et al., 2013 <sup>38</sup>	E: 12 (100%)  C: 13 (100%)	52.8	E: 34.9 ± 3.5  C: 33.8 ± 4.1	NR	Sedentary	Obesity	No	NR	

Izadi et al., 2017 <sup>39</sup>	E: 15 (46.7%) C: 15 (40%)	61.6	E: 25.2 ± 0.6 (Men) 25.7 ± 0.7 (Women) C: 25.2 ± 0.8 (Men) 25.3 ± 1.2 (Women)	NR	Untrained	No	No	NR
Koga et al., 1992 <sup>40</sup>	E: 10 (100%) C: 5 (100%)	49.0	NR	NR	NR	No	No	NR
Maruf et al., 2014 <sup>41</sup>	E: 45 (NR) C: 43 (NR)	52.0	E: 27.5 ± 5 C: 25.4 ± 4.7	NR	NR	No	No	Knee joint pain (n=2)
Miura et al., 1994 <sup>42</sup>	E: 17 (88.2%) C: 10 (90%)	49.0	NR	NR	NR	No	No	NR
Ramos et al., 2018 <sup>43</sup>	E: 12 (83.3%) C: 12 (83.3%)	60.6	E: 30.5 ± 1.5 C: 33.1 ± 2.8	NR	NR	Obesity	No	NR
Tanabe et al., 1989 <sup>44</sup>	E: 21 (52.4%) C: 10 (50%)	48.9	NR	NR	NR	NR	No	NR
Tsai et al., 2002 <sup>45</sup>	E: 12 (41.7%) C: 11 (54.5%)	47.9	E: 26.1 ± 4.5 C: 25.0 ± 1.8	NR	Untrained	No	No	NR
Tsai et al., 2004 <sup>46</sup>	E: 52 (53.8%) C: 50 (54%)	49.1	E: 23.6 ± 1.8 C: 23.8 ± 2.2	NR	Untrained	No	No	NR

Note: E - exercise group. C - control group. CONT- continuous. INT - interval. NR- not reported. BMI- body mass index. DM2- diabetes mellitus 2.\*\*Soltani et al.,2019 and Tanaka et al., 1997 - Number of randomized individuals, because the number of analyzed was not reported in the study.

### 3.3 Characteristics of interventions

#### 3.3.1 General characteristics

The general characteristics of the interventions is presented in Table 2. In the case of aerobic training, indoor cycling was the most reported modality (35.7%), followed by running / walking on the treadmill (25%) and soon after swimming (7.14%), aquatic exercises (7.14%) and dance (3.6%). Regarding the methods applied to training, of the 28 aerobic training groups, only five (17.9%) used interval training, while the other 23 (82.1%) used continuous training. The total duration of the interventions ranged from 6 to 37 weeks and the sessions lasted from 20 to 60 minutes, performed 3 to 4 times a week.

Table 2  
Characteristics of the interventions.

Study	Intervention period	Modality	Method	Session Duration	Weekly frequency	Intensity
<b>Progressive aerobic training</b>						
Abdelaal and Mohamad, 2014 <sup>23</sup>	12 weeks	Treadmill (not defined whether walking or running)	Continuous	B: 20-35min F: 40-50 min	3	B: 60-65% HRmax F: 70-75% HRmax
Baghaiee et al., 2018 <sup>24</sup>	12 weeks	NR	Continuous	B: 25 min F: 45 min	3	B: 50% HRmax F: 70% HRmax
Farahani et al., 2010 <sup>25</sup>	10 weeks	Aquatic exercise	Continuous	35 min	3	B: 60-65% HRmax F: 70-75% HRmax
Hagberg et al., 1989 <sup>26</sup>	37 weeks	Walking/running (Treadmill)/ Cycle Ergometer	Continuous	45-60 min	3	B: NR F: 85% VO <sub>2</sub> max
Kokkinos et al., 1995 <sup>27</sup>	16 weeks 32 weeks	Cycle Ergometer	Continuous	20-60 min	3	60-80% HRmax
Lamina et al., 2010 <sup>28</sup>	8 weeks	Cycle Ergometer	Continuous	B: 45 min F: 60 min	NR	B: 60% HRmax F: 79% HRmax
			Interval	B: 45 min F: 60 min	3	60-79% HRmax
Latosik et al., 2014 <sup>29</sup>	8 weeks	Nordic walking	Continuous	45 min	NR	B:40-60% HRmax F: 38-69% HRmax
Meirelles et al., 2009 <sup>30</sup>	12 weeks	Walking/ running	Continuous	40 min	3	B: 75% HRmax F: 85% HRmax

Note: B – beginning. F – final. Min – minutes. HRmax – maximum heart rate. VO<sub>2</sub>max - maximum volume of oxygen. VO<sub>2</sub> peak - peak oxygen volume. HRres – heart rate reserve. – rating perceived exertion.

Study	Intervention period	Modality	Method	Session Duration	Weekly frequency	Intensity
Soltani et al., 2019 <sup>31</sup>	8 weeks	Walking/running (Treadmill)	Interval	27 min	3	B: 80% VO <sub>2</sub> peak F: 100% VO <sub>2</sub> peak
				32 min		B: 75% VO <sub>2</sub> peak F: 90 VO <sub>2</sub> peak
Tanaka et al., 1997 <sup>32</sup>	10 weeks	Swimming	Continuous	B: 30 min F: 45 min	3	60% HRres
Turner et al., 2000 <sup>33</sup>	28 weeks	Walking/running / Cycle Ergometer	Continuous	30–50 min	4	B: 60–70% HRmax F: 70–80% HRmax
Wong et al., 2018 <sup>34</sup>	20 weeks	Swimming	Continuous	B: 25–30 min	3 to 4	B: 60% HRmax
				F: 40–45 min		F: 70–75% HRmax
<b>Non-progressive aerobic training</b>						
Arca et al., 2014 <sup>35</sup>	12 weeks	Cycle Ergometer	Continuous	20 min	3	50–60% HRres
		Aquatic exercise				
He et al., 2018 <sup>36</sup>	12 weeks	Walking	Continuous	60 min	3	45–50% VO <sub>2</sub> max
Hong et al., 2018 <sup>37</sup>	12 weeks	Walking/running (Treadmill)	Continuous	60 min	4	60% VO <sub>2</sub> max
Khalid et al., 2013 <sup>38</sup>	8 weeks	Walking (Treadmill)	Continuous	20 min	3	60–75% HRmax
Izadi et al., 2017 <sup>39</sup>	6 weeks	Cycle Ergometer	Interval	35 min	3	85–90% HRres
Koga et al., 1992 <sup>40</sup>	10 weeks	Cycle Ergometer	Continuous	60 min	3	50% VO <sub>2</sub> max
Maruf et al., 2014 <sup>41</sup>	12 weeks	Dance	Interval	35 min	3	50–70% HRres
Miura et al., 1994 <sup>42</sup>	10 weeks	Cycle Ergometer	Continuous	60 min	3	40–60% VO <sub>2</sub> max

Note: B – beginning. F – final. Min – minutes. HRmax – maximum heart rate. VO<sub>2</sub>max - maximum volume of oxygen. VO<sub>2</sub> peak - peak oxygen volume. HRres – heart rate reserve. – rating perceived exertion.

Study	Intervention period	Modality	Method	Session Duration	Weekly frequency	Intensity
Ramos et al., 2018 <sup>43</sup>	12 weeks	Athletics Track (not defined whether walking or running)	Continuous	50 min	3	60% HRmax/ 4–6 RPE (OMNI)
Tanabe et al., 1989 <sup>44</sup>	10 weeks	Cycle Ergometer	Continuous	60 min	3	40–60% VO <sub>2</sub> max
Tsai et al., 2002 <sup>45</sup>	12 weeks	Walking/ (Treadmill)	Continuous	30 min	3	60–70% HRres
Tsai et al., 2004 <sup>46</sup>	10 weeks	Walking/running (Treadmill)	Continuous	30 min	3	60–70% HRres

Note: B – beginning. F – final. Min – minutes. HRmax – maximum heart rate. VO<sub>2</sub>max - maximum volume of oxygen. VO<sub>2</sub> peak - peak oxygen volume. HRres – heart rate reserve. – rating perceived exertion.

### 3.3.2 Progressive aerobic training

Regarding aerobic training with progression, 15 exercise groups<sup>23–34</sup> were analyzed, with the majority (80%) of the studies applying continuous training protocols. The total duration of interventions ranged from 8 to 37 weeks and the duration of sessions from 20 to 60 minutes, with two studies<sup>28,32</sup> that progressed only in duration not showing the number of progressions made. Regarding the weekly frequency of training sessions, one study<sup>33</sup> reported four weekly sessions, 11 exercise groups<sup>23–28,30–32</sup> had three weekly sessions, one exercise group<sup>34</sup> had a frequency of three to four weekly sessions and two<sup>28,29</sup> did not report this information. No study reported progression in weekly frequency. Regarding intensity, seven exercise groups<sup>25,26,29–31,33</sup> had only progression for this variable, with the most widely used method for prescribing the maximum heart rate (HRmax), applied in 11 exercise groups<sup>23–25,27–30,33,34</sup>, followed by peak oxygen consumption (VO<sub>2</sub>peak), maximum oxygen consumption (VO<sub>2</sub>max) and reserve heart rate (HRres).

### 3.3.3 Non-progressive aerobic training

Regarding aerobic training without progression, 13 aerobic exercise groups<sup>35–46</sup> were analyzed, of which only two (15.4%) used interval training<sup>39,41</sup>. A single study showed a frequency of four training sessions per week<sup>37</sup>, while all others used three sessions per week. The total duration of the interventions ranged from 6 to 12 weeks and the duration of the sessions ranged from 20 to 60 minutes. For intensity, the most used method for prescription was HRres, applied in six studies<sup>35,39,41,45,46</sup>, followed by VO<sub>2</sub>max, HRmax and rating of perceived exertion (RPE).

## 3.4 Analysis of the risk of bias

Among all the included studies, only 16.7% carried out the process of randomization and allocation confidentiality of the participants in the groups in an appropriate manner, 75% did not provide enough information to determine the randomization process and almost 80% failed to provide details regarding allocation secrecy. Still, only 25% of the studies were carried out with blinded evaluators, 58.3% of the studies described sample losses and 20.8% adopted analysis by intention to treat. Data on risk of bias separated by group with and without progression can be seen in Table 3.

Table 3  
Risk of bias

Study	Random sequence generation	Allocation concealment	Blinding of outcome assessment	Description of sample losses	Intention-to-treat analysis
<b>Progressive aerobic training</b>					
Abdelaal and Mohamad, 2014 <sup>23</sup>	Low	Low	Low	Low	Low
Baghaiee et al., 2018 <sup>24</sup>	Unclear	Unclear	Unclear	High	Unclear
Farahani et al., 2010 <sup>25</sup>	High	Unclear	Unclear	High	Unclear
Hagberg et al., 1989 <sup>26</sup>	Unclear	Unclear	Unclear	Low	Unclear
Kokkinos et al., 1995 <sup>27</sup>	Unclear	Unclear	Unclear	Low	High
Lamina et al., 2010 <sup>28</sup>	Unclear	Unclear	Low	Low	High
Latosik et al., 2014 <sup>29</sup>	Unclear	Unclear	Unclear	Low	High
Meirelles et al., 2009 <sup>30</sup>	Unclear	Unclear	Unclear	High	Low
Soltani et al., 2019 <sup>31</sup>	Unclear	Unclear	Unclear	Low	Unclear
Tanaka et al., 1997 <sup>32</sup>	Unclear	Unclear	Low	High	Unclear
Turner et al., 2000 <sup>33</sup>	High	High	Unclear	Low	Unclear
Wong et al., 2018 <sup>34</sup>	Low	Low	Low	Low	Low
<b>Non-progressive aerobic training</b>					
Arca et al., 2014 <sup>35</sup>	Unclear	Unclear	Unclear	High	Unclear
He et al., 2018 <sup>36</sup>	Unclear	Unclear	Unclear	High	High
Hong et al., 2018 <sup>37</sup>	Unclear	Unclear	Unclear	High	Unclear
Khalid et al., 2013 <sup>38</sup>	Low	Low	Low	Low	High
Izadi et al., 2017 <sup>39</sup>	Unclear	Unclear	Unclear	Low	High
Koga et al., 1992 <sup>40</sup>	Unclear	Unclear	High	High	Unclear
Maruf et al., 2014 <sup>41</sup>	Low	Unclear	Unclear	Low	Low
Miura et al., 1994 <sup>42</sup>	Unclear	Unclear	Unclear	Low	Unclear
Ramos et al., 2018 <sup>43</sup>	Unclear	Low	Unclear	High	Unclear
Tanabe et al., 1989 <sup>44</sup>	Unclear	Unclear	Unclear	High	Low
Tsai et al., 2002 <sup>45</sup>	Unclear	Unclear	Unclear	Low	High
Tsai et al., 2004 <sup>46</sup>	Unclear	Unclear	Low	Low	High

### 3.5 Effect of interventions

### 3.5.1 Effect of aerobic training (SBP and DBP)

The aerobic training analyzed in general, totaling 716 included participants, demonstrated a reduction in SBP with a magnitude of 10.56 mmHg (95% CI -14.083, -7.026;  $p < 0.001$ ;  $I^2$ : 98%) and in DBP of 5.84 mmHg (95% CI -8.226, -3.465;  $p < 0.001$ ;  $I^2$ : 97%).

### 3.5.2 Effect of progressive aerobic training (SBP and DBP)

The results related to aerobic training with progression were analyzed in 15 studies, showing a reduction in SBP of 10.67 mmHg (95% CI -15.421, -5.926;  $p < 0.001$ ;  $I^2$ : 99%) and in DBP of 5.49 mmHg (95% CI -8.663, -2.310;  $p < 0.001$ ;  $I^2$ : 99%) (Fig. 2).

### 3.5.3 Effect of different progressions (SBP and DBP)

Analyzing only the studies that progressed in intensity, there was a decrease in SBP of 12.89 mmHg (95% CI -20.134, -5.648;  $p < 0.001$ ;  $I^2$ : 64%) and in DBP of 7.09 mmHg (95% CI -11.707, -2.478;  $p = 0.003$ ;  $I^2$ : 69%), while for progression only in duration, a reduction in SBP of 13.98 mmHg was found (95% CI -24.238, -3.716;  $p = 0.008$ ;  $I^2$ : 36%) and in DBP 5.07 mmHg (95% CI -7.288, -2.843;  $p < 0.001$ ;  $I^2$ : 0%). When analyzing the progression in the intensity and duration variables together, statistically significant reductions were found only in the SBP (-8.28 mmHg; 95% CI -15.089, -1.479;  $p = 0.017$ ;  $I^2$ : 100%). In DBP, the reduction was 4.48 mmHg, without statistical significance (95% CI -9.100, 0.132;  $p = 0.057$ ;  $I^2$ : 99%).

### 3.5.4 Effect of non-progressive aerobic training (SBP and DBP)

Regarding the effect of aerobic training without progression, adopted in 13 studies, a reduction was found in SBP of 10.17 mmHg (95% CI -12.213, -8.120;  $p < 0.001$ ;  $I^2$ : 0%) and in DBP of 6.51 mmHg (95% CI -9.147, -3.868;  $p < 0.001$ ;  $I^2$ : 61%) (Fig. 3).

### 3.5.5 Effect of aerobic training on subgroups (SBP and DBP)

Subgroup analyses show the effects of aerobic training on SBP and DBP separately under different conditions, between female and male, between subjects with and without comorbidities, between subjects with and without the use of antihypertensive drugs, between different weekly durations of intervention, between methods (continuous and interval), between different modalities and between aquatic and terrestrial environment.

Among the subgroups, in absolute terms, aerobic training provided the greatest reduction magnitude both in SBP (-12.01 mmHg; 95% CI -12.56, -11.46;  $p < 0.001$ ;  $I^2$ : 0%) and in DBP (-7.94 mmHg; 95% CI -10.58, -5.29;  $p < 0.001$ ;  $I^2$ : 15%) when the exercise was performed in the aquatic environment. The lowest magnitude of SBP reduction after aerobic training was observed in those individuals who did not use any antihypertensive medication (-8.18 mmHg; 95% CI -14.58, -1.78;  $p = 0.012$ ;  $I^2$ : 99%). For DBP, the lowest magnitude of reduction after aerobic training was observed in the subgroup of men (-2.80 mmHg; 95% CI -4.76, -0.85;  $p = 0.005$ ;  $I^2$ : 76%) (Table 4).

Table 4  
Meta-analysis results.

Sub-analysis	N	Systolic blood pressure				Diastolic blood pressure			
		Mean difference (CI 95%)	p value	Heterogeneity		Mean difference (CI 95%)	p value	Heterogeneity	
				I <sup>2</sup>	p value			I <sup>2</sup>	p value
<b>Sex</b>									
Men	9	-9.89 (-17.11; -2.67)	0.007	89%	< 0.001	-2.80 (-4.76; -0.85)	0.005	76%	< 0.001
Women	7	-11.98 (-12.52; -11.43)	< 0.001	0%	0.471	-5.81 (-9.36; -2.26)	0.001	75%	< 0.001
<b>Comorbidities</b>									
With comorbidities	6	-10.17 (-13.56; -6.79)	< 0.001	41%	0.132	-7.76 (-11.14; -4.37)	< 0.001	67%	0.010
Without comorbidities	15	-10.46 (-13.10; -7.83)	< 0.001	28%	0.153	-4.59 (-6.57; -2.61)	< 0.001	64%	< 0.001
<b>Antihypertensive drugs</b>									
User	10	-10.47 (-14.63; -6.31)	< 0.001	63%	0.004	-6.44 (-9.95; -2.93)	< 0.001	80%	< 0.001
Non-user	8	-8.18 (-14.58; -1.78)	0.012	99%	< 0.001	-6.45 (-11.2; -1.65)	0.008	99%	< 0.001
<b>Intervention duration</b>									
< 12 weeks	13	-11.37 (-14.67; -8.08)	< 0.001	34%	0.110	-5.04 (-7.50; -2.57)	< 0.001	71%	< 0.001
12 to 24 weeks	12	-10.80 (-16.01; -5.58)	< 0.001	99%	< 0.001	-6.37 (-10.23; -2.52)	0.001	99%	< 0.001
> 24 weeks	3	-8.73 (-15.84; -1.62)	0.016	0%	0.546	-6.37 (-10.81; -1.93)	0.005	0%	0.842
<b>Method</b>									
Continuous	23	-10.62 (-14.52; -6.71)	< 0.001	99%	< 0.001	-6.10 (-8.78; -3.42)	< 0.001	98%	< 0.001
Interval	5	-10.32 (-16.08; -4.56)	< 0.001	48%	0.101	-4.62 (-6.43; -2.82)	< 0.001	0%	0.686
<b>Modality</b>									
Walking/running	11	-11.20 (-14.61; -7.78)	< 0.001	66%	0.001	-7.65 (-10.42; -4.88)	< 0.001	81%	< 0.001
Cycle ergometer	9	-10.89 (-15.76; -6.02)	< 0.001	51%	0.038	-4.01 (-6.31; -1.71)	< 0.001	55%	0.022
Various modalities	2	-11.12 (-20.24; -2.01)	0.017	0%	0.466	-7.61 (-13.74; -1.48)	0.015	0%	0.911
<b>Training location</b>									
N – Number of analyzes. CI 95% - confidence interval. I <sup>2</sup> - indicates the percentage of heterogeneity.									

	Systolic blood pressure				Diastolic blood pressure				
Dry-land	23	-11.06 (-13.53; -8.59)	< 0.001	54%	0.001	-6.23 (-8.25; -4.22)	< 0.001	82%	< 0.001
Aquatic	4	-12.01 (-12.56; -11.46)	< 0.001	0%	0.666	-7.94 (-10.58; -5.29)	< 0.001	15%	0.315

N – Number of analyzes. CI 95% - confidence interval.  $I^2$  - indicates the percentage of heterogeneity.

### 3.5.6 Meta-regression

According to the results of the meta-regression analyses, only age showed an association with the reduction of SBP ( $\beta$ : -0.323; CI -0.339, -0.307;  $p < 0.001$ ), it being considered a predictor in reducing this variable as a result of aerobic training. Thus, the older the sample, the greater the reduction in SBP after the aerobic training period. The variables BMI, number of antihypertensive users, baseline SBP, weekly training frequency, weekly duration and intervention period were not associated with SBP reduction. No variable was associated with a reduction in DBP due to aerobic training (Table 5).

Table 5  
Meta-regression results

Moderator	Number of studies	Systolic blood pressure			Diastolic blood pressure		
		B	CI 95%	p-value	B	CI 95%	p-value
Mean age (years)	23	-0.323	-0.339; -0.307	< 0.001	-0.121	-0.337; 0.095	0.273
Body mass index (kg/m <sup>2</sup> )	21	0.192	-0.645; 1.028	0.653	-0.269	-0.827; 0.288	0.344
Antihypertensives users (n)	19	-0.028	-0.248; 0.193	0.805	0.071	-0.105; 0.247	0.428
SBP basal (mmHg)	28	-0.234	-0.482; 0.014	0.065	-	-	-
DBP basal (mmHg)	28	-	-	-	-0.116	-0.453; 0.220	0.498
Weekly frequency	26	-1.407	-9.057; 6.242	0.718	-1.525	-6.791; 3.741	0.570
Weekly length (min)	27	0.016	-0.045; 0.077	0.604	0.018	-0.022; 0.059	0.368
Intervention period (weeks)	28	0.107	-0.295; 0.508	0.603	-0.114	-0.366; 0.138	0.376

## 4 Discussion

This systematic review with meta-analysis aimed to analyze the effects of aerobic training, with and without progression, on the SBP and DBP of hypertensive adults. Our main results show that both aerobic training strategies (with and without progression) were effective in reducing BP and that older age is a factor associated with greater BP reductions due to aerobic training in hypertensive individuals.

The general results of the present study (aerobic training vs. control group) are in line with results from other meta-analyses, which showed an average reduction of 8 to 12 mmHg in SBP and 5 to 6 mmHg in DBP in hypertensive adults<sup>11-13</sup>. Thus, our results reinforce the importance of aerobic training as a primary strategy for the treatment of hypertension, since the reduction in BP resulting from this practice is similar to that achieved with treatment with antihypertensive drugs<sup>47</sup>. These

results are clinically relevant since a 10 mmHg decrease in SBP is associated with a 20% reduction in the risk of developing cardiovascular disease, 27% in the occurrence of stroke and 13% in the risk of mortality<sup>48</sup>.

Although there is no difference in the BP reduction between aerobic training with and without progression, reductions of greater magnitudes occurred in studies that progressed in the duration and intensity variables separately. The studies that progressed in intensity<sup>25,26,29-31,33</sup> showed reductions of 12.89 mmHg (SBP) and 7.09 mmHg (DBP) and achieved the highest percentages of intensity compared to the other studies. Studies that progressed in duration<sup>28,32</sup>, on the other hand, showed reductions of 13.98 mmHg in SBP and 5.07 mmHg in DBP, and achieved the longest durations in comparison to all studies with and without progression. The studies that progressed in both<sup>23,24,27,28,34</sup> showed more modest reductions in SBP (8.28 mmHg), with no significant reduction in DBP, and achieved session durations longer than the other studies, however the percentage of intensity was below that observed in general, both in with progression and without progression studies. Although the greatest reductions in SBP occur with studies that have progressed in duration, it is possible that the intensity of training is an important modulator of BP reduction, since both studies that have progressed in duration and those that have progressed in intensity have achieved or maintained a high intensity of training. In addition, our results showed a response of greater magnitude in studies with progression in duration, for SBP, and in intensity, for DBP, which may be associated with different mechanisms of action. Bearing in mind that the performance of these mechanisms in response to training is still unknown<sup>49</sup>, it is not possible to state the reason associated with these differences.

The literature points to exercise intensity as a determining factor for BP changes in response to training programs<sup>7,50</sup>, indicating a dose-response relationship, so that higher intensities of training promote greater reductions in BP<sup>51</sup>. As for the duration of the session, there seems to be no dose-response relationship, as longer durations do not necessarily indicate greater reductions in BP, with beneficial effects occurring even with shorter periods of exercise<sup>52</sup>. However, although some studies have investigated the effects of different intensities and durations of exercise, there is insufficient evidence to determine the relationship of these variables with the BP response<sup>53</sup>, especially when not analyzed as isolated doses, but in relation to their manipulations throughout interventions. In the general analysis of our results, the greatest reduction occurred in the study by Meirelles et al. (2009)<sup>30</sup>, both for SBP (-26.3 mmHg) and for DBP (-13.4 mmHg), having reported progression in intensity and reached high intensity (85% HRmax). In addition, although there was no progression in duration, the length of the sessions was intermediate when compared to the other studies (40 minutes).

Although the evidence regarding progression is not concrete, the manipulation of training variables, such as duration and intensity, are recommended, and must respect a gradual process<sup>20</sup>, especially in intensity progression<sup>50</sup>. This strategy, in addition to reducing the risks of musculoskeletal injuries and cardiovascular events, favors greater participation by the participant in training<sup>20</sup>. In addition, other precautions must be considered in this process, such as the levels of BP the person has, recent changes in antihypertensive drugs, effects caused by exercise and medications, in addition to the presence of other diseases and related conditions<sup>50</sup>.

With regard to the subgroup analysis by sex, the effects of the interventions were effective for both men and women, and, in absolute terms, the magnitude of reduction observed for women was greater in SBP (11.98 mmHg) and DBP ( 5.81 mmHg), although there was no statistical difference between the groups. Turnbull et al.<sup>54</sup>, in a meta-analysis, demonstrated that men and women have BP reductions of similar magnitudes, thus demonstrating that training methods do not need to differ between sexes. For analysis between practitioners with and without comorbidities, both groups showed significant BP reductions, with similar magnitudes. This finding demonstrates great clinical relevance, considering that hypertensive patients with comorbidities, which present more serious health risks and greater chances of developing coronary artery disease (CAD)<sup>55</sup>, benefit from the training as much as those without comorbidities.

Regarding the results by users and nonusers of antihypertensive drugs, both showed significant and similar reductions in SBP and DBP, emphasizing that aerobic training also has great hypotensive potential, being able to further optimize the treatment of hypertension, reducing the risks of complications and improving the clinical picture of hypertensive patients<sup>56</sup>.

Reinforcing these results, the meta-regression analysis showed that the use of antihypertensive drugs was not a moderator in reducing BP during aerobic training. However, different dosages and classes of antihypertensive drugs were used in the studies included in this review, which makes it difficult to understand the effects of these factors on the pressure responses observed. Similar to our results, meta-analysis by Sardeli et al.<sup>57</sup> also found that medication use did not affect BP reduction in response to training. However, this result was not specific to aerobic training and included few studies. Studies evaluating the effects of drug therapy and exercise on BP variables mainly focus on outcomes separately and have conflicting results. Thus, the evidence regarding the interaction between the use of medications and pressure responses to exercise is still scarce<sup>53</sup>.

With regard to the duration of the interventions, it was shown that regardless of the aerobic training being performed for short or long periods (< 12 weeks, 12–24 weeks and > 24 weeks), the BP reductions are similar. Likewise, a systematic review by Cao et al.<sup>13</sup> demonstrated that interventions of less than 8 weeks, between 8 and 12 weeks and of more than 12 weeks were similarly effective in decreasing BP. On the other hand, Cornelissen and Smart (2013)<sup>11</sup> observed that aerobic training periods of less than 12 weeks produced greater reductions in SBP and DBP when compared to longer periods, which could be related to the greater adherence of participants to shorter. However, we should consider the importance of the continuity of the training, in order to maintain the benefits achieved. Considering the divergence of the available findings, there is a need for more studies with good methodological quality to better understand the role of the duration of the intervention in the nondrug treatment of hypertensive patients.

As for the training methods, the continuous and the interval methods promoted similar reductions in SBP (-10.62 mmHg; -10.32 mmHg, respectively) and DBP (-6.10 mmHg; -4.62 mmHg, respectively), showing that both are effective. Another recent meta-analysis, carried out with the hypertensive population<sup>58</sup>, showed reductions in SBP for both training methods when compared to control groups (continuous: -3.70 mmHg; interval: -5.64 mmHg), but without difference between training groups. For DBP, reduction was also found after continuous (-2.41 mmHg) and interval (-4.80 mmHg) training when compared to control groups, but the magnitude of DBP reduction in the interval method was significantly greater when compared to the continuous one.

Regarding the training modality, our study shows that the SBP and DBP reduce in a similar way regardless of whether the aerobic exercise is performed with walking / running (-11.20 mmHg), on cycle ergometers (-10.89 mmHg) or combining the training modalities (-11.12 mmHg). This finding has an important practical application, as it demonstrates that exercise professionals can choose the form of aerobic exercise according to the patient's preference, thus being able to favor adherence due to the ease of access to a certain modality or to specific clinical conditions (i.e., using a cycle ergometer due to difficulty mobility with support of their own weight), without prejudice to the reduction in BP.

As for the training location, conducting training in water may be an alternative for the hypertensive population, as it has also shown slightly higher magnitudes of BP reductions (SBP - terrestrial: -11.06 mmHg; aquatic: -12.01 mmHg; DBP - terrestrial: -6.23 mmHg; aquatic: -7.94 mmHg) in absolute terms, without statistical differences. Another study of systematic review also observed that training in water reduces SBP and DBP in a similar way to terrestrial training in adults and the elderly, with 54.5% of the sample classified as hypertensive and 27.3% with pre-hypertensive<sup>59</sup>. It is noteworthy that studies comparing exercises performed in different media and evaluating different outcomes in hypertensive patients are still scarce, especially in the case of chronic effects.

The meta-regression analysis showed a significant association only for age and SBP responses, indicating that older individuals showed greater magnitude reductions in SBP after aerobic training. Since the prevalence of hypertension is higher at older ages<sup>60</sup>, the results of the present study suggest that the practice of aerobic training is an important nondrug strategy for reducing BP in the elderly, which has been observed previously<sup>61</sup>. However, our results were different from those evidenced by previous studies<sup>11,57,62</sup>. There is still disagreement in the literature regarding the influence of age on the effects of BP reduction in response to aerobic training, so that other factors must also be considered.

An important point to be highlighted in the present study is that most studies analyzed with progression used HRmax to prescribe the intensity of exercise<sup>23-25,27-30,33,34</sup> while only one study without progression used this method<sup>38</sup>. Since HRmax is a marker with limitations, we can explain, in part, why the studies that performed progression did not find greater chronic reductions in BP, since the prescribed intensity may have been underestimated in these studies. That is, not progressing violates a training principle, but using more suitable methods for prescribing intensity (such as VO2max and HRres) seems to mitigate the effects of the lack of progression in training.

Finally, our study exposes some limitations that need to be highlighted. Although the general analysis has a considerable number of studies, some subanalyses were carried out with a small number of studies. When assessing methodological quality, the set of studies analyzed did not clearly report most of the information, and of the five evaluation criteria, three were reported unclearly in more than 50% of the studies, making it difficult to assess the risk of bias. Another limitation is related to the lack of important information in the studies, which prevent association with the results, such as disease duration, antihypertensive drugs used and the training status of the participants.

On the other hand, the present study has some strengths. As far as we know, this is a first meta-analysis that assesses the effects of the progression of aerobic training in patients with hypertension, with a significant number of participants being analyzed. The analysis of possible moderators of the effect using the meta-regression analysis is also a strong point of the study. In practical terms, although some guidelines recommend the progression of training, more precise information is lacking in relation to the way to progress. In this regard, the present study presents results that will possibly assist in the prescription of exercises, such as manipulation and the increase of the variables of the training, especially session length and intensity, thus maximizing the beneficial effects of exercise on BP.

## 5 Conclusion

Aerobic training promotes a reduction in SBP and DBP levels in adults with hypertension, regardless of whether there is progression of the training variables. However, when manipulating the training variables, a response of greater magnitude seems to occur with the progression in duration, for SBP, and in intensity, for DBP. Nevertheless, although there is no chronic difference, the progression of the training variables must be considered, in order to potentiate the effects caused by aerobic training on the pressure response.

## Declarations

### Availability of data and material

Please contact the authors for data requests.

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### Author's contribution

GTB - Participated in the literary search, data extraction, in date analysis, interpretation of dates for the work and writing of the manuscript.

IH - Participated in the literary search, data extraction, in date analysis, interpretation of dates for the work and writing of the manuscript.

JCC - Participated in the literary search, data extraction, interpretation of dates for the work and writing of the manuscript.

BAV - Participated in the literary search, data extraction, interpretation of dates for the work and writing of the manuscript.

RSD - Participated in the initial study design, interpretation of dates for the work and critical review of the manuscript.

AMG - Participated in the initial study design, interpretation of dates for the work and critical review of the manuscript.

All authors reviewed final version of the manuscript, takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors read and approved the final manuscript.

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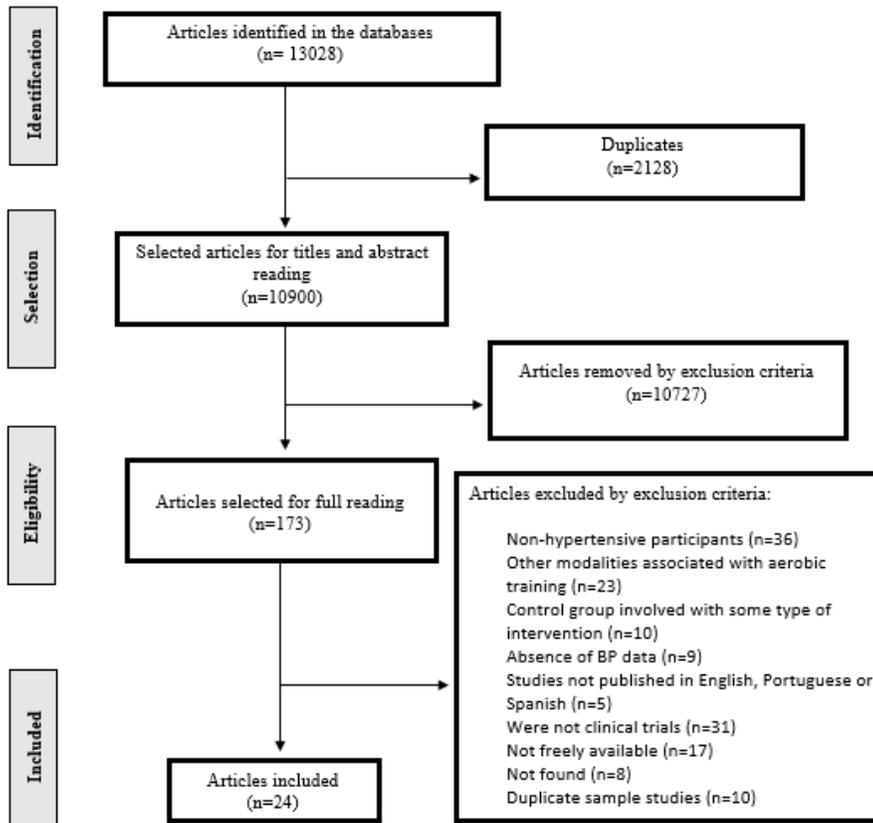
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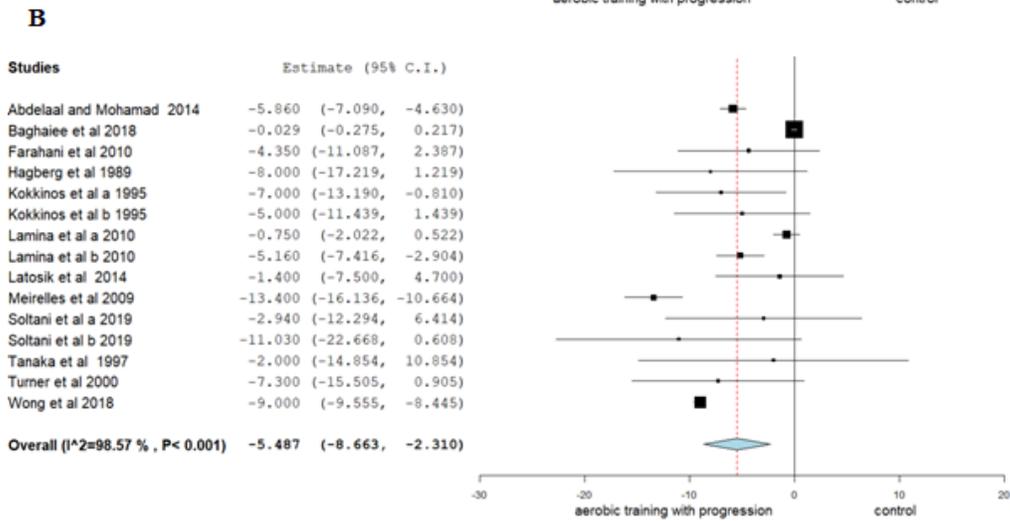
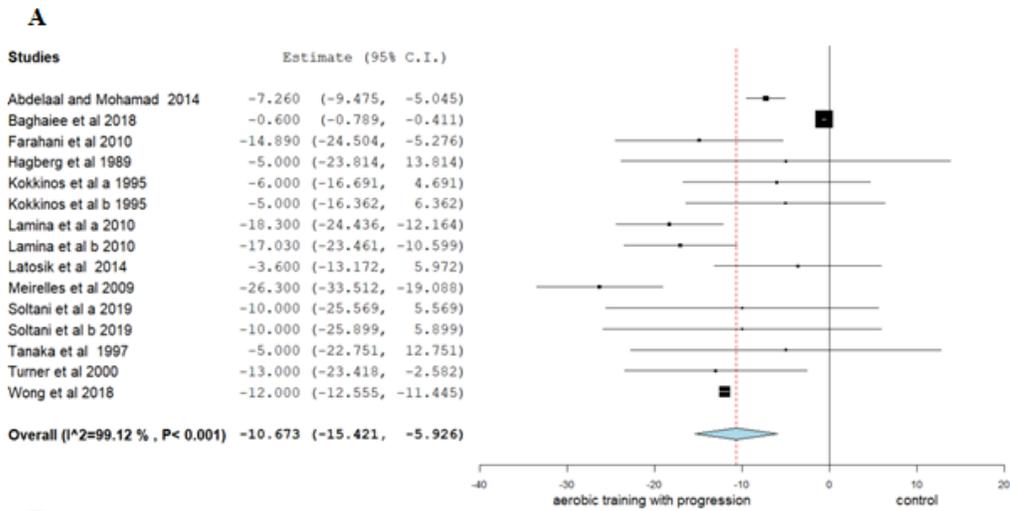
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## Figures



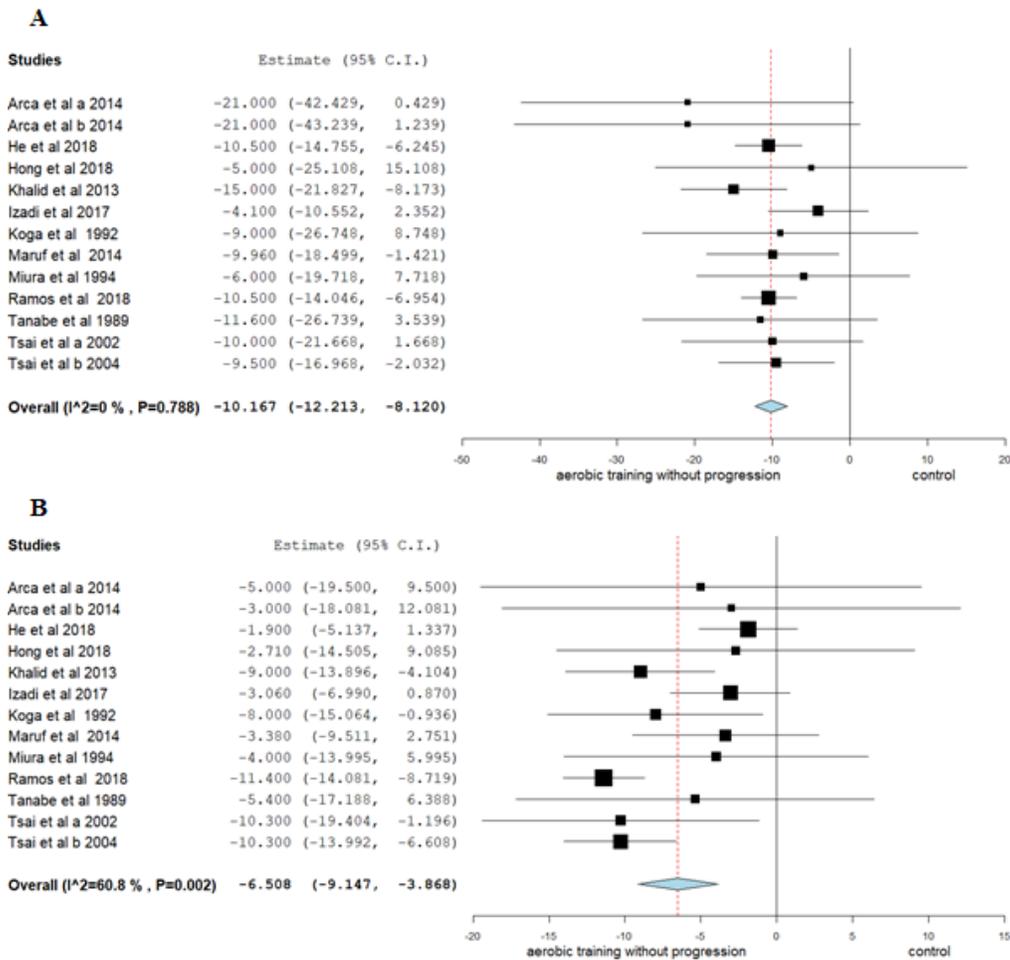
**Figure 1**

Flowchart with information on the different phases of the systematic review



**Figure 2**

Mean differences in SBP (A) and DPB (B) observed between aerobic training with progression compared to control (without intervention). Study-specific estimates (black square); pooled estimates of random-effects meta-analyses (blue diamond).CI indicates confidence interval



**Figure 3**

Mean differences in SBP (A) and DBP (B) observed between aerobic training without progression compared to control (without intervention). Study-specific estimates (black square); pooled estimates of random-effects meta-analyses (blue diamond).CI indicates confidence interval

## Supplementary Files

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