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SYSTEMATIC REVIEW

Effects of High-Intensity Interval Training Versus Moderate-Intensity Continuous Training On Blood Pressure in Adults with Pre- to Established Hypertension: A Systematic Review and Meta-Analysis of Randomized Trials

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Abstract

Background Aerobic exercise reduces blood pressure (BP), but it is unknown whether a high-intensity training approach can elicit a greater BP reduction in populations with elevated BP. This systematic review compared the efficacy of high-intensity interval training (HIIT) versus moderate-intensity continuous training (MICT) for reducing BP in adults with pre- to established hypertension.

Methods Five electronic databases (MEDLINE, EMBASE, CENTRAL, PEDro, and SPORTDiscus) were searched for randomized trials comparing the chronic effects of HIIT versus MICT on BP in individuals with resting systolic BP $\geq$ 130 mmHg and/or diastolic BP $\geq$ 85 mmHg and/or under antihypertensive medication. Random-effects modelling was used to compare changes from pre- to post-intervention in resting and ambulatory BP between HIIT and MICT. Changes from pre- to post-intervention in maximal oxygen uptake ($\dot{V}O_{2max}$) between HIIT and MICT were also meta-analyzed. Data were reported as weighted mean difference (MD) and 95% confidence interval (CI).

Results Ambulatory BP was excluded from the meta-analysis due to the limited number of studies (two studies). Comparing changes from pre- to post-intervention, no differences in resting systolic BP (MD − 0.22 mmHg [CI 95%, − 5.36 to 4.92], p = 0.93, I^2 = 53%) and diastolic BP (MD − 0.38 mmHg [CI 95%, − 3.31 to 2.54], p = 0.74, I^2 = 0%) were found between HIIT and MICT (seven studies; 164 participants). HIIT improved $\dot{V}O_{2max}$ to a greater magnitude than MICT (MD 2.13 ml/kg/min [CI 95%, 1.00 to 3.27], $p < 0.01$, I^2 = 41%) with similar completion rates of the intervention and attendance at the exercise training sessions (nine studies; 245 participants). Limited data were available to compare the incidence of adverse events between HIIT and MICT.

Conclusion HIIT and MICT provided comparable reductions in resting BP in adults with pre- to established hypertension. HIIT was associated with greater improvements in $\dot{V}O_{2max}$ when compared to MICT. Future randomized trials should investigate the efficacy of HIIT versus MICT for reducing ambulatory BP in adults with pre- to established hypertension.

Registration PROSPERO registration (2016: CRD42016041885).

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Key Points

High-intensity interval training (HIIT) and moderate-intensity continuous training (MICT) provide comparable reductions in resting blood pressure in adults with pre- to established hypertension.

Limited information is available to assess the efficacy of HIIT versus MICT for reducing ambulatory blood pressure in adults with pre- to established hypertension.

HIIT improves cardiorespiratory fitness to a greater magnitude than MICT.

Completion rates of the intervention and attendance at the exercise training sessions are similar when HIIT and MICT programs are performed in supervised settings over a short-term period (16 weeks or less).

1 Background

Hypertension is the most common condition seen in primary care [1]. Worldwide, high blood pressure (BP) affects approximately 40% of adults and accounts for 9.4 million deaths every year mainly due to heart diseases and stroke [2]. Thus, it is necessary to optimize the treatment of high BP in order to prevent future cardiovascular morbidity and mortality. From a clinical perspective, there are pharmacological and non-pharmacological approaches to treat high BP [3, 4]. Physical exercise is a cornerstone in the non-pharmacological therapy for those with prehypertension (i.e., systolic BP between 130 and 139 mmHg and/or diastolic BP between 85 and 89 mmHg) [3, 4] and hypertension (i.e., systolic BP $\geq$ 140 mmHg and/or diastolic BP $\geq$ 90 mmHg and/or under antihypertensive medication) [3–7].

In the last two decades, systematic reviews and meta-analyses of randomized controlled trials (RCTs) have reported positive effects of aerobic exercise training for decreasing resting and ambulatory BP [8–11]. Despite this, little is known about the effects of exercise with different FITT (i.e., frequency, intensity, time, type) principles on BP in those with pre- to established hypertension. Recently, Pescatello et al. [6, 7] summarized the existing recommendations made by various professional committees and organizations, such as the American College of Sports Medicine, American Heart Association, Canadian Hypertension Education Program, European Society of Hypertension, and others on exercise prescription for the hypertensive population in accordance with the FITT principle. Currently, high-intensity interval training (HIIT) is not recommended by these clinical associations for the treatment of hypertension. Most guidelines recommend a moderate intensity approach [6, 7], which could be attributed to the feasibility of moderate exercise for most inactive adults with pre- to established hypertension, especially in unsupervised settings, and the absence of a clear benefit-to-risk ratio of exercising at high intensity to reduce BP in these individuals. The authors found an emerging body of evidence showing that BP reduction from exercise training seems to be dose-dependent and is related to exercise intensity. Pescatello et al. [6, 7] suggest that future exercise prescription guidelines for the management of BP should be expanded to include vigorous intensity aerobic exercise training. However, more research to establish the benefits and risks of high intensity exercise in adults with pre- to established hypertension is needed to support such a guideline revision.

HIIT, defined as repeated high-intensity interval bouts between 80% and 100% of peak heart rate (HR_{peak}) interspersed with recovery periods or light exercise [12], has been proposed as an alternative approach to moderate-intensity continuous training (MICT) to improve cardiovascular health in individuals with cardiovascular diseases [13, 14]. Previous meta-analyses have reported that HIIT is superior to MICT in improving cardiorespiratory fitness in patients with cardiovascular diseases (e.g., coronary heart disease, heart failure) [12, 15, 16]. Furthermore, a meta-analysis conducted by Ramos et al. [17] showed that HIIT improves flow-mediated dilation in individuals with impaired vascular function (i.e., individuals with obesity, hypertension, metabolic syndrome, type 2 diabetes, and coronary artery disease) to a greater magnitude than MICT. However, to the best of our knowledge, there is no systematic review comparing the effects of HIIT versus MICT on brachial BP in those with pre- to established hypertension. Therefore, the aim of this systematic review and meta-analysis is to compare the efficacy of HIIT versus MICT for reducing resting and ambulatory BP in adults with pre- to established hypertension. As a secondary aim, we compared the efficacy of HIIT versus MICT for improving maximal oxygen uptake ($\dot{V}O_{2max}$) and the completion rate of the intervention, attendance at the exercise training sessions, and safety (i.e., reported adverse events) with the HIIT and MICT programs.

2 Methods

2.1 Literature Search Strategy

A systematic search of RCTs was conducted according to the Cochrane Handbook for Systematic Reviews of Interventions [18] and PRISMA guidelines [19], and registered in the PROSPERO International prospective register of systematic reviews (protocol 2016: CRD42016041885). An initial search was completed in July 2016 on the databases of MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), PEDro, and SPORTDiscus, with an update in April 2017 (omitting CENTRAL). The MEDLINE (Ovid) search strategy was developed by a librarian experienced in systematic review searching, and peer reviewed by another librarian using the Peer Review Electronic Search Strategy (PRESS) standard [20]. The MEDLINE search was then adapted for the other databases and limited to English language, human studies, date range of 1996 to present, and RCTs using the Cochrane Collaboration RCT filter. Figure 1 presents the MEDLINE (Ovid) search strategy and all strategies are publically available via institutional repository [21].

Initially, two independent reviewers (ECC and JLH) checked all titles and abstracts identified in the electronic databases to include eligible articles for the full-text analysis. The agreement between the reviewers for the title/abstract screening was high (kappa = 0.839; $p < 0.001$). Moreover, both reviewers checked the reference lists of published systematic reviews and meta-analyses about HIIT available on MEDLINE to identify additional articles. Both reviewers then reviewed the potential eligible articles for inclusion. In case of disagreement between the first two reviewers, a third independent reviewer (DSK) helped to resolve the issue by consensus. Figure 2 presents the PRISMA flow diagram of this methodology.

2.2 Eligibility Criteria

The following eligibility criteria, according to the PICOS (Population, Intervention, Comparator, Outcomes, and Study design) question, were considered for inclusion of the articles in this systematic review.

2.2.1 Population

The review included adults ($\geq$ 18 years) with pre- to established hypertension [3, 4]; i.e., the mean values of baseline resting systolic BP $\geq$ 130 mmHg and/or diastolic BP $\geq$ 85 mmHg and/or under antihypertensive medication(s). For ambulatory BP, the mean values of baseline 24-hour systolic BP $\geq$ 130 mmHg and/or diastolic BP $\geq$ 80 mmHg were used as inclusion criteria [3, 4]. The mean values of baseline BP were adopted for the inclusion criteria following the same procedures of the previous systematic reviews on the effects of exercise training on resting [10] and ambulatory [8, 11] BP. Studies including individuals with additional risk factors (e.g., high cholesterol, overweight, obesity, prediabetes, etc.) or known cardiometabolic diseases (e.g., type 2 diabetes, coronary heart disease, heart failure, etc.) were eligible for inclusion.

2.2.2 Intervention

HIIT was defined according to the scheme proposed by Weston et al. [12]: repeated high-intensity interval bouts between 80% and 100% of HR_{peak} interspersed with recovery periods or light exercise [12]. Studies using percentage of $\dot{V}O_{2max}$, oxygen uptake reserve ($\dot{V}O_{2reserve}$), heart rate reserve ($HR_{reserve}$), or rating of perceived exertion (RPE) to define exercise intensity were included when the values were equivalent to 80–100% of HR_{peak} according to the American College of Sports Medicine (ACSM) [22]. Only HIIT interventions that included a minimum of 4 weeks of training were eligible for the analysis. Exercise training regimes that included a combination of HIIT and resistance training or nutritional interventions were not included.

2.2.3 Comparator

MICT was a comparator of HIIT and it included exercise interventions with intensity between 64 and 76% of HR_{peak} performed continuously. Studies that prescribed exercise intensity as a percentage of $\dot{V}O_{2max}$, $\dot{V}O_{2reserve}$, $HR_{reserve}$, or RPE equivalent to 64–76% of HR_{peak} were included as MICT [22]. Only MICT interventions that included a minimum of 4 weeks of training were eligible for the analysis. Exercise training regimes that included a combination of MICT and resistance training or nutritional interventions were not included.

2.2.4 Outcomes

Resting BP and/or ambulatory BP were the primary outcomes. $\dot{V}O_{2max}$, completion rate of the intervention (i.e., patients who concluded the intervention divided by patients who began the intervention), attendance at the exercise training sessions (i.e., performed sessions divided by planned sessions), and safety (i.e., reported adverse events) were secondary outcomes.

Search strategy
1 hypertension/
2 (antihypertens$ or hypertens$ or prehypertens$ or anti-hypertens$ or pre-hypertens$).tw.
3 exp blood pressure/
4 ((blood or arterial or systolic or diastolic) adj2 pressure?).kw,tw.
5 (bp or dbp or sbp).tw.
6 prehypertension/
7 or/1-6
8 exercise/
9 exercise therapy/
10 physical exertion/
11 (high-intensity adj3 (interval? OR exercis$ OR intermittent OR train$)).kw,tw.
12 HIIT.kw.
13 (exercise training).kw.
14 aerobic adj (interval? OR capacity).tw,kw.
15 (high adj5 (interval? OR exercis$ OR intermittent OR train$ OR intensity OR exert$)).tw,kw.
16 (interval? adj3 (train$ OR exercise$)).tw,kw.
17 or/8-16
18 (controlled clinical trial or randomized controlled trial).pt.
19 clinical trials as topic.sh.
20 (randomi#ed or randomly or RCT?1 or placebo$).tw.
21 ((singl$ or doubl$ or trebl$ or tripl$) adj (mask$ or blind$ or dumm$)).tw.
22 trial.ti.
23 or/18-22 [Cochrane Collaboration RCT filter]
24 exp Animals/ not (exp Animals/ and Humans/) [Human filter]
25 (comment or editorial or interview or news).pt.
26 (letter not (letter and randomized controlled trial)).pt.
27 25 or 26 [Opinion filter]
28 7 and 17
29 28 and 23
30 29 not 27
31 30 not 24
32 limit 31 to English language and yr=1996-2016

Fig. 1 MEDLINE (Ovid) search strategy

2.2.5 Study Design

Randomized trials published in English over the last 20 years (from January 1996 to June 2016) were considered.

2.3 Study Quality Assessment

The TESTEX (Tool for the assEssment of Study qualiTy and reporting in Exercise) scale [23], which is a specific tool for assessing the methodological quality of the exercise training studies, was used to assess each individual study for quality and reporting. Briefly, TESTEX examines

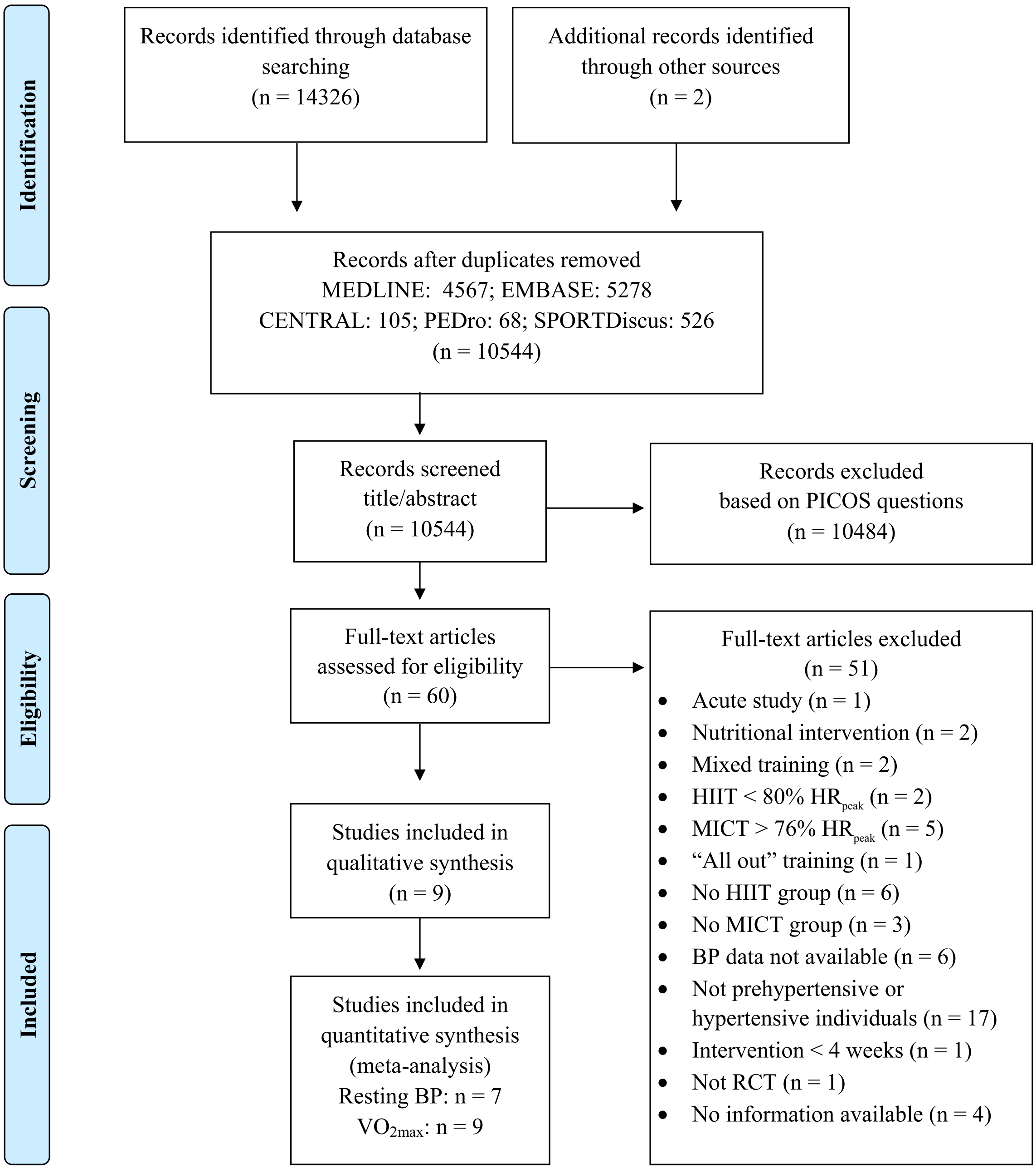

Fig. 2 PRISMA flow diagram of the selection of articles. *HIIT* high-intensity interval training, *MICT* moderate-intensity continuous training, *HR* heart rate, *BP* blood pressure, *RCT* randomized controlled trial, $\dot{V}O_{2max}$ maximal oxygen uptake, *PICOS* Population, Intervention, Comparator, Outcomes, and Study design, HR_{peak} peak heart rate, *CENTRAL* Cochrane Central Register of Controlled Trials

12 criteria (five criteria for study quality and seven criteria for reporting) and the quality assessment uses a 15-point scale (five points for study quality and 10 points for reporting) developed to facilitate a comprehensive review of exercise training trials [23].

2.4 Qualitative Synthesis

Data were extracted in duplicate and the information was cross-checked by two independent reviewers (ECC and JLH). Sample characteristics (participant’s health status, age, sex, body mass index, BP level, method used to measure BP and $\dot{V}O_{2max}$), medication use, intervention and training characteristics (modality, setting, supervision, duration, frequency, intensity, exercise time spent per week), primary outcomes (resting and ambulatory BP), secondary outcomes ($\dot{V}O_{2max}$, completion rate of the intervention, attendance at the exercise training sessions and safety), and quality assessment and reporting of included studies were extracted using a data extraction form (spreadsheet format). A data extraction form was created and tested by the review team prior to full data extraction. In case of disagreement between the first two reviewers (ECC and JLH), a third independent reviewer (DSK) helped to resolve the issue by consensus. Missing data were requested from the authors of the original data.

2.5 Quantitative Synthesis

Pre- to post-intervention changes in resting BP, ambulatory BP, and $\dot{V}O_{2max}$ were used for the head-to-head (pairwise) meta-analysis between the HIIT and MICT interventions. Data were reported as weighted mean difference (MD) and 95% confidence interval (CI). The use of weighted mean differences ("difference in means") was based on the adequateness of this standard statistic when the outcome measurements in all studies are made on the same scale [18]. The Higgins I^2 statistic was calculated to estimate the statistical heterogeneity between the studies. Values above 75% and $p < 0.10$ were used to indicate high heterogeneity [24]. A random-effects model was conducted in the presence of high or low statistical heterogeneity for the between-interventions meta-analyses. The meta-analysis was conducted using Review Manager software (RevMan 5.3, Nordic Cochrane, Denmark). For all analyses, the significance level was set at $p < 0.05$.

3 Results

Table 1 shows the sample characteristics of the nine studies included in this systematic review (total sample size of 245). Seven studies [25–31] compared the effects of HIIT (60.0% men; age 57.8 ± 8.6 years; body mass index (BMI) 30.6 ± 2.1 kg/m^2) versus MICT (49.4% men; age 56.1 ± 11.7 years; BMI 30.4 ± 2.3 kg/m^2) on resting BP. These studies included patients with chronic heart failure [25, 29], coronary heart disease [31], metabolic syndrome [26, 30], abdominal obesity [27], and prediabetes [28]. Two trials [32, 33] compared the effects of HIIT (65.3% men; age 59.9 ± 10.4 years; BMI 27.6 ± 1.1 kg/m^2) versus MICT (67.4% men; age 61.0 ± 10.5 years; BMI 28.0 ± 0.1 kg/m^2) on ambulatory BP. These trials involved patients with chronic heart failure [32] and hypertension stage 1–2 [33]. However, due to the limited number of studies comparing the effects of HIIT versus MICT on ambulatory BP, this primary outcome was excluded from the quantitative synthesis (i.e., meta-analysis).

Six studies reported the medication use (Table 2) of participants [25, 26, 29–32], and two studies did not report medication use [27, 28]. In one study [33] involving patients with stage 1–2 hypertension, the antihypertensive drugs were terminated and the patients were observed for a washout period of 1 month before inclusion in the study.

Table 3 outlines the characteristics of HIIT and MICT interventions in the included studies. Most studies included a 12- to 16-week intervention [26, 27, 29, 30, 32, 33] and were conducted in laboratory settings [26, 30, 33] or in hospital/cardiac rehabilitation centers [25, 29, 31, 32] under direct supervision [25, 29–33]. Participants in included studies performed the exercise training sessions mostly on a treadmill [25, 26, 30–33] three times per week [25, 28–33]. Exercise time performed per week, including warm-up and cool-down, was on average ∼ 23% lower in the HIIT interventions compared to the MICT interventions (∼ 113 ± 39 vs. ∼ 147 ± 25 min).

Table 4 shows the assessment of study quality and reporting of included studies. The studies achieved an average score of 9.8/15 on the TESTEX Scale. Absence of allocation concealment [25, 28–33] and intention-to-treat analysis [26, 28–33] were the most common issues observed in the included studies.

3.1 Between-Intervention Effects

3.1.1 Effects of HIIT Versus MICT on Resting Blood Pressure

Comparisons of the changes from pre- to post-intervention between HIIT and MICT revealed no significant differences in resting systolic BP (MD − 0.22 mmHg [CI 95%, − 5.36 to 4.92], $p = 0.93$). A moderate heterogeneity was detected for this analysis ($I^2 = 53\%$; $p = 0.04$). Likewise, comparisons of the changes from pre- to post-intervention between HIIT and MICT revealed no significant differences in resting diastolic (MD − 0.38 mmHg [CI 95%, − 3.31 to 2.54], $p = 0.74$). Low heterogeneity was detected for this analysis ($I^2 = 0\%$; $p = 0.80$). Forest plots for changes in resting systolic and diastolic BP are shown in Fig. 3.

3.1.2 Effects of HIIT Versus MICT on Maximal Oxygen Uptake

Comparisons of the changes from pre- to post-intervention between HIIT and MICT revealed significant differences in $\dot{V}O_{2max}$ in favour of HIIT interventions (MD 2.13 ml/kg/min [CI 95%, 1.00 to 3.27], $p < 0.01$). A moderate heterogeinety was detected for this analysis ($I^2 = 41\%$; $p = 0.09$). A forest plot for changes in $\dot{V}O_{2max}$ is shown in Fig. 4.

Table 1 Sample characteristics of included studies

References	Sample characteristics	HIIT			MICT			Blood pressure measurement	$\dot{V}O_{2max}$ measurement
		Sample (*n*); Age (years); Sex (M/F)	BMI (kg/m^2)	Baseline BP (mmHg)	Sample (*n*); Age (years); Sex (M/F)	BMI (kg/m^2)	Baseline BP (mmHg)		
Angadi et al. (2015) [25]	Patients with CHF and preserved EF	9; 69.0 ± 6.1; 8/1	29.8 ± 5.1	134.0 ± 14.0 85.0 ± 8.0	6; 71.5 ± 11.7; 4/2	29.3 ± 2.8	134.0 ± 24.0 78.0 ± 7.0	Resting/method NR	Cardiopulmonary exercise test on a treadmill
Ramos et al. (2016) [26]	Individuals with metabolic syndrome	18; 57.0 ± 7.0; 11/7	31.0 ± 6.0	136.0 ± 17.0 84.0 ± 9.0	17; 55.0 ± 11.0; 12/5	33.0 ± 6.0	134.0 ± 12.0 89.0 ± 10.0	After 10 min resting in a supine position/oscillometric method	Cardiopulmonary exercise test on a cycle ergometer or treadmill[a]
Ramos et al. (2016) [26]	Individuals with metabolic syndrome	15; 57.0 ± 11.0; 10/5	32.0 ± 5.0	127.0 ± 14.0 83.0 ± 8.0	–	–	–	After 10 min resting in a supine position/oscillometric method	Cardiopulmonary exercise test on a cycle ergometer or treadmill[a]
Cheema et al. (2015) [27]	Individuals with abdominal obesity	6; 43.0 ± 19.0; 3/3	32.0 ± 5.9	137.0 ± 12.0 89.0 ± 8.0	6; 36.0 ± 15.0; 2/4	30.8 ± 2.6	127.0 ± 4.0 89.0 ± 7.0	In a seated position/auscultatory method	Cardiopulmonary exercise test on a treadmill
Jung et al. (2015) [28]	Individuals with prediabetes	15; 51.0 ± 11.0; 4/11	33.1 ± 7.7	133.0 ± 21.0 82.0 ± 7.0	17; 51.0 ± 10.0; 1/16	32.8 ± 5.0	131.0 ± 8.0 83.0 ± 8.0	Resting/method NR	Cardiopulmonary exercise test on a cycle ergometer
Fu et al. (2013) [29]	Patients with CHF	15; 67.5 ± 1.8; 10/5	NR	141.0 ± 2.0 83.0 ± 2.0	15; 66.3 ± 2.1; 9/6	NR	142.0 ± 3.0 82.0 ± 3.0	Resting/method NR	Cardiopulmonary exercise test on a cycle ergometer
Tjonna et al. (2008) [30]	Individuals with metabolic syndrome	8; 55.3 ± 13.2; 4/4	29.8 ± 5.5	144.0 ± 5.0 95.0 ± 3.0	11; 52.0 ± 10.6; 4/7	29.4 ± 4.9	131.0 ± 6.0 88.0 ± 4.0	After 5 min resting in a seated position/auscultatory method	Cardiopulmonary exercise test on a treadmill
Rognmo et al. (2004) [31]	Patients with CAD	8; 62.9 ± 11.2; 6/2	26.7 ± 4.1	140.0 ± 20.0 72.0 ± 11.0	9; 61.2 ± 7.3; 8/1	26.9 ± 2.7	146.0 ± 19.0 79.0 ± 10.0	Resting/method NR	Cardiopulmonary exercise test on a treadmill
Iellamo et al. (2014) [32]	Patients with CHF secondary to CAD	18; 67.2 ± 6.0; 16/2	28.3 ± 3.0	123.8 ± 14.0 85.4 ± 6.0	18; 68.4 ± 8.0; 15/3	28.1 ± 2.0	120.2 ± 16.0 85.9 ± 11.0	24 h ABPM at baseline and 2 days after the last exercise session/oscillometric method	Cardiopulmonary exercise test on a treadmill

Table 1 continued

References	Sample characteristics	HIIT			MICT			Blood pressure measurement	$\dot{V}O_{2max}$ measurement
		Sample (*n*); Age (years); Sex (M/F)	BMI (kg/m^2)	Baseline BP (mmHg)	Sample (*n*); Age (years); Sex (M/F)	BMI (kg/m^2)	Baseline BP (mmHg)		
Molsen-Hansen et al. (2012) [33]	Hypertensive patients	31; 52.5 ± 7.4; 16/15	26.8 ± 4.1	153.0 ± 12.3 93.0 ± 8.2	28; 53.6 ± 6.5; 16/12	27.9 ± 3.2	151.0 ± 12.1 92.0 ± 5.9	24 h ABPM at baseline and least 1 day after the last exercise session/oscillometric method	Cardiopulmonary exercise test on a treadmill

Data are mean ± SD

HIIT high-intensity interval training, *MICT* moderate-intensity continuous training, *BMI* body mass index, *BP* blood pressure, *$\dot{V}O_{2max}$* maximal oxygen uptake, *CHF* chronic heart failure, *EF* ejection fraction, *CAD* coronary artery disease, *ABPM* ambulatory blood pressure monitoring, *NR* not reported, *M* male, *F* female, *SD* standard deviation

[a]The cardiopulmonary exercise tests were performed either on a cycle or treadmill ergometer, depending on the participant's training preference during the supervised sessions or orthopedic limitations presented

3.1.3 *Completion Rate of the Intervention, Attendance at the Exercise Training Sessions and Reported Adverse Events in HIIT and MICT Programs*

Table 5 describes the completion rate of the intervention, attendance at the exercise training sessions, and reported adverse events in the included studies. Overall, the completion rate of the intervention (HIIT: 82.7 ± 12.9%; MICT: 81.8 ± 9.7%) and attendance at the exercise training sessions in the HIIT and MICT programs (HIIT: 88.9 ± 4.3%; MICT: 85.2 ± 6.7%) were similar. Regarding adverse events, three studies did not report this information [28–30], three studies reported no adverse events in both HIIT and MICT groups [25, 26, 32], and three studies reported some adverse events [27, 31, 33]. However, only Cheema et al. [27] clearly stated that two participants from the HIIT group had musculoskeletal injuries (elbow epicondylitis and gastrocnemius muscle strain) related to the intervention. Rognmo et al. [31] reported one dropout in the HIIT group due to ankle fracture and one dropout in the MICT group due to knee injury. Molmen-Hansen et al. [33] reported three dropouts in the HIIT group because of pain and one dropout in the MICT group due to a myocardial infarction when the participant was at home. However, in both of these studies [31, 33] the authors did not state clearly if the adverse events were directly associated with the training interventions.

4 Discussion

To our knowledge, this is the first systematic review to directly compare the efficacy of HIIT versus MICT for reducing BP in adults with pre- to established hypertension. The main findings were: (1) the exercise-training-induced reductions in resting systolic and diastolic BP were similar between HIIT and MICT. The limited number of studies did not allow comparison of the effects of HIIT and MICT on ambulatory BP; (2) HIIT was associated with greater improvements in $\dot{V}O_{2max}$ when compared to MICT; (3) similar completion rates of the intervention and attendance at the exercise training sessions were observed for HIIT and MICT programs; and (4) there are limited data to establish the incidence of adverse events attributed to HIIT and MICT interventions in adults with pre- to established hypertension.

We found a mean reduction from pre- to post-intervention of 6.3 and 5.8 mmHg for resting systolic BP and 3.8 and 3.5 mmHg for resting diastolic BP in the HIIT and MICT programs, respectively, with no differences between these interventions. Therefore, the data indicate that both HIIT and MICT improve BP to a similar extent in adults

Table 2 Participants receiving medication

References	Year	ACEI/ARB		Alpha/beta-blocker		Diuretics		CCB		Statins		Antiplatelets		Antihyperglycemics	
		HIIT	MICT	HIIT	MICT	HIIT	MICT	HIIT	MICT	HIIT	MICT	HIIT	MICT	HIIT	MICT
Angadi et al. [25][a]	2015	5/9	3/6	6/9	4/6	4/9	4/6	2/9	4/6	6/9	4/6	5/9	4/6	4/9	0/6
Ramos et al. [26]	2016	11/18	8/17	1/18	0/17	NR	NR	2/18	1/17	9/18	6/17	3/18	3/17	6/18	5/17
Ramos et al. [26]	2016	9/15	–	0/15	–	NR	–	4/15	–	9/15	–	4/15	–	5/15	–
Cheema et al. [27]	2015	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Jung et al. [28]	2015	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Fu et al. [29][b]	2013	12/15	12/15	14/15	14/15	8/15	7/15	10/15	9/15	NR	NR	NR	NR	NR	NR
Tjonna et al. [30]	2008	2/12	1/10	1/12	1/10	NR	NR	1/12	1/10	2/12	0/10	1/12	0/10	1/12	1/10
Rognmo et al. [31]	2004	[c]	[c]	[c]	[c]	[c]	[c]	[c]	[c]	[c]	[c]	[c]	[c]	NR	NR
Iellamo et al. [32][d]	2014	16/18	17/18	16/18	14/18	13/18	11/18	NR	NR	13/18	15/18	3/18	4/18	NR	NR
Molsen-Hansen et al. [33]	2012	[e]	[e]	[e]	[e]	[e]	[e]	[e]	[e]	NR	NR	NR	NR	NR	NR

HIIT high-intensity interval training, *MICT* moderate-intensity continuous training, *ACEI/ARB* angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, *CCB* calcium-channel blocker, *NR* not reported

[a]Warfarin: HIIT = 3/9; MICT = 2/6

[b]Digoxin: HIIT = 3/15; MICT = 4/15

[c]Medications received by the patients from both HIIT and MICT groups included beta-blockers (41%), antiplatelet agents (88%), statins (94%), ACEIs (35%), CCBs (6%), long-acting nitrates (12%), and diuretics (12%). Medication was not different between groups

[d]Warfarin: HIIT = 3/18; MICT = 3/18; Aldosterone receptors blockers: HIIT = 7/18; MICT = 10/18

[e]Blood pressure medications were terminated and the patients were observed for a washout period of 1 month before inclusion in the study

with pre- to established hypertension. A meta-analysis conducted by Cornelissen and Smart [10], which examined the effects of endurance, dynamic resistance, combined endurance and resistance training, and isometric resistance training on resting BP in adults, reported that continuous aerobic exercise training reduces resting systolic and diastolic BP by a mean 2.1 and 1.7 mmHg for prehypertensives and by a mean 8.3 and 5.2 mmHg for hypertensives. Greater reductions in resting BP were found for interventions with a duration less than 24 weeks, involving exercise training sessions between 30 and 45 min, and weekly exercise time less than 210 min. That meta-analysis found similar reductions in resting systolic and diastolic BP for moderate and high-intensity aerobic exercise training interventions. Interestingly, all studies included in our systematic review described intervention durations of 4–16 weeks and weekly exercise time $\leq$ 200 min (51–200 min), and most investigations involved exercise training sessions between 30 and 45 min (all MICT interventions and ~ 80% of HIIT interventions). We herein extend this body of knowledge summarizing that both HIIT and MICT have comparable efficacy to promote reductions in resting BP in adults with pre- to established hypertension.

With regard to the effects of HIIT versus MICT on ambulatory BP, which was also previously established as a primary outcome for this systematic review, due to the limited number of studies found (n = 2), it was considered advisable to omit the quantitative synthesis (i.e., meta-analysis) since this would have introduced more imprecision than resolution. We therefore only presented a descriptive summary for ambulatory BP, but we underscore that out-of-office measures of BP, especially ambulatory BP monitoring, have a stronger association with cardiovascular events and mortality than office BP measurement [3, 4]. We strongly indicate the need for future RCTs to compare the efficacy of HIIT and MICT in reducing ambulatory BP in adults with pre- to established hypertension. Also, given the clinical relevance of central BP (i.e., measured in the ascending aorta), which represents the true load imposed on the heart, brain, kidney and large arteries [4], it also should be considered in future RCTs.

Table 3 Characteristics of high-intensity interval training and moderate-intensity training interventions of included studies

References	Year	Duration (weeks)	Modality	Setting	Supervision	HIIT			MICT		
						Training characteristics	Frequency (days/week)	Exercise time[a] (min/week)	Training characteristics	Frequency (days/week)	Exercise time[a] (min/week)
Angadi et al. [25]	2015	4	Treadmill	CRC	Yes	4 × 4 min intervals at 85–90% HRmax, interspersed by 3 min active recovery at 50% HRmax	3	120	30 min 70% HRmax	3	135
Ramos et al. [26][b]	2016	16	Treadmill or cycle	Laboratory and home	Mixed	1 × 4 min interval at 85–95% HRmax / RPE 15–17, interspersed by 3 min active recovery at 50–70% HRmax	3	51	30 min 60–70% HRmax / RPE 11–13	5	150
Ramos et al. [26][b]	2016	16	Treadmill or cycle	Laboratory and home	Mixed	4 × 4 min intervals at 85–95% HRmax / RPE 15–17, interspersed by 3 min active recovery at 50–70% HRmax	3	114	–	–	–
Cheema et al. [27][c]	2015	12	HIIT: Boxing MICT: Walking	HIIT: Gym MICT: Home	HIIT: Yes MICT: No	3 × 2 min intervals at RPE 15–17 for 5 boxing exercises, interspersed by 1 min of rest (standing or pacing)	4	200	45 min "walking as quickly as possible"	4	200
Jung et al. [28][d]	2015	4	Self-selected	Home	No	10 × 1 min intervals at 90% HRmax, interspersed by 1 min active recovery	3	75	50 min 65% HRmax	3	150
Fu et al. [29]	2013	12	Cycle	Hospital	Yes	5 × 3 min intervals at 80% HRR, interspersed by 3 min active recovery at 40% HRR	3	108	30 min 60% HRR	3	108
Tjonna et al. [30]	2008	16	Treadmill	Laboratory	Yes	4 × 4 min intervals at 90% HRmax, interspersed by 3 min active recovery at 70% HRmax	3	120	47 min 70% HRmax	3	141
Rognmo et al. [31]	2004	10	Treadmill	Hospital	Yes	4 × 4 min intervals at 85–95% HRmax, interspersed by 3 min active recovery at 65–75% HRmax	3	99	41 min 65–75% HRmax	3	123
Iellamo et al. [32]	2014	12	Treadmill	CRC	Yes	4 × 4 min intervals at 75–80% HRR, interspersed by 3 min active recovery at 45–50% HRR	3	129	30–45 min 45–60% HRR	3	150–195

Table 3 continued

References	Year	Duration (weeks)	Modality	Setting	Supervision	HIIT			MICT		
						Training characteristics	Frequency (days/week)	Exercise time[a] (min/week)	Training characteristics	Frequency (days/week)	Exercise time[a] (min/week)
Molsen-Hansen et al. [33]	2012	12	Treadmill	Laboratory	Yes	4 × 4 min intervals at 90–95% HRmax, interspersed by 3 min active recovery at 60–70% HRmax	3	114	47 min 70% HRmax	3	141

HIIT high-intensity interval training, *MICT* moderate-intensity continuous training, *CRC* cardiac rehabilitation center, *HRmax* maximal heart rate, *HRR* heart rate reserve, *RPE* rating of perceived exertion

[a] Exercise time per week includes warm-up and cool-down periods

[b] Participants from both HIIT and MICT groups performed two supervised sessions per week in the laboratory. HIIT group performed one unsupervised exercise session per week and MICT performed three unsupervised exercise sessions per week. Unsupervised sessions consisted of outdoor or indoor activities including swimming, walking, running, and rowing

[c] HR responses were monitored using a HR monitor in the HIIT group (i.e., boxing group). The HR responses during the high-intensity intervals varied from 86 to 89% of participant's age-predicted HR_{max}. Participants from the MICT group (i.e., walking group) were instructed how to manually monitor their HR. These data were recorded in a logbook. Mean HR during walking training varied from 64 to 77% of participant's age-predicted HR_{max}

[d] Duration: Previously, participants performed seven supervised exercise sessions in the laboratory and three unsupervised exercise sessions over two consecutive weeks. This period was not included because participants performed the baseline assessments after the laboratory training; Modality: Participants self-selected the exercise modality (walking outdoors, elliptical machine, treadmill walking, or stationary cycling) for each exercise session; Setting = After the first two consecutive weeks of supervised laboratory training the participants performed unsupervised exercise sessions at home; Intensity: During the supervised exercise sessions the participants of the HIIT group reached 82 ± 3% HR_{max} and the participants of the MICT group reached 67 ± 5% HR_{max}. No data were provided for the unsupervised training days

Table 4 Assessment of study quality and reporting of included studies

Reference	Year	Study quality					Score (0–5)	Study reporting										Score (0–10)	Total score (0–15)
		1	2	3	4	5		6a	6b	6c	7	8a	8b	9	10	11	12		
Angadi et al. [25]	2015	+	−	−	+	+	3	−	+	+	+	+	+	+	NC	+	+	8	11
Ramos et al. [26]	2016	+	+	+	+	+	5	−	+	+	−	+	+	+	NC	+	+	7	12
Cheema et al. [27]	2015	+	+	+	+	+	5	−	+	+	+	+	+	+	NC	−	−	6	11
Jung et al. [28]	2015	+	−	−	+	−	2	−	−	+	−	+	+	+	NC	+	+	6	8
Fu et al. [29]	2013	+	−	−	+	−	2	+	−	−	−	+	+	+	−	+	+	6	8
Tjonna et al. [30]	2008	+	−	−	+	+	3	−	−	+	−	+	+	−	−	+	+	5	8
Rognmo et al. [31]	2004	+	+	−	+	+	4	−	+	+	−	+	+	+	NC	+	+	6	10
Iellamo et al. [32]	2014	+	+	−	+	−	3	+	+	+	−	+	+	+	NC	+	+	8	11
Molsen-Hansen et al. [33]	2012	+	+	−	+	−	3	−	+	−	−	+	+	+	−	+	+	6	9

Study quality: 1 = Eligibility criteria specified; 2 = Randomization specified; 3 = Allocation concealment; 4 = Groups similar at baseline; 5 = Blinding of assessor (for at least one key outcome)

Study reporting: 6 = Outcome measures assessed in 85% of participants (6a = 1 point if completion rate is > 85%; 6b = 1 point if adverse events are reported; 6c = 1 point if exercise attendance is reported); 7 = Intention-to-treat analysis; 8 = Between-group statistical comparisons reported (8a = 1 point if between-group statistical comparisons are reported for the primary outcome measure of interest; 8b = 1 point if between-group statistical comparisons are reported for at least one secondary outcome measure); 9 = Point measures and measures of variability for all reported outcome measures; 10 = Activity monitoring in control groups; 11 = Relative exercise intensity remained constant; 12 = Exercise volume and energy expenditure

\+ meet the criteria; − do not meet the criteria, *NC* no control group

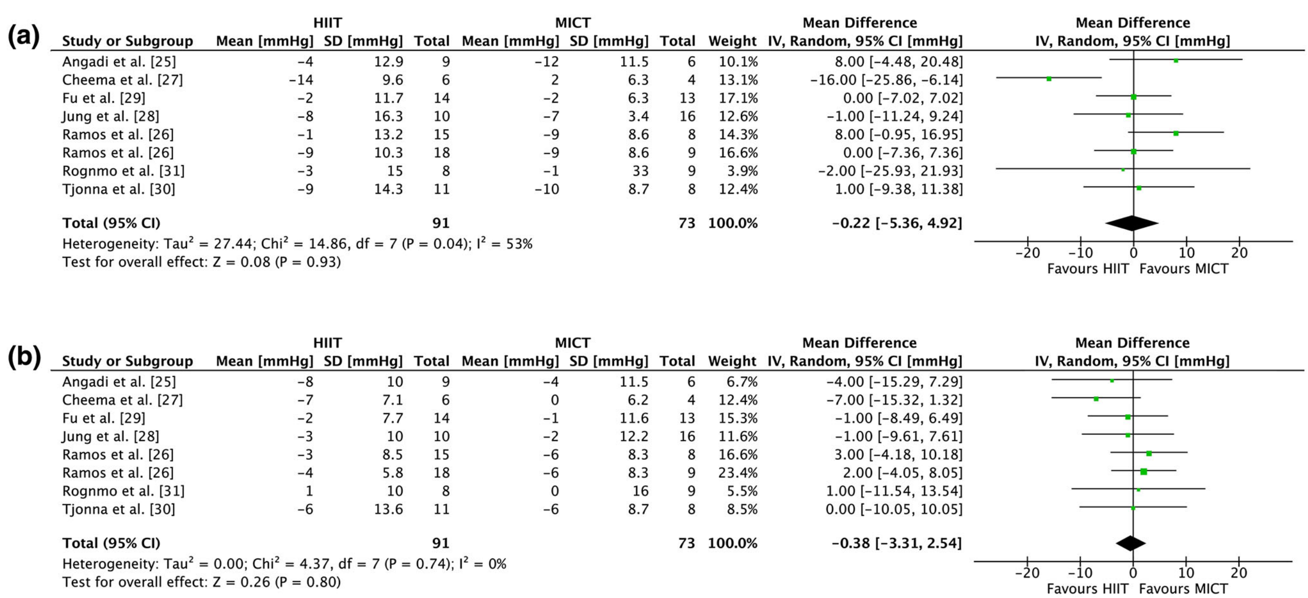

Fig. 3 Forest plot of the between-group comparison of the effects of high-intensity interval training (HIIT) versus moderate-intensity continuous training (MICT) interventions on resting systolic blood pressure (**a**) and diastolic blood pressure (**b**). *SD* standard deviation, *CI* confidence interval, *IV* random effects

From a clinical perspective, reduction in systolic BP decreases the risk of cardiovascular disease events and mortality [34–36]. A reduction of 5 mmHg in systolic BP reduces the mortality due to stroke by 14%, mortality due to coronary heart disease by 9%, and all-cause mortality by 7% [34]. Ettehad et al. [35] observed that a reduction of 10 mmHg in systolic BP reduced the risk of stroke by 27%, coronary heart disease by 17%, heart failure by 28%, and all-cause mortality by 13%. More recently, Bundy et al. [36] showed a linear association between the magnitude of systolic BP reduction and the risk of both cardiovascular disease and all-cause mortality. We observed that

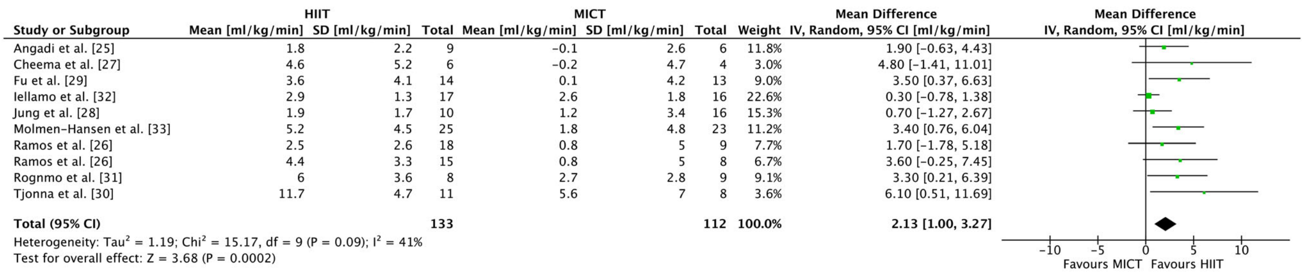

Fig. 4 Forest plot of the between-group comparison of the effects of high-intensity interval training (HIIT) versus moderate-intensity continuous training (MICT) interventions on maximal oxygen uptake. *SD* standard deviation, *CI* confidence interval, *IV* random effects

Table 5 Completion rate of the intervention, attendance at the exercise training sessions and reported adverse events in included studies

References	Year	HIIT			MICT		
		Completion rate of the intervention (%)	Attendance at exercise training sessions (%)	Reported adverse events	Completion rate of the intervention (%)	Attendance at exercise training sessions (%)	Reported adverse events
Angadi et al. [25]	2015	90.0	≥ 92.0	0	66.7	≥ 92.0	0
Ramos et al. [26]	2016	75.0	91.0	0	80.9	88.0	0
Ramos et al. [26]	2016	62.5	87.0	0	–	–	–
Cheema et al. [27]	2015	100	79.0	2 participants had musculoskeletal injury	66.7	82.0[a]	0
Jung et al. [28]	2015	66.7	89.0	NR	94.1	71.0	NR
Fu et al. [29]	2013	93.3	NR	NR	86.7	NR	NR
Tjonna et al. [30]	2008	91.7	90.0[b]	NR	80.0	90.0[b]	NR
Rognmo et al. [31]	2004	72.7	94.3[c]	1 dropout due to ankle fracture[d]	90.0	84.7[c]	1 dropout due to a knee injury[d]
Iellamo et al. [32]	2014	94.4	87.8	0	88.9	83.6	0
Molsen-Hansen et al. [33]	2012	80.7	≥ 90.0[e]	3 dropouts because of pain[d]	82.1	≥ 90.0[e]	1 dropout due to a myocardial infarction at home[d]

HIIT high-intensity interval training, *MICT* moderate-intensity continuous training, *NR* not reported

[a]Including the participants that withdrew the attendance at exercise training sessions was 55%

[b]The training groups (i.e., HIIT and MICT) attended 90 ± 2% of the scheduled training sessions

[c]The authors did not state if these adverse events were directly associated with the training interventions

[d]The completion criterion was at least 90% of attendance in the training program

[e]The completion criterion was at least 70% of attendance in the training program. Only one participant from the HIIT group was excluded because of low attendance (< 70% of training attendance)

4–16 weeks of exercise training based on a HIIT or MICT approach was associated with resting systolic BP reductions by more than 5 mmHg, which suggests that risk for adverse cardiovascular events and mortality may be also derived. This observation was made based on seven published articles that included only HIIT or MICT training regimes and excluded combination approaches (such as exercise plus diet-induced weight loss, resistance training or health promotion counseling) that would have confounded the interpretation of the data. However, it should be noted that in most studies (see Table 2) the participants were utilizing medications that improve BP control, such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium-channel blockers, beta-blockers, and diuretics. None of the included studies reported significant medication changes during the exercise interventions. In order to improve the analysis and interpretation of findings, we suggest future studies report in detail medication status at baseline as well as changes in medication status during the interventions.

Five studies included in our systematic review [25–27, 30, 33] compared the effects of HIIT versus MICT on parameters of vascular function. All these studies observed that HIIT interventions improved the parameters of vascular function more than MICT. Three studies [25, 30, 33] showed greater improvements in endothelial function (assessed by brachial artery flow-mediated dilation) and two studies [26, 27] showed greater improvements in arterial stiffness, assessed by augmentation index [27] and aortic reservoir pressure [26], in HIIT interventions compared to MICT interventions. These data reinforce the previous findings that HIIT improves vascular function, assessed by brachial artery flow-mediated dilation, to a greater extent than MICT [17]. This suggests that HIIT may reduce peripheral vascular resistance, an important determinant of high BP, to a greater magnitude than MICT. Thus, exercise prescriptions for adults with pre- to established hypertension should be optimized by recommending HIIT, given that endothelial dysfunction and increased peripheral vascular resistance are commonly present in this clinical population [37–39]. Our data strengthen the literature supporting the notion that exercise recommendations should include exercise at high intensity with brief durations (i.e., work bouts at $\geq$ 80% of HR_{peak} interspersed with recovery periods) in addition to moderate intensity with longer durations (i.e., $\geq$ 30 min at $\sim$ 65–75% of HR_{peak}) for the management of BP in adults with pre- to established hypertension.

The effect of HIIT versus MICT on $\dot{V}O_{2max}$ was assessed as the secondary outcomes of this systematic review. Our results showed that HIIT interventions improved $\dot{V}O_{2max}$ to a greater degree than MICT interventions. Cardiorespiratory fitness is an independent predictor of cardiovascular and all-cause mortality [40, 41]. Lee et al. [41] observed that every 3.5 ml/kg/min (i.e., 1 metabolic equivalent) improvement in cardiorespiratory fitness was associated with 19 and 15% lower risk of cardiovascular and all-cause mortality, respectively, in the Aerobics Center Longitudinal Study (n = 14,345; follow-up = 11.4 years). Therefore, improvements in cardiorespiratory fitness should be considered as a goal in clinical practice, especially for unfit individuals [40]. Based on our results and previous studies involving healthy individuals [42, 43] and patients with cardiovascular diseases [12, 16, 44], it seems that exercise performed at high intensity with brief durations is better than moderate intensity with longer durations to improve $\dot{V}O_{2max}$.

Completion rates of the intervention, attendance at the exercise training sessions, and adverse events in HIIT and MICT programs were also assessed as secondary outcomes. For the completion rate of the intervention and attendance at the exercise training sessions we observed similar results between HIIT and MICT programs. Completion rates of the intervention were above 80% and attendance at the exercise training sessions was above 85% for both HIIT and MICT programs. It should be noted that almost all interventions [25–27, 29–33] were performed in a supervised setting during a short-term period (16 weeks or less). Thus, under these conditions and probably with encouragement from research staff the high level of effort required to perform HIIT (i.e., perceived exertion “hard” to “very hard”) [25–27, 29, 30] did not impact negatively on individuals’ completion of the intervention and attendance at the exercise training sessions. However, these findings cannot be translated directly to settings with no supervision or encouragement. Limited data were reported from the included studies regarding adverse events during HIIT and MICT interventions. It is still unclear whether participants could have a higher incidence of adverse events during HIIT than during MICT due to its vigorous to near-maximal nature. Even so, the few data available indicate a low incidence of adverse events during HIIT, which is similar to the low incident rates of adverse events attributed to MICT. Further research is needed to compare the completion rates of the intervention and attendance at the exercise training sessions and incidence of adverse events between HIIT and MICT interventions in inactive/unfit individuals in settings with no supervision or encouragement. Effectiveness trials to assess the impact of HIIT in adults with pre- to established hypertension should be considered in the future. As previously stated by Gray et al. [45], longer-term studies including low cost and easily accessible HIIT protocols are needed to translate the use of HIIT from research settings into the public sector where it can inform health and physical activity guidelines. Lastly, future intervention studies should report measures of intervention fidelity, such as compliance with the prescribed intensity to improve study interpretation and translation [46].

This systematic review has some limitations that should be taken into account. It included a limited number of randomized trials and most of these had a small sample size (15 participants or less per intervention; total sample size of 245 individuals). As prespecified in our review registry (PROSPERO; protocol 2016: CRD42016041885), we included studies based on BP means indicating pre- to established hypertension. However, we cannot rule out that such samples could be mixed and have included some normotensive individuals. Most included studies failed to report the method of allocation concealment and did not conduct an intention-to-treat analysis. Intention-to-treat analysis is particularly important to avoid overestimation of the efficacy of an intervention due to the exclusion of participants who dropped out or who were excluded from the statistical analysis because they presented a low attendance at the intervention [47]. Moreover, it should be noted that some studies [25, 28, 29, 31] failed to report the BP measurement method. Therefore, our results should be interpreted with caution.

5 Conclusion

HIIT and MICT seem to provide similar reductions in resting systolic (mean 6.3 vs. 5.8 mmHg) and diastolic (mean 3.8 vs. 3.5 mmHg) BP in adults with pre- to established hypertension. This reduction in resting systolic BP is associated with a 7–14% lower risk of all-cause mortality, stroke, and coronary heart disease [34]. We also found that HIIT interventions improved $\dot{V}O_{2max}$ to a greater magnitude (mean 4.3 vs. 1.6 ml/kg/min) than MICT, with similar completion rates of the intervention (82.7 vs. 81.8%) and attendance at exercise training sessions (88.9 vs. 85.2%). Limited data were available about the incidence of adverse events during HIIT and MICT interventions. Future multicenter, long-term RCTs designed to compare the effects of HIIT versus MICT on BP, especially ambulatory BP, in a large sample of adults with pre- to established hypertension should be conducted.

Compliance with Ethical Standards

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Conflict of interest Eduardo Caldas Costa, Jacqueline Hay, Dustin Kehler, Kevin Boreskie, Rakesh Arora, Daniel Umpierre, Andrea Szwajcer, and Todd Duhamel declare that they have no conflicts of interest relevant to the content of this review.

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