

## SYSTEMATIC REVIEW

**Effects of physical activity on heart rate variability in adults with overweight or obesity: A systematic review and meta-analysis***Efecto del ejercicio físico sobre la variabilidad de la frecuencia cardiaca en adultos con sobrepeso u obesidad. Revisión sistemática y metaanálisis*Lubin Betancur-Sepúlveda<sup>1</sup>  Jhon Freddy Ramírez-Villada<sup>1</sup>  Carlos Mario Arango-Paternina<sup>1</sup> <sup>1</sup> Universidad de Antioquia - Instituto Universitario de Educación Física y Deportes - Medellín - Colombia.

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**Abstract**

**Introduction:** Cardiovascular autonomic dysfunction is a cardiovascular risk factor associated with various health conditions, mainly in individuals with overweight and obesity. In this regard, heart rate variability (HRV) is one of the tools that allow evaluating the activity of the autonomic nervous system (ANS), facilitating the physiological characterization and diagnosis of any individual.

**Objective:** To determine the effect of physical activity on HRV in adults with overweight or obesity (>18 years old).

**Materials and methods:** Systematic review. Cochrane, Medline, Embase, Lilacs, and PEDro databases were systematically searched using the following search strategy: study types: randomized controlled trials (RCTs) assessing the effect of exercise-based interventions on HRV parameters in individuals with overweight and obesity; publication period: January 2015 to June 2021; language: English; search terms: MeSH terms combined with Boolean operators “AND” and “OR”. The review protocol was registered in PROSPERO (code: CRD42021224027). Risk of bias was assessed using the Cochrane risk of bias assessment tool. A random-effects meta-analysis was performed to estimate the pooled effect for each outcome variable (HRV parameter) when the pooling of data was possible. Subgroup analyses were also performed to make comparisons between the different interventions. A significance level of  $p < 0.05$  was considered.

**Results:** The initial searches yielded 2 650 studies; of these, only 10 RCTs met the inclusion criteria. There were no statistically significant differences between the intervention and control groups in terms of changes in the HRV parameters: standard deviation of normal-to-normal R-R (NNN) intervals (SDNN): (weighted mean difference [WMD]=1.30, 95%CI: -5.93 to 8.53;  $p=0.72$ ); root mean square of successive R-R interval differences (RMSSD): (WMD=0.79, 95%CI: -0.29 to 1.87;  $p=0.15$ ); high frequency (HF): (WMD=6.67, 95%CI: 1.71 to 11.63;  $p=0.008$ ), and low frequency (LF): (WMD=-0.32, 95%CI: -0.73 to 0.10;  $p=0.13$ ).

**Conclusions:** Physical activity did not affect any of the HRV parameters studied in adults with overweight or obesity.

**Resumen**

**Introducción.** La disfunción autonómica cardiaca es un factor de riesgo cardiovascular asociado a diversas condiciones de salud, principalmente en personas con sobrepeso y obesidad. Al respecto, la variabilidad de la frecuencia cardiaca (VFC) es una de las herramientas que permite evaluar la actividad del sistema nervioso autónomo (SNA), facilitando así la caracterización fisiológica y el diagnóstico de cualquier individuo.

**Objetivo.** Determinar el efecto del ejercicio físico sobre la VFC en adultos (>18 años) con sobrepeso u obesidad.

**Materiales y métodos.** Revisión sistemática. Se realizaron búsquedas sistemáticas en Cochrane, Medline, Embase, Lilacs y PEDro mediante la siguiente estrategia de búsqueda: tipos de estudio: ensayos aleatorios controlados (ECA) que evaluaron el efecto de las intervenciones basadas en ejercicio físico sobre los parámetros de VFC en adultos con sobrepeso u obesidad; período de publicación: de enero 2015 a junio 2021; idioma: inglés; términos de búsqueda: términos MeSH combinados con los operadores booleanos “AND” y “OR”. El protocolo fue registrado en PROSPERO (código: CRD42021224027). El riesgo de sesgo se evaluó mediante la herramienta Cochrane de evaluación del riesgo de sesgo. Se realizó un metaanálisis de efectos aleatorios para estimar el efecto agrupado de cada variable de resultado (parámetro VFC) cuando fue posible agrupar los datos. También se realizaron análisis de subgrupos para hacer comparaciones entre las diferentes intervenciones. Se consideró un nivel de significancia de  $p < 0.05$ .

**Resultados.** Las búsquedas iniciales arrojaron 2 650 estudios; de estos, 10 ECA cumplieron los criterios de inclusión. No hubo diferencias estadísticamente significativas entre los grupos de intervención y control en los parámetros de la VFC: desviación estándar de los intervalos R-R normales (SDNN): (diferencia de medias ponderadas: [DMP]=1.30, IC95%: -5.93 a 8.53;  $p=0.72$ ); raíz de la media cuadrática de las diferencias de los intervalos R-R sucesivos (RMSSD): (DMP=0.79, IC95%: -0.29 a -1.87;  $p=0.15$ ); alta frecuencia (AF): (DMP=6.67, IC95%: 1.71 a 11.63;  $p=0.008$ ), y baja frecuencia (BF): (DMP=-0.32, IC95%: -0.73 a 0.10;  $p=0.13$ ).

**Conclusiones:** El ejercicio físico no afectó ninguno de los parámetros de la VFC estudiados en adultos con sobrepeso u obesidad.

## Introduction

Cardiovascular autonomic dysfunction is a cardiovascular disease (CVD) risk factor associated with the occurrence of health conditions such as hyperglycemia, high blood pressure, sudden death, and diabetes mellitus, therefore posing a higher risk of death.<sup>1</sup> The use of heart rate variability (HRV) has been proposed to monitor patients with cardiac autonomic dysfunction.<sup>2</sup> HRV is a simple tool that describes the oscillations between heart beats (R-R intervals), accounting for the influence of the autonomic nervous system (ANS) on the sinus node and allowing the evaluation of its cardiovascular health-related behavior.<sup>3</sup> Heart arrhythmia has been associated with low HRV,<sup>4</sup> especially in patients with overweight or obesity, in whom a direct relationship between all-cause mortality and ANS impairment has been described.<sup>5</sup> Indeed, one of the consequences of overweight and obesity is the deterioration of cardiac autonomic function (CAF), which is manifested by decreased vagal activity and elevated sympathetic nervous system (SNS) function.<sup>6</sup>

Physical activity (PA) is one of the most promising non-pharmacological interventions to prevent health complications in patients with overweight and obesity.<sup>7</sup> For instance, there is evidence showing that moderate-intensity continuous training (MICT) increases vagal tone, decreases resting HR, activates the parasympathetic nervous system (PNS), and favors autonomic control;<sup>8</sup> dynamic strength training (DST) improves metabolic and cardiopulmonary health;<sup>9</sup> and high-intensity interval training (HIIT) enhances physical and physiological fitness and contributes to reducing CVD risk factors.<sup>10</sup> However, there is insufficient scientific support to conclusively link the positive effect of such interventions on HRV in this population. These limitations are related to the high heterogeneity of components of PA programs in terms of frequency, intensity, duration (time), and types (FITT) of exercise.<sup>11,12</sup>

Considering the wide range of PA-based proposals for the complementary treatment of overweight or obesity, it is necessary to conduct a systematic review to identify the most appropriate FITT planning-related variables and contents of such interventions, as well as perform a meta-analysis of the contribution of PA to the modification of HRV, which would make it possible to evaluate the relevance of these models for the control and regulation of patients with overweight or obesity. Hence, the objective of this systematic review was to determine the effect of PA on HRV in adults (>18 years old) with overweight or obesity, while a secondary objective was to determine which training model (HIIT, MICT, and strength-based exercise training models) best modulates HRV in this population based on the evidence reported by randomized clinical trials (RCT).

## Materials and methods

This systematic review and meta-analysis were performed following the recommended guidelines for reporting this type of study and the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 statement.<sup>13</sup> The systematic review protocol was registered in PROSPERO on December 01, 2020 (protocol code: CRD42021224027).

## Search strategy

Systematic searches were conducted between February and March 2021 in the Cochrane, Medline, Embase, Lilacs, and PEDro databases using the following search strategy: Study types: RTCs assessing the effects of PA on HRV in adults (>18 years old) with overweight

and/or obesity; publication period: from January 2015 to June 2021; search terms: “Heart Rate Control”, “Autonomic Nervous System”, “Exercise Physical”, “High Intensity Interval Training”, “Obesity”, “Overweight”, “randomized controlled trial”, alone and in combination using the “AND” and “OR” Boolean operators. The search strategy was first implemented in Medline and then adapted to the other databases. In addition, a snowball search was conducted to identify other RCTs meeting the selection criteria.

### Eligibility and study selection

A data collection and selection form for each RCT was handled independently by two reviewers (JFV and CMA). To identify eligible RCTs, title and abstract screening were performed, followed by full-text reading by the two reviewers separately to verify compliance with the established inclusion criteria. Disagreements were discussed by the three authors (LFB, JFV, and CMA) until a consensus was reached.

### Selection criteria and data extraction

#### *Study types*

Only RCTs following the PICOT (patient, intervention, comparison, outcome, and [sometimes] time) framework with two or more parallel groups were included. Uncontrolled studies and those conducted in animals were excluded.

#### *Type of participants*

Only RCTs involving apparently healthy men and women (i.e., with a clinically controlled disease or without a diagnosis of any disease) and older than 18 years with overweight or obesity were included in the review.

#### *Type of interventions*

RCTs describing interventions lasting four or more weeks, regardless of whether they reported or not the FITT of HIIT, MICT, and DST protocols, and the comparison model or control group, were included.

#### *Type of outcomes*

We looked for RCTs reporting the following intervention outcomes as part of their main and surrogate outcomes: outcomes on HRV, time domain parameters such as R-R intervals, standard deviation of normal-to-normal R-R (NN) intervals (SDNN), percentage of adjacent R-R intervals that differed from each other by more than 50 milliseconds (pNN50), root mean square of successive R-R intervals differences (RMSSD), and frequency domain parameters (low frequency [LF], high frequency [HF], and LF/HF ratio).

### Data analysis

Once the RCTs meeting the inclusion criteria were selected, strict criteria were followed for their assessment, and the resulting data were documented: sample size (n), mean and standard deviation (SD) values, last name of the first author, year of publication,

evaluation method, and HRV parameters (R-R intervals, SDNN, pNN50, HF, LF, and LF/HF ratio). Likewise, outcomes of interest, description of instruments, data collection protocol, and methods utilized were extracted. This information was collected independently by each of the three authors in a Microsoft Excel database (V2020); then, these databases were compared to identify discrepancies, review them, and based on this process, obtain a database with final data.

Finally, the Consensus on Exercise Reporting Template (CERT)<sup>14</sup> was used for reporting PA interventions, as it is a helpful instrument for assessing the completeness of interventions and allows the replication of the research and enriches its results.

### Risk of bias

The risk of bias of the studies included in the review was independently assessed by LFB, JFV, and CMA according to the criteria described in the Cochrane Handbook and using the Risk of Bias Tool (Version 5.1.0).<sup>15</sup> Each criterion was scored as low, high, or unclear risk.

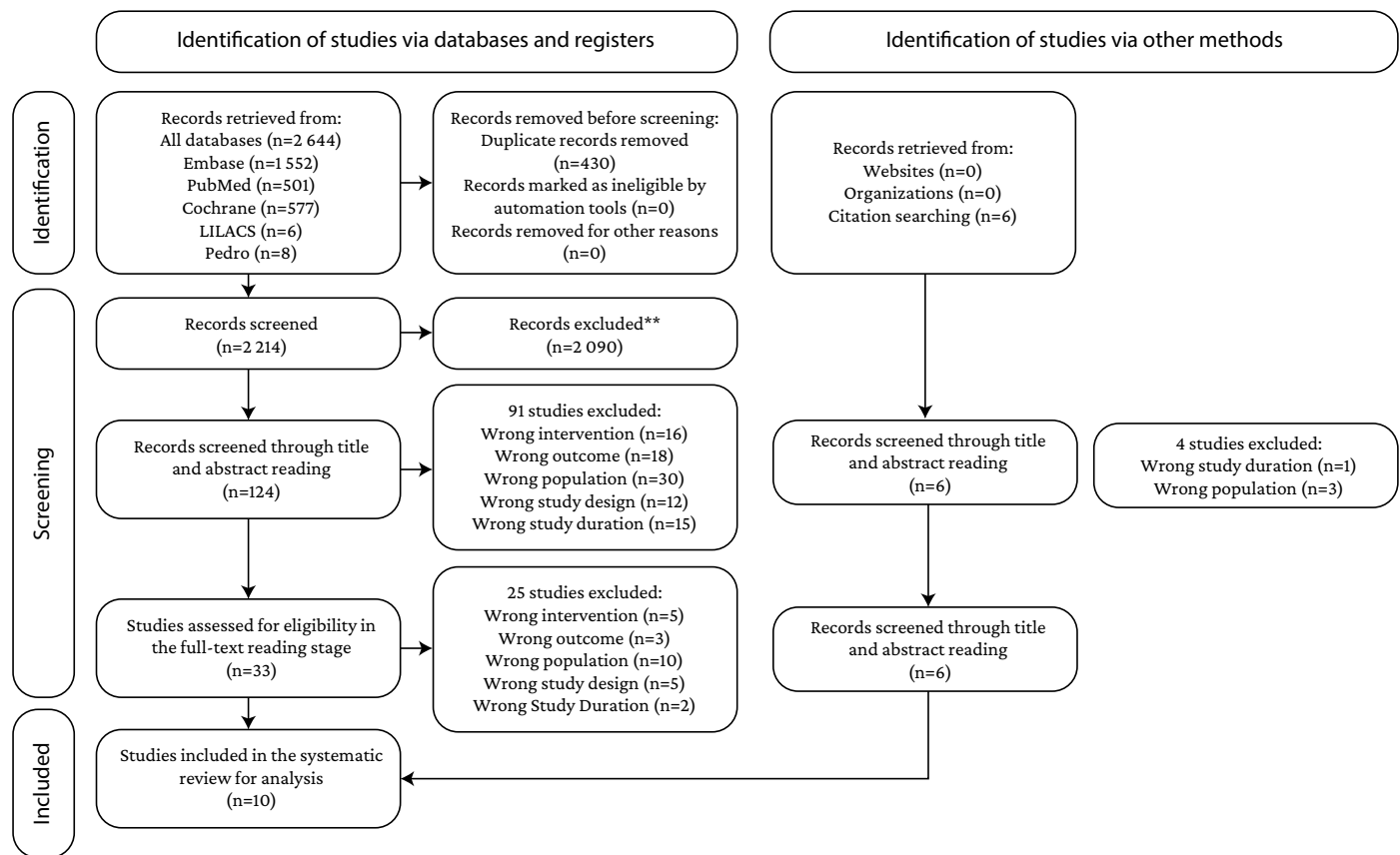
### Statistical analysis

The Cochran's Q test and the I<sup>2</sup> test were applied since the primary outcomes were continuous variables. The standardized mean difference  $\pm$  (SD), with its corresponding 95% confidence interval (CI), was considered as the effect size, and a  $p < 0.05$  was established as the significance level. The change in the measurement of HRV time and frequency parameters was assessed, and forest plots were used to detect and quantify heterogeneity among studies. Heterogeneity was considered to be low and moderate if I<sup>2</sup> values  $< 25\%$  and between 25-50% were obtained, respectively, while high heterogeneity was established in the case of  $p < 0.05$  or I<sup>2</sup>  $> 50\%$  values. All statistical analyses were performed using RevMan 5.3 software (Cochrane Collaboration). A random effects meta-analysis was carried out to calculate pooled effects for each outcome variable. Subgroup analyses were then performed comparing differences: HIIT and MICT versus the control group in HF, LF, RMSSD, and SDNN; HIIT versus MICT in HF, LF, and RMSSD, and DST versus MICT and functional strength training (FRT) in HF and LF.

## Results

### Studies included in the systematic review

The initial searches yielded 2 650 articles (577 in Cochrane, 1 552 in Embase, 501 in Pubmed, 6 in Lilacs, and 8 in PEDro). These searches, as well as their results, were imported into the Rayyan software. Once duplicates ( $n=430$ ) were removed, 2 090 articles were discarded in the title screening stage since they did not meet the inclusion criteria; 91 of the remaining 129 were discarded for the same reason in the abstract screening stage. Then, after performing a full-text reading of the remaining 33 studies, 25 were excluded. In addition, a snowball search was conducted in the 8 RCTs that met the inclusion criteria, and 2 more eligible studies were identified and included for final analysis. Therefore, 10 RCTs<sup>16-25</sup> were included in this systematic review and meta-analysis. The study selection process is shown in Figure 1.



**Figure 1.** Study selection flowchart.

Source: Own elaboration.

As shown in Table 1, the included RCTs were conducted in different countries (Australia, Brazil, Denmark, England, Italy, Lithuania, New Zealand, Republic of South Korea, and Saudi Arabia), and all 10 reported HRV parameters in patients with overweight and obesity,<sup>16,18,25</sup> type 2 diabetes mellitus,<sup>17,19,20,22,24</sup> and metabolic syndrome<sup>21,23</sup> as primary outcomes. In total, there were 398 participants, 205 were assigned to the HIIT, MICT, or DST intervention group and 193 to the control group. The mean age in the intervention group was 52.72 years, and in the control group, 52.27. All interventions lasted between 8 and 16 weeks: 12-week interventions in 5 studies,<sup>19,20,22-24</sup> 16-week interventions in 4 RCTs,<sup>16-18,21</sup> and 8-week intervention in one study.<sup>25</sup>

**Table 1.** Characteristics of the studies included in the review.

Study, Country	Patient group intervention				Exercise				HRV measures	Adherence-Compliance program	Other outcomes *
	Condition	Sample size	Age, (mean ± SD)	% Male	Type/group	Intensity	Session time / Supervised	Duration (months) / Frequency (day/week)			
Ramos <i>et al.</i> <sup>21</sup> 2017 Australia	MetS	16	56±8	47%	HIIT	HIIT, 4 × 4-minute intervals at 85-95% [HRpeak], * 3 min active recovery	38 min/session, preceded by 10 min warm-up, 3-min cooldown / partially supervised	4 months/3 days/week	SDNN, RMSSD,	HIIT, 89% MICT, 89%	HRrest, HRpeak, HRreserve, VO2absolute (L·min <sup>-1</sup> ), VO2relative (mL·kg <sup>-1</sup> ·min <sup>-1</sup> ), Weight (kg), Total body fat (%)
		19	54±11	56%	MICT	MICT 30 min at 60-70% [HRpeak], 30 min/session	30 min/session, preceded by 10 min warm-up, 3min cooldown / partially supervised	4 months/5 days/week	pNN50, HF, LF, LF/HF		
Cassidy <i>et al.</i> <sup>22</sup> 2019 England	Type 2 diabetes mellitus	11	59±3	88%	HIIT	HIIT, 38 min RPE reached: 16-17 ("very hard"). Five 2min intervals and 3min recovery	38min/session, preceded by 5 min warm-up, 5 min cooldown / not supervised	3 months/3 days/week	SDNN, HF, LF, LF/HF	100%	HRpeak, Weight (kg), BMI
		11	60±3	99%	Control group	No physical activity, just the usual	N/A	N/A			
Kang <i>et al.</i> <sup>20</sup> 2016 Republic of Korea	Type 2 diabetes mellitus	8	56.0±7.4	0%	MICT	MICT 30min/session at 60%, [HRreserve], RT 30min/session 60-80% IRM	30min/session (MICT) 30min/session and (RT), in both cases preceded by warm-up and stretching for 10-min., 10-min cooldown /not supervised	3 months/3 days/week	SDNN, RMSSD, HF, LF, LF/HF	N/R	VO2relative (mL·kg <sup>-1</sup> ·min <sup>-1</sup> ), Weight (kg), Total body fat (%)
		8	57.5±4.6	0%	Group control	No physical activity, just the usual	N/A	N/A			
Rodrigues <i>et al.</i> <sup>18</sup> 2020 Brazil	Overweight and Obesity	26	52±5.8 35.6±4.2	28%	HIIT	4HIIT,4×4-minute intervals at 85-95% [HRmax], * 3 min active recovery	40 min/session preceded by 10 warm-up, 3-min cooldown / supervised	4 months/3 days/week	SDNN, RMSSD, HF, LF, LF/HF	HIIT and MICT 75%	HRrest, HRreserve, VO2absolute (L·min <sup>-1</sup> ), VO2relative (mL·kg <sup>-1</sup> ·min <sup>-1</sup> ), BMI
		19	52±5.8 35.6±4.2	36%	MICT	MICT 30 min at 60-70% [HRmax], 30 min/session	30 min/session preceded/heated by 10 minutes and ended with a 3-minute cooldown / supervised	4 months/5 days/week			
Turri-Silva <i>et al.</i> <sup>23</sup> 2020 Brazil	MetS	19	52.31±6.56	53%	FRT	FRT and CRT 30% and 40% of IRM (3 weeks), sets and reps increased weekly, reaching 2 sets, 16 rep, and 90% of IRM. The interval between sets was 40 to 90s	N/R /supervised	2.5 months/3 days/week	SDNN, RMSSD, HF, LF	N/R	Other outcomes not reported
		19	53.4±5.22	68%	CRT						
Bellavere <i>et al.</i> <sup>17</sup> 2018 Italy	Type 2 diabetes mellitus	19	57.1±1.6	68%	AER	AER 60-65% [HRreserve]	60min/session/supervised	4 months/3 days/week	HF, LF, LF/HF	AER 86±3.4% RES 89±3.7%	HRrest (bpm)
		11	51.4±2	68%	RES	RES 3 sets of 10 reps at 70% -80% 1-RM/1min recovery	60min/session/supervised				
Zlibinaite <i>et al.</i> <sup>25</sup> 2020 Lithuania	Overweight and Obesity	17	44.8±6.5	0%	AER on a bicycle.	AER aerobic training on a bicycle. HR obtained at 50% to 60% of VO2max	60min/session, 50min/session preceded by 5 min warm-up, 5min cooldown /supervised	2 months/5 days/week	RMSSD, HF, LF	AER and Group control (95.7% [5.6%])	Weight (kg), BMI
		16	48.8±5.3	0%	Control group	No physical activity, just the usual	N/A	N/A			
Hallman <i>et al.</i> <sup>16</sup> 2017 Denmark	Overweight and Obesity	57	44.9±9.2	24.6%	AER	AER, ≥60% of VO2max	30min/session/supervised	4 months/3 days/week	SDNN, RMSSD, HF, LF	64%-Loss-(15-19) AER-Control group.	HRrest (bpm), BMI
		59	45.7±8.1	23.7%	Control group	No physical activity, just the usual.	N/A	4 months/5 health lectures/week			
Ahmed <i>et al.</i> <sup>19</sup> 2019 Saudi Arabia	Type 2 diabetes mellitus	20	52.4±4.6	100%	HIIT	HIIT,4×4-minute intervals at 80-90% [HRmax], * 3 min active recovery at 50%-60% [HRmax]	HIIT, 38 min/session, 30min/session, preceded by 3 min warm-up, 3 min cooldown / supervised	3 months/3 days/week	SDNN, RMSSD, HF, LF	HIIT 100%	HRrest (bpm), VO2relative (mL·kg <sup>-1</sup> ·min <sup>-1</sup> ), Weight (kg), BMI
		20	51.8±5.1	100%	Control group	No physical activity, just the usual.	N/A	N/A			
Wormgoor <i>et al.</i> <sup>24</sup> 2018 New Zealand	Type 2 diabetes mellitus	12	52.2±7.1	100%	HIIT + RT	HIIT-interspersed with twelve 1-minute sets at 95% eWLmax 1-minute recovery sets, alternating with 8 sets of 30 sec at 120% eWLmax interspersed with 2:15 minute recovery sets -RT-3 sets of 10 reps at 75% of IRM	60 min/session. 28 min/session, preceded by 2:30 min warm-up, 2:30 min cooldown, and 30 min (RT) / supervised	3 months/3 days/week	LF/HF	HIIT + RT 91.2±9.9% MICT + RT 90.4±6.8%	Other outcomes not reported.
		11	52.5±7		MICT + RT	MICT- 26 min at 55% of eWLmax - RT- 3 sets of 10 rep at 75% of IRM	60 min/session.26 min/session, preceded by 3 min warm-up, 3 min cooldown, / 30 min (RT) / supervised				

MetS: metabolic syndrome; HIIT: high-intensity interval training; MICT: moderate-intensity continuous training; FRT: functional resistance training; RPE: rating of perceived exertion; CRT: conventional resistance training; AER: aerobic training; RT: resistance training; eWLmax: estimated maximum workload; RES: strength training; HR: heart rate; HRmax: maximum heart rate; HRpeak: peak heart rate; eWLmax: maximal workload; IRM: one-repetition maximum; HRrest: resting heart rate; HRreserve: heart rate reserve; VO2max: maximum oxygen consumption; VO2absolute: absolute oxygen consumption; VO2relative: relative oxygen consumption; BMI: body mass index; SDNN: standard deviation of R-R intervals; RMSSD: root mean square of successive R-R intervals; pNN50: percentage of adjacent NN intervals that differed from each other by more than 50 milliseconds; LF: low frequency; HF: high frequency; LF/HF: LF/HF ratio.

Source: Own elaboration.

## Interventions

Out of the 10 studies, 5 used the HIIT protocol as the intervention method,<sup>18,19,21,22,24</sup> 4 used the MICT protocol,<sup>16,17,20</sup> and 1 used the DST method.<sup>23</sup> The intensity of the MICT protocol in both the intervention and the control group ranged between 60 and 70% [HRpeak, HRreserve, or HRmax], while in the HIIT protocol, it ranged between 80 and 95% [HRpeak or HRmax]. Five studies compared HIIT or MICT with a control group,<sup>16,19,20,22,25</sup> 3 compared HIIT with MICT,<sup>18,21,24</sup> and 2 compared two strength protocols with MICT.<sup>17,23</sup> The duration of each training session varied from 30 to 60 minutes in the case of MICT interventions; training sessions in HIIT and DST protocols lasted 38 and 30 minutes, respectively. Regarding the frequency of the interventions, training sessions were carried out between 3 and 5 days per week in MICT interventions and 3 days per week in both HIIT and DST protocols.

## Reporting of the interventions - Consensus on Exercise Reporting Template

The assessment of the reporting of the interventions was carried out using the CERT checklist. The average score of the RCTs was 14 (73.68% compliance), and all described the FITT of the intervention and the means used for its execution. The full report is shown in Table 2.

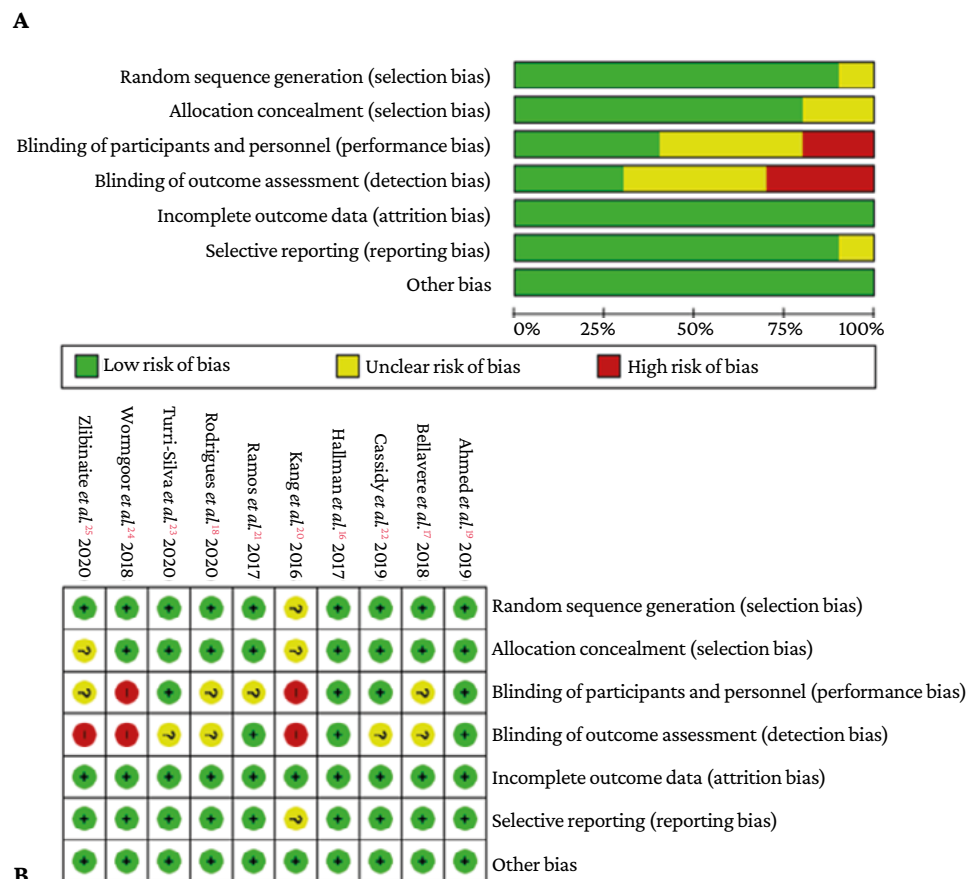
**Table 2.** Consensus on Exercise Reporting Template (CERT) summary of findings.

N°	Study ID	(n) Intervention	Multidisciplinary team	CERT items																	Total	%			
				1	2	3	4	5	6	7a	7b	8	9	10	11	12	13	14a	14b	15			16a	16b	
1	Ramos <i>et al.</i> <sup>21</sup> 2017	16	Medical research team	1	1	1	1	1	1	1	1	1	0	0	1	1	1	1	1	0	1	0	15	79%	
2	Cassidy <i>et al.</i> <sup>22</sup> 2019	11	Medical research team	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	0	1	1	1	17	89%	
3	Kang <i>et al.</i> <sup>20</sup> 2016	8	N/R	1	0	1	0	0	0	0	1	1	0	0	0	1	1	1	1	0	1	0	1	9	47%
4	Rodrigues <i>et al.</i> <sup>18</sup> 2020	26	Medical research team	1	1	1	1	1	1	1	1	1	0	0	1	1	1	1	1	0	1	0	15	79%	
5	Turri-Silva <i>et al.</i> <sup>23</sup> 2020	19	Medical research team	1	1	1	1	0	0	1	1	1	0	1	0	1	1	1	0	1	0	1	13	68%	
6	Bellavere <i>et al.</i> <sup>17</sup> 2018	19	Medical research team	1	1	1	1	1	0	1	1	1	0	0	1	1	1	1	0	1	1	1	15	79%	
7	Zlibinaite <i>et al.</i> <sup>25</sup> 2020	17	Medical research team	1	0	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	17	89%	
8	Hallman <i>et al.</i> <sup>16</sup> 2017	57	Medical research team	0	1	1	1	1	0	0	0	0	0	0	0	1	0	1	0	0	1	0	7	37%	
9	Ahmed <i>et al.</i> <sup>19</sup> 2019	20	Medical research team	1	1	1	1	0	0	1	1	1	0	0	1	1	1	1	1	1	1	1	15	79%	
10	Wormgoor <i>et al.</i> <sup>24</sup> 2018	12	Medical research team	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	1	1	1	17	89%	

Source: Own elaboration.

### Evaluation of risk of bias

The risk of bias was assessed as per the criteria described in the Cochrane Handbook and using the risk of bias tool (Version 5.1.0).<sup>15</sup> Most studies did not explicitly stated if there was blinding of personnel (medical staff and researchers) and participants: 3 RCTs had a high risk of bias,<sup>20,24,25</sup> 4 had an unclear risk,<sup>17,18,22,23</sup> and 3 had a low risk of bias in these 2 domains.<sup>20,24,25</sup> Regarding random sequence generation, 9 studies had a low risk of bias,<sup>16-19,21-24</sup> and 1 had an unclear risk.<sup>20</sup> Concerning allocation concealment, 2 RCTs had unclear risk,<sup>20,25</sup> and the remaining 8 had a low risk of bias.<sup>16-19,21-24</sup> Finally, all studies had a low risk of attrition, reporting, and other biases (Figure 2). Overall, the quality of the 10 RCTs was moderate to high.



**Figure 2.** (A) Quality assessment of included studies. (B) Risk of bias of the studies identified; specificity the 10 RCTs. “+” represents low risk of bias; “?” represents unclear risk of bias; “-” represents high risk of bias. Source: Own elaboration.

### Outcomes

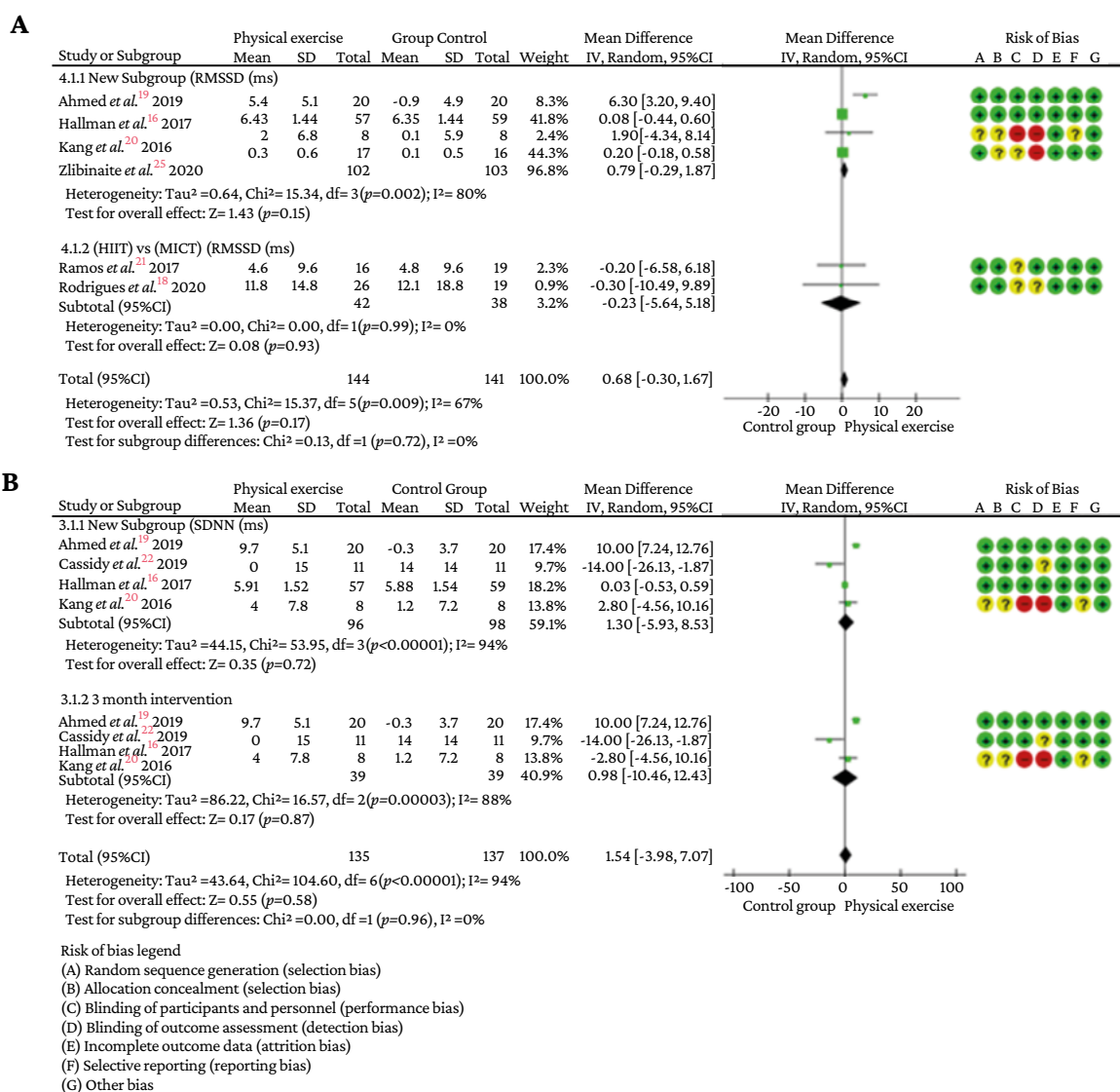
#### HRV measurements

All studies reported measurements for the time domain and frequency domain parameters. SDNN data were reported in 7 studies,<sup>16,18-23</sup> RMSSD in 7 studies,<sup>16,18-21,23,25</sup> and HF and LF in 9 studies.<sup>16-23,25</sup>



Effect of PA on HRV-RMSSD

The pooled effect for RMSSD was reported in 4 studies<sup>16,19,20,25</sup> assessing the changes produced by the intervention (HIIT or MICT) in comparison with the control group, and in 2 RCTs<sup>18,21</sup> comparing the effect of HIIT versus that of MICT. Heterogeneity was high in the HIIT or MICT versus control group subgroup ( $I^2=80\%$ ,  $p=0.002$ ). Although a slight difference in favor of these two PA models compared to the control group was observed in the random effects model, results show that changes in RMSSD were not statistically significant in the intervention group (weighted mean difference [WMD]=0.79, 95%CI: -0.29 to 1.87;  $p=0.15$ ). On the other hand, heterogeneity was low ( $I^2=0\%$ ,  $p=0.99$ ) in the HIIT versus MICT subgroup, and results of the random effects model showed that there were no statistically significant differences in favor of either model. It seems that both HIIT and MICT show the same results (WMD=-0.23; 95%CI: -5.64 to 5.18;  $p=0.93$ ) (Figure 3).



**Figure 3.** A) Summary of the meta-analysis of the effect of HIIT and MICT on RMSSD in patients with overweight and obesity, stratified by the HIIT and MICT versus control group subgroup, and the HIIT versus the MICT subgroup. B) Summary of the random effects meta-analysis of the effect of HIIT or MICT on SDNN in patients with overweight and obesity, stratified by overall pooled result and 3-month intervention. Squares denote study-specific outcome estimates, and the square size represents the study's specific weight. Horizontal lines and figures in parentheses represent the 95%CI. Diamonds indicate summary results with the corresponding 95%CI.

Source: Own elaboration.

### Effect of PA on HRV-SDNN

Four RCTs evaluated changes in SDNN after the intervention (HIIT (n=2)<sup>19,22</sup> or MICT (n=2)<sup>16,20</sup> in comparison with the control group; the intervention lasted 3 months in 3 studies,<sup>19,20,22</sup> and 4 months in the remaining one.<sup>16</sup> A significantly high heterogeneity was found in the overall pooled result and the 3-month intervention subgroup ( $I^2=94%$ ;  $p=0.00001$  and  $I^2=88%$ ;  $p=0.0003$ , respectively). The random effects model showed that there were no significant differences between the intervention group and the control group in terms of SDNN changes in both the overall pooled result (WMD=1.30, 95%CI: -5.93 to 8.53;  $p=0.72$ ) and the 3-month intervention subgroup (WMD=0.98, 95%CI: -10.46 to 12.43;  $p=0.87$ ) (Figure 3).

### Effect of PA on HRV-HF

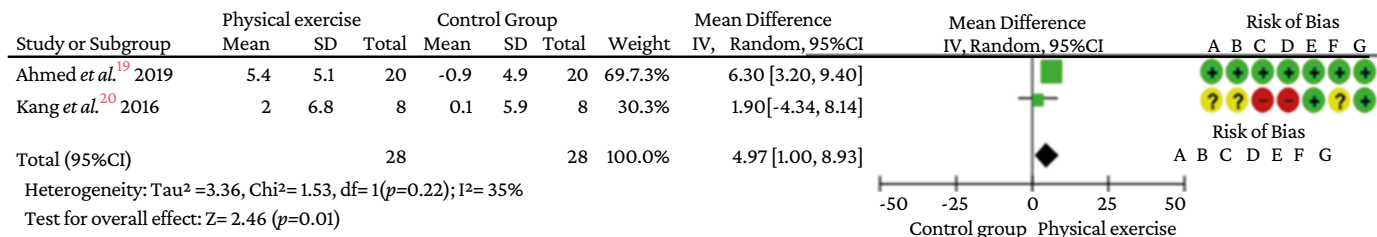
HF was reported in 3 studies<sup>19,20,22</sup> that evaluated changes in this HRV parameter after the intervention with HIIT or MICT compared to the control group. A significantly high heterogeneity was found in this subgroup ( $I^2=97%$ ;  $p=0.00001$ ). The effects of HIIT and MICT on HF were compared in 2 studies,<sup>19,21</sup> and heterogeneity between these 2 RCTs was low ( $I^2=0%$ ;  $p=0.57$ ). Finally, DST versus MICT and FRT were compared in 2 other studies;<sup>17,23</sup> heterogeneity in this subgroup was high ( $I^2=88%$ ;  $p=0.004$ ). The results of the random effects model in these 3 subgroups showed that none of these intervention models had statistically significant effects on HF: HIIT or MICT versus control group (WMD=6.67, 95%CI: 1.71 to 11.63;  $p=0.008$ ), HIIT versus MICT (WMD=0.17, 95%CI: -0.28 to 0.61;  $p=0.57$ ), and DST versus MICT and FRT (WMD=0.91 95%CI: -0.67 to 2.50;  $p=0.26$ ) (Figure 4).

### Effects of PA on HRV-LF

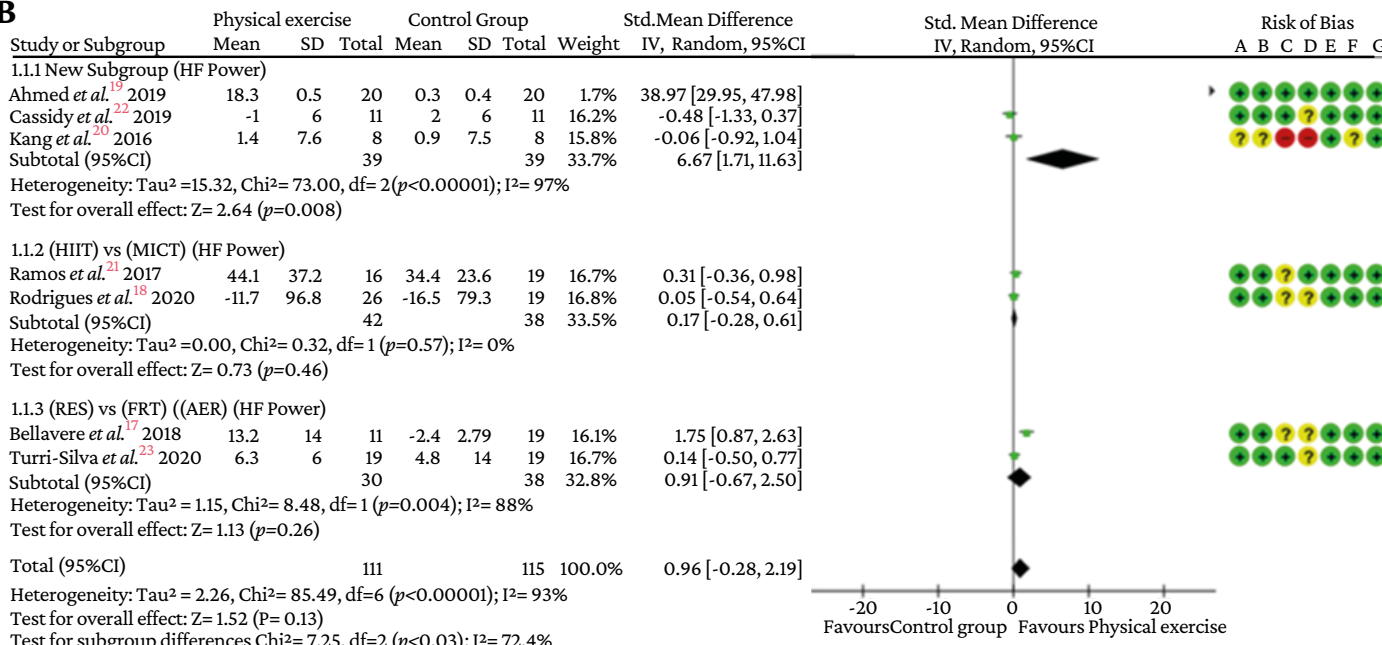
The pooled effect on LF was reported in 3 studies<sup>19,20,22</sup> that assessed changes in this HRV parameter after the intervention with HIIT or MICT compared with the control group. In this subgroup, heterogeneity was low ( $I^2=0%$ ;  $p=0.58$ ), and there were no significant differences between groups in the random effects model (WMD=-0.32, 95%CI: -0.73 to 0.10;  $p=0.13$ ). The effects of HIIT and MICT on LF were compared in 2 studies.<sup>18,21</sup> In this subgroup, heterogeneity was high ( $I^2=78%$ ;  $p=0.03$ ) and, according to the results of the random effects model, there were no statistically significant changes in favor of either model. It seems that both HIIT and MICT show the same results in terms of changes in LF (WMD=10.72, 95%CI: -39.89 to 61.34;  $p=0.68$ ) (Figure 5).

Regarding the quality of the evidence, the comparisons made by the 10 RCTs (either between them or with the control group) were deemed to be of poor quality. Therefore, the certainty of the evidence decreased. Both the lack of blinding and errors in the randomization of participants led to this grading. Besides, the wide confidence intervals, the high heterogeneity among studies, and the small sample size of each study also contributed to the fact that the outcomes reported by the RCTs, which are of great importance to those in charge of developing clinical practice, were finally graded as having a poor quality of evidence. The summary of findings according to the GRADE approach is shown in Table 3.

**A**



**B**

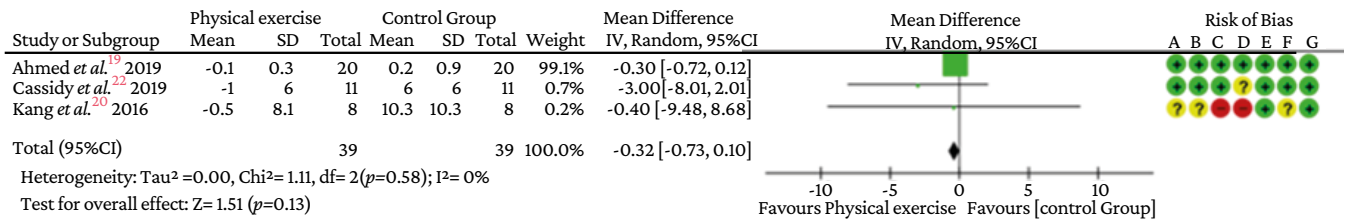


- Risk of bias legend
- (A) Random sequence generation (selection bias)
  - (B) Allocation concealment (selection bias)
  - (C) Blinding of participants and personnel (performance bias)
  - (D) Blinding of outcome assessment (detection bias)
  - (E) Incomplete outcome data (attrition bias)
  - (F) Selective reporting (reporting bias)
  - (G) Other bias

**Figure 4.** A) Summary of the meta-analysis on the effect of HIIT or MICT on RMSSD in patients with overweight and obesity and stratified by the 12-week intervention versus control group subgroup. B) Summary of the meta-analysis on the pooled effect of HIIT or MICT versus control group, HIIT versus MICT, and DST versus MICT, FRT on HF individuals with overweight and obesity.

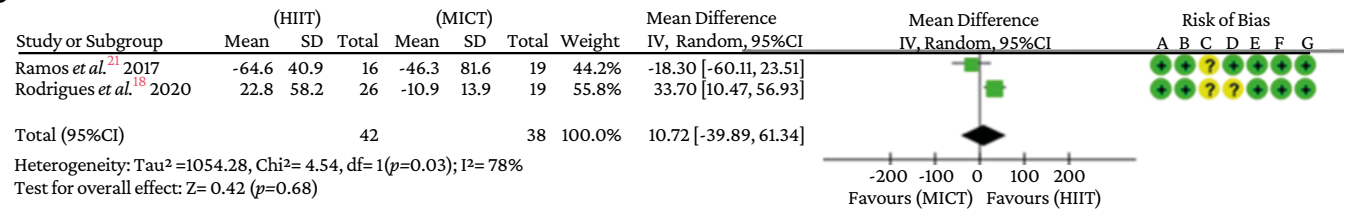
Source: Own elaboration.

**A**



Risk of bias legend  
 (A) Random sequence generation (selection bias)  
 (B) Allocation concealment (selection bias)  
 (C) Blinding of participants and personnel (performance bias)  
 (D) Blinding of outcome assessment (detection bias)  
 (E) Incomplete outcome data (attrition bias)  
 (F) Selective reporting (reporting bias)  
 (G) Other bias

**B**



Risk of bias legend  
 (A) Random sequence generation (selection bias)  
 (B) Allocation concealment (selection bias)  
 (C) Blinding of participants and personnel (performance bias)  
 (D) Blinding of outcome assessment (detection bias)  
 (E) Incomplete outcome data (attrition bias)  
 (F) Selective reporting (reporting bias)  
 (G) Other bias

**Figures 5.** A) Summary of the meta-analysis on the pooled effect of HIIT and MICT versus control group. B) Summary of the meta-analysis on the pooled effect of HIIT versus MICT on LF in individuals with overweight and obesity.  
 Source: Own elaboration.

**Table 3.** Grading of Recommendations Assessment, Development, and Evaluation (GRADE) summary of findings.

No. of studies	Certainty assessment					No. of patients		Effect Absolute (MD 95%CI)	Certainty	Importance
	Risk of bias	Inconsistency	Indirect evidence	Imprecision	Other considerations	Physical exercise	Control group			
SDNN ms (follow-up: 4 months; evaluated with ECG 12 Leads 5/minutes)										
4	Serious	Very serious	Not serious	Very serious	None	96	98	1.3 ms higher (5.93-8.53)	⊕○○○ Very low	Important
RMSSD ms (follow-up: 4 months; evaluated with: ECG 12 Leads 5/minutes)										
4	Very serious	Very serious	Not serious	Very serious	None	102	103	0.79 ms higher (5.43-4.62)	⊕○○○ Very low	Important
RMSSD ms HIIT vs. MICT (follow-up: 4 months; evaluated with: ECG 12 Leads 5/minutes)										
3	Serious	Not serious	Not serious	Very serious	None	61	50	0.4 ms lower (5.43-4.62)	⊕○○○ Very low	Important
RMSSD ms HIIT, MICT vs. Control Group (follow-up: 4 months; evaluated with: ECG 12 Leads 5/minutes)										
2	Serious	Not serious	Not serious	Very serious	None	28	28	4.97 ms higher (1-8.93)	⊕○○○ Very low	Important
RMSSD ms MICT vs. Control Group (follow-up: 4 months; evaluated with: ECG 12 Leads 5/minutes)										
3	Very serious	Not serious	Not serious	Very serious	None	82	83	0.16 ms higher (0.14-0.47)	⊕○○○ Very low	Important

**Table 3.** Grading of Recommendations Assessment, Development, and Evaluation (GRADE) summary of findings. (Continued)

No. of studies	Certainty assessment					No. of patients		Effect	Certainty	Importance
	Risk of bias	Inconsistency	Indirect evidence	Imprecision	Other considerations	Physical exercise	Control group	Absolute (MD 95%CI)		
<b>HF Power ms (follow-up: 4 months; evaluated with: ECG 12 Leads)</b>										
3	Serious	Very serious	Not serious	Very serious	None	39	39	6.67 ms higher (1.71-11.63)	⊕○○○ Very low	Important
<b>HF ms HIIT vs. MICT (follow-up: 4 months; evaluated with: ECG 12 Leads 5/minutes)</b>										
2	Serious	Not serious	Not serious	Very serious	None	42	38	0.17 ms higher (0.28-0.61)	⊕○○○ Very low	Important
<b>LF ms (follow-up: 4 months; evaluated with: ECG 12 Leads 5/minutes)</b>										
3	Serious	Not serious	Not serious	Very serious	None	39	39	0.32 ms lower (0.73 0.1)	⊕○○○ Very low	Important
<b>LF ms HIIT vs. MICT (follow-up: 4 months; evaluated with: ECG 12 Leads)</b>										
2	Not serious	Very serious	Not serious	Very serious	None	42	38	10.72 ms higher (39.89-61.34)	⊕○○○ Very low	Important

CI: confidence interval; MD: mean difference; ms: milliseconds

Source: Own elaboration.

## Discussion

The aim of this study was to determine the effect of HIIT and MICT models on HRV in adults with overweight or obesity (>18 years old) based on the evidence reported by RCTs. The literature review stage allowed summarizing the existing evidence of the effects of different PA modalities on autonomic control of cardiovascular function in individuals with overweight and obesity. The high heterogeneity found among the studies included in this review and the small number of participants in each study limited the analysis and the possibility of drawing conclusions in favor or against any PA model in relation to changes produced in the main variables that modulate the ANS.

A total of 10 RCTs (398 participants) reporting the effects of PA interventions on the main variables that modulate the ANS as their outcomes were included in this systematic review. The mean age of the participants was 52.72 years (intervention group) and 52.27 (control group), and 218 were males. Although the number of studies for each exercise modality and each outcome variable was unequal, the results showed that the effects were not statistically significant, except for the 12-week HIIT or MICT intervention versus control group subgroup ( $p=0.008$ ), thus preventing us from concluding in favor of any of these two models in terms of positive changes in HRV parameters. PA interventions produced changes in all the HRV parameters analyzed, which is in line with what has been reported in the literature.<sup>26</sup>

Results of the meta-analysis showed that, compared to the control group, 12-week MICT or HIIT interventions did not cause statistically significant changes in SDNN. In the case of RMSSD, a slight difference, although not statistically significant, was observed in favor of these two exercise models in comparison with the control group. However, when the 12-week HIIT or MCIT intervention versus control group subgroup<sup>19,20</sup> was analyzed, a significant change in RMSSD in favor of these two interventions was found (WMD=4.97, 95%CI: 1.00 to 8.93;  $p=0.01$ ). Finally, when these two training models were compared (HIIT versus MICT subgroup), there were no statistically significant differences in favor of either model. It appears that both models may produce positive changes in this HRV parameter in individuals with overweight and obesity. It should be noted that SDNN and RMSSD represent the vagal nervous system, and that reductions in these parameters are associated with increased risk of cardiovascular morbidity and mortality.<sup>27</sup>

In the case of HF and LF, there were no statistically significant differences in favor of PA interventions (HIIT and MICT) compared to the control group. In addition, there were no differences in favor of any intervention models in the HIIT versus MICT and the DST versus MICT and FRT subgroups.

Although it is clear that HF represents the PNS, there is not yet a consensus about LF since some studies consider it an index that allows evaluating sympathetic activity, while others state that it is a parameter that reflects both sympathetic and parasympathetic activity.<sup>28</sup> It is worth noting that in terms of interpretation, an increased LF suggests that there are no positive changes in HRV, as it would mean a sustained increase in SNS activity.<sup>18</sup>

Consequently, even though there is evidence of the positive changes caused by PA interventions in the ANS,<sup>26</sup> considering that any cardiovascular adaptation requires an increase in cardiac vagal modulation and a decrease in SNS activity to be deemed as beneficial, the mechanisms through which these changes occur are still unknown.<sup>29</sup> In fact, there is still controversy about the physiological benefits of PA interventions with the ANS since some authors, such as Sousa Fortes *et al.*,<sup>30</sup> in a study conducted in 31 young adults from Brazil (aged 18-25 years) to assess the effect of two different resistance training methods (clustering and multi-sets) on HRV, describe physiological changes related to the reduction of metabolite concentrations and proinflammatory cytokines production levels after exercising, while others such as Grässler *et al.*,<sup>31</sup> in a systematic review that included 26 studies evaluating the effects of PA interventions (endurance, resistance, high-intensity, coordinative, or multimodal training) on HRV, report decreased norepinephrine levels in the blood after exercising, which would lead to CAF balance. In addition, body weight changes after completion of PA interventions could also promote positive changes in HRV.<sup>29</sup>

Furthermore, while one of the objectives of this study was to determine which PA training model, HIIT or MICT, best modulates changes in the ANS of individuals with overweight and obesity, the results show that neither model is superior to the other in terms of their effects on the HRV parameters that were assessed. There were no statistically significant differences when they were compared, perhaps due to the high heterogeneity among the studies comparing these two training models or their small sample size. Even so, it is worth noting the changes produced by PA interventions make it possible to infer that HIIT, MICT, and DST could lead to positive changes in RMSSD and HF, important parameters that modulate HRV.

It is worth noting that the results of the present study should be interpreted with caution, that more RCTs assessing the effects of PA interventions on the variables analyzed here are required, and that such studies must maximize control bias measures since situations such as the presence of high or unclear risk of bias give rise to doubts regarding the outcomes assessed, so potentially valuable information might be lost. Furthermore, due to the small number of studies, heterogeneity was substantial in each analysis; moreover, not all RCTs provided information on the means and their SDs using the same unit of measurement, which might reduce the statistical power of the meta-analyses and induce biases in the estimates.

Finally, there is currently no clear evidence on which training models (HIIT and MICT) modulate HRV the best, as studies claim HIIT is better or vice versa. For example, Ramos *et al.*,<sup>21</sup> in a research conducted in Australia in 56 people with metabolic syndrome who completed a 16-week HIIT or MICT program, claim HIIT was superior to MICT. Nevertheless, according to a recent systematic review conducted by Picard *et al.*<sup>11</sup> (21 studies; 523 participants), MICT benefits in modulating HRV were superior to those of HIIT.

The findings of the present study are in agreement with those of some individual studies, such as the one conducted by Kang *et al.*<sup>20</sup> in South Korea in 16 women with type 2 diabetes mellitus, and systematic reviews such as the one by Picard *et al.*,<sup>11</sup> which have reported that results regarding the effects of any PA intervention on the ANS after its completion are inconclusive and are not statistically significant.

The reporting of the interventions by the RCTs included for analysis was evaluated using the CERT tool. The average score of the 10 RCTs was 14 (i.e., a 73.68% compliance in the CERT scoring scale: 0-19), all provided information on the FITT of the PA training models, and most of them explained how the interventions were supervised and provided data on the participants' adherence. This information implies that all studies met sufficient CERT checklist items for their interventions to be replicable. Therefore, findings are a valuable resource to help decision-makers and medical staff in developing and implementing these interventions in clinical practice.<sup>14</sup>

On the other hand, in terms of the methodological quality of the RCTs included in this review, most of them did not provide explicit information about the blinding of personnel and participants and how outcomes were evaluated, which reduced the certainty of the evidence. In addition, although the overall quality of the 10 studies was moderate to high, these findings could lead to an overestimation of the effect, so they should be cautiously interpreted. Likewise, it should be noted that publication bias was not assessed because the number of studies grouped by variable in the meta-analysis was <10.<sup>10</sup>

Lastly, this systematic review highlights the need to strictly increase the methodological quality of primary studies, since the gaps in the reporting of interventions weaken the quality of evidence, which were rated using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.

Some of the limitations of this study include the fact that there may be a risk of publication bias, as only studies indexed in the Cochrane, Medline, Embase, Lilacs, and PEDro databases were searched. Also, the absence of a person specialized in library science during the literature search stage, as well as the fact that only papers published in English and within the last 5 years at the time of conducting the search were considered, could have limited the amount of information retrieved and relevant data might have been left out. In addition, including studies conducted in people with type 2 diabetes mellitus and metabolic syndrome, along with the small number of studies included for analysis and the small sample size of each study, could have contributed to the high heterogeneity among studies and the inability to make strong assertions regarding the effects of PA interventions on HRV parameters in the target population.

## Conclusions

Physical activity did not affect any of the HRV parameters studied in adults with overweight or obesity. In addition, it seems that both HIIT and MICT-based interventions for individuals with overweight and obesity could lead to similar changes in most of the variables modulating the ANS.

## Conflicts of interest

None stated by the authors.

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