ISSN 0120-4157

Biomédica

Revista del Instituto Nacional de Salud

Citación provisional:

Arboleda-Serna VH, Feito Y, Patiño-Villada FA, Vargas-Romero AV, Arango-Vélez EF. Effects of a high-intensity interval training compared to moderate-intensity continuous training on maximal oxygen consumption and blood pressure in healthy men: A randomized controlled trial. Biomédica. 2019;39(3).

Recibido: 12-04-18

Aceptado: 31-10-18

Publicación en línea: 12-12-18

Effects of a high-intensity interval training compared to moderate-intensity continuous training on maximal oxygen consumption and blood pressure in healthy men: A randomized controlled trial

High-intensity interval training in healthy men

Efecto del entrenamiento por intervalos de alta intensidad comparado con continúo moderado sobre el consumo máximo de oxígeno y la presión arterial en hombres sanos: ensayo clínico aleatorio

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Introduction: Aerobic exercise generates increased cardiorespiratory fitness (CF), which results in a protective factor for cardiovascular disease. High-intensity interval training (HIIT) might cause higher increases on CF in comparison with moderate-intensity continuous training (MICT); nevertheless, current evidence is not conclusive.

Objective: To compare the effects of a low-volume HIIT and a MICT on maximal oxygen consumption (VO_{2max}), systolic blood pressure (SBP), and diastolic blood pressure (DBP) during a period of eight weeks in healthy men between 18-44 years of age.

Materials and methods: A randomized controlled trial was conducted. Forty-four volunteers were randomized to HIIT (n=22) or MICT (n=22). Both groups performed 24 sessions on a treadmill. The HIIT group completed 15 bouts of 30 seconds [90-95%, maximal heart rate (HR_{max})], while the MICT group completed 40 minutes of continuous exercise (65-75% HR_{max}).

Results: Intra-group analysis showed an increase in VO_{2max} of 3.5 ml/kg/min. [confidence interval (CI) 95%, 2.02 to 4.93; p=0.0001] in HIIT and 1.9 ml/kg/min. (CI 95%, -0.98 to 4.82; p=0.18) in MICT. However, the difference between the two groups was not statistically significant (1.01 ml/kg/min. IC 95%, -2.16 to 4.18, p=0.52). MICT generated a greater reduction in SBP compared to HIIT [median 8 mmHg (p<0.001)]. Finally, no statistically significant differences were found between the groups for DBP.

Conclusions: Results indicate no significant change in VO_{2max} was observed with a low-volume HIIT protocol versus MICT after 24 sessions. In contrast, MICT provided a greater reduction in SBP compared to HIIT.

This study is registered as a clinical trial via ClinicalTrials.gov with identifier number: NCT02288403

Key words: High-intensity interval training; blood pressure; exercise; cardiorespiratory fitness, randomized controlled trial.

Introducción. El ejercicio aeróbico incrementa la capacidad cardiorrespiratoria (CCR), considerada factor protector para enfermedades cardiovasculares. El entrenamiento de intervalos de alta intensidad (HIIT) podría causar mayores incrementos en la CCR comparado con entrenamiento continúo moderado (ECM), sin embargo, la actual evidencia no es concluyente.

Objetivo. Comparar los efectos de un HIIT de bajo volumen y un ECM sobre el consumo máximo de oxígeno (VO_{2max}), la presión arterial sistólica (PAS) y la presión arterial diastólica (PAD) durante ocho semanas, en hombres sanos entre 18-44 años.

Materiales y métodos. Ensayo clínico controlado con asignación al azar. Cuarenta y cuatro voluntarios fueron asignados al azar a HIIT (n=22) o ECM (n=22). Ambos grupos ejecutaron 24 sesiones en tapiz rodante. El grupo HIIT completó 15 cargas de 30 segundos [90-95%, de la frecuencia cardiaca máxima (FCmáx)], ECM realizó 40 minutos continuos (65-75% FCmáx).

Resultados. Análisis intra-grupo mostró un aumento en $VO_{2máx}$ de 3.5 ml/kg/min. [intervalo de confianza (IC) 95%, 2.02 a 4.93; p=0.0001] en HIIT, y 1.9 ml/kg/min. (IC95, -0.98 a 4.82; p=0.18) en ECM. Sin embargo, las diferencias entre grupos no fueron estadísticamente significativas (1.01 ml/kg/min. IC95%, -2.16 a 4.18, p= 0.52). El ECM generó una mayor reducción en la PAS comparado con HIIT [mediana 8 mmHg (p<0.001)]. Finalmente, no se hallaron diferencias estadísticamente significativas entre grupos para PAD.

Conclusiones. Los resultados indican que no hay diferencias en el efecto sobre $VO_{2máx}$ con un protocolo HIIT de bajo volumen versus ECM. Por el contrario, ECM provee una reducción mayor en la PAS comparado con HIIT. Registrado en ClinicalTrials.gov, código: NCT02288403.

Palabras clave: entrenamiento de intervalos de alta intensidad; presión sanguínea; ejercicio; capacidad cardiovascular, ensayo clínico controlado aleatorio.

Maximum oxygen consumption (VO_{2max}) is considered the main indicator to evaluate cardiorespiratory fitness (CRF) (1,2). VO_{2max} is directly related to cardiovascular health, and its increase is associated with a reduced risk of death from cardiovascular disease and for all-cause mortality (3-5). Moderate-intensity continuous training (MICT) has been the most widely used method to increase VO_{2max} in the past. However, in recent years, high-intensity interval training (HIIT) methods have been practiced by individuals with different health conditions, and its use is increasing (6,7). Currently, the gain in VO_{2max} achieved with HIIT versus MICT is under discussion. Some studies have shown that HIIT generated faster and more significant adaptations in VO_{2max} when compared to MICT (8-14), while other investigations have found less pronounced increases in VO_{2max} with HIIT, indicating some limitations exist with these types of programs (15-17). Nonetheless, it should be noted that the protocols used in these HIIT studies were comprised of short periods of load and more extensive recovery periods compared to other interventions (9,10,14,18,19).

High blood pressure is a common health condition that is associated with increases in the incidence of all-cause mortality and CVD. Cornelissen and Smart (20) reported a decrease in SBP and BPD of 3.5 mmHg (95% CI, 2.3-4.6) and 2.5 mmHg (95% CI, 1.7-3.2) with aerobic exercise, respectively. Moreover, studies comparing continuous training and HIIT among non-exercisers hypertensive controls, reported significant decreases in SBP of 8-mmHg in all groups (12), and mean decreases in SBP and DBP with HIIT of 12 and 8 mmHg, respectively, compared with continuous workouts that achieved non-significant reductions of 4.5 and 3.5 mmHg (21). Although exercise is a fundamental aspect in the primary prevention, treatment and control of hypertension, the optimal frequency, intensity, time, and type of exercise to reduce SBP and BPD values are still unclear (22). Therefore, the primary objective of this study was to compare the effect of a low-volume HIIT program versus a MICT program in VO_{2max} among healthy men. The secondary objective was to identify the effect of both exercise programs on systolic (SBP) and diastolic blood pressure (DBP). We hypothesize that those in the HIIT group would have significant greater improvements in VO_{2max} and BP responses compared to the MICT group.

Materials and Methods

This two-arm randomized control trial (RCT) with parallel groups was developed following the CONSORT statement for randomized trials of non-pharmacological treatment (23), and it is registered as a clinical trial with identified number NCT02288403.

Participants were recruited via posters, word of mouth, social media, and email around the academic community of a Public University in Medellin, Colombia. For this study, men between the ages of 18 and 44 years, who did not meet the physical activity recommendations of 150 minutes of aerobic exercise per week, were asked to participate. Those who responded and agreed to participate voluntarily in the study were asked to sign an informed consent form. The University Research Ethics Committee approved all forms and study protocols. Individuals with any of the following characteristics were excluded from the study: those who practiced HIIT, smoked, had a history of pulmonary, metabolic or cardiovascular disease, arrhythmias, heart failure, hypertension, diabetes mellitus, were being treated with anticoagulants, beta blockers, calcium antagonists, bronchodilators, steroids, or had cognitive, sensory, neuromotor, and/or musculoskeletal disorders that could affect their participation in any of the study protocols. All subjects were evaluated by a sports medicine physician, who authorized their participation in the study according to the criteria mentioned above.

For the purpose of this study, we were interested in examining changes in maximal oxygen consumption (VO_{2max}) between the two groups. We evaluated VO_{2max} via graded exercise test on a treadmill (Trackmaster® model TMX 425C) using a portable gas analyzer (K4b^2 Cosmed Inc., IL, USA). We were also interested in examining changes in both SBP and DBP between the groups. Blood pressures (SBP and DBP) was measured with an Omron® M3 HEM-7200-E (Omron Healthcare, Co., Ltd., Kyoto, Japan) automatic blood pressure monitor. A detailed description of the study design along with specific details of the protocols utilized to measure the primary and secondary outcomes have been published elsewhere (24). Briefly, participants were randomly assigned to a high-intensity interval-training (HIIT) group, or moderate-intensity continuous training (MICT) group. All training sessions for groups were monitored using a heart rate monitor (Polar FT1; Polar, Lake Success, NY) and supervised by a qualified trainer on alternate days (3 times/week) for eight-weeks. Prior to their assigned exercise session, all participants completed a five-minute warm up at 50-60% maximal heart rate (MHR), and completed their respective session with a three-minute cool-down at 40-50% MHR.

The MICT group was prescribed a 40-minute treadmill session at 65-75% of MHR throughout the eight-week intervention. In addition, they were encouraged to continue with their regular daily routines but were discouraged to engage in any other form of exercise. They were provided an Omron HJ-112 (Bannockburn, IL) pedometer to monitor their daily ambulatory activity. The HIIT group underwent 15 bouts of 30 seconds at 90–95% MHR followed by 60 seconds of recovery at an equivalent speed to achieve 50-55 % of maximal oxygen consumption on a treadmill. We used percentage of VO_{2max} for recovery in order to determine an accurate speed during the recovery period for each participant, considering that 60-seconds is not enough time for the heart rate to decrease and provide an accurate measurement of recovery. We considered using this method to provide a more accurate estimate of recovery intensity. A qualified trainer was present throughout each session to ensure participants reached and maintained the desired intensity. The speed of the treadmill was adjusted manually while the elevation was maintained constant at 10%. In addition, following their respective interventions, all participants preformed a resistance-training program three times per week, following established guidelines (22) with a qualified trainer. The purpose of this non-differential co-intervention was simply to introduce participants to the benefits of resistance training. Considering its intensity, we believe this intervention did not have any influence in any of the primary or secondary outcomes (24).

In order to control selection bias and minimize confounding variables, a randomization sequence was generated through four- and six-size permuted blocks, with a 1:1 ratio between the groups (25). The concealment was made by means of numbered, sealed envelopes, and the volunteers were assigned to either the HIIT or the MCIT group according to the order of entry in the study. An investigator without direct contact with any of the study participants completed the blinding procedures. In addition, in order to control information bias, those responsible for recruitment, evaluation, and analysis of the outcome data were blinded to the group assignment and only completed the testing sessions. The staff responsible for conducting the exercise intervention was trained according to the protocols designed for each program. The initial and final evaluations of the outcomes were made at the same time of day, and the interventions were carried out individually (24). Identification codes were used for the participants, and all the information was stored in file cabinets and password-secured computers only available to the researchers.

In order to determine an appropriate sample size, a mean difference in VO_{2max} of 3.5 ml/kg/min with standard deviations (SD) of 2.6 and 4.6 for the HIIT and MICT groups, respectively (10), was considered as a minimal difference to reduce CVD risk (3,4). We used a 95% confidence level, an alpha error of 5% and a beta error of 20%, assuming a 1:1 ratio between the groups. Using Epidat software (version 4.0), a sample of 20 individuals per group, plus 10% for potential losses, was calculated.

Intention-to-treat analyses were conducted for comparisons between groups. In addition, sensitivity analyses [per-protocol analysis (PP)] were completed for subjects who completed ≥70% of the training sessions. Normality test, homoscedasticity test, and linearity tests were considered as basic assumptions for the use of t-tests and analysis of covariance (ANCOVA) (26) to control for the baseline value of VO_{2max} and adjust for possible confounding variables. Logarithmic transformations and Box-Cox transformations were performed only for secondary outcomes (SBP and DBP). However, it was not possible to comply with the parametric assumptions. As summary measures, means and SD were used. The Mann-Whitney U Test was adopted when the assumptions for parametric analyses could not be obtained; in this case, the values are reported in medians and interquartile ranges (IQR). Two-tailed statistical significance tests with a $p<0.05$ and a 95% confidence level (95% CI) were used. Multiple imputation techniques were applied to the management of missing data for VO_{2max}, SBP, and DBP (27). All calculations were performed with the STATA software (version 13).

Results

Data were collected between March 2015 and May 2016. A total of 135 individuals, who responded to our request to participate were evaluated. Of those who responded, 26 did not meet the selection criteria, three did not agree to participate and 62 did not enter the study for other reasons (primarily due to time difficulties to comply with the sessions). The final sample consisted of 44 men, distributed evenly between the HIIT and MICT groups (N=22 for HIIT group, and N=22 for MICT group; see Fig 1).

Participant baseline characteristics are presented in table 1. At baseline, the HIIT group was significantly older and heavier than the MICT group. In addition, the HIIT group had a significantly higher body mass index (BMI), waist circumference (WC), and fat mass (%FM) than the MICT group. Fat–free mass (FFM) was significantly higher in the MICT group compared to the HIIT group. In the other variables evaluated, no differences were found between the groups (see Table 1). Regarding the losses to follow–up, two were reported in the HIIT group and one in the MICT group (see Fig 1).

For these three subjects, multiple imputation techniques described above were used, and were conducted with intention-to-treat analyses.

After adjusting for baseline (BL) values, age, BMI, weight, and height there was no significant difference in the primary outcome (VO_{2max}) between the HIIT and MICT groups (difference (Δ) 0.98 ml/kg/min; 95%CI -2.26 to 4.23, p=0.54) (table 2). VO_{2max} increased significantly in those who received the HIIT intervention [39.2 ± 6.0 ml/kg/min vs. 42.7 ± 6.0 ml/kg/min; Δ 3.5 ml/kg/min (95%CI, 2.02 to 4.93; p=0.0001)], while in the MICT group, the increase of this variable did not reach significance [(VO_{2max} change 1.9 ml/kg/min (95%CI, -0.98 to 4.82; p=0.18)]. When analyzing the VO_{2max} changes individually, it was possible to identify that the participants of the HIIT group presented an average gain of 9.4% vs. 6.0% found in the subjects in the MICT protocol (p=0.67), with a positive intervention response of 81.8% in HIIT, compared to 59% for MICT (p=0.09).

In the PP analyses (those who completed ≥70% of the programmed training sessions), no differences were found in the primary outcome (VO_{2max}) between groups post–trainings (HIIT: 44.0 ± 5.8 ml/kg/min vs. MICT: 45.1 ± 8.9 ml/kg/min; p= 0.74). In the intra–group analyses, statistically significant differences and important practical differences were found in both those who received the HIIT intervention (40.4 ± 6.0 ml/kg/min vs. 44.0 ± 5.8; p= 0.0004), as well as in the MICT group (41.7 ± 9.8 ml/kg/min vs. 45.1 ± 8.9; p= 0.03).

SBP and DBP values did not meet the assumption needed to utilize the ANCOVA test. Therefore, the non-parametric Mann-Whitney U Test was used. In the ITT analyses, a lower value of SBP was found post-intervention (PI) in those in the MICT group [HIIT: 124.5 mmHg (IQR 120.0–129.5) vs. MICT: 116.5 mmHg (IQR 115.0–119.0); median difference 8 mmHg; p <0.001). In addition, no significant differences were found after eight-weeks in DBP between the groups (HIIT: 79.2 mmHg (IQR 76.0–85.0) vs. MICT: 79.0 mmHg (IQR 71.5–83.0); median difference 0.2 mmHg; p= 0.15) (see Table 2).

In the intra–group analyses, no median differences were observed in SBP for those who received the HIIT intervention [120.7 mmHg (IQR 116.0–133.5) vs. 124.5 mmHg (IQR 120.0 - 129.5); median difference 3.8 mmHg; p=0.15], or in DBP [79.2 mmHg (IQR 76.0–85.0) vs. 79.2 mmHg (IQR 76.0–85.0); p=0.40]. In the MICT group, SBP was significantly reduced after the intervention (118.2 mmHg (IQR 116.0–126.0) vs. 116.5 mmHg (IQR 115.0–119.0); median difference -1.7 mmHg; p=0.02), while DBP did not change (77.7 mmHg (IQR 70.5–87.5) vs. 79.0 mmHg (IQR 71.5–83.0); median difference 1.3 mmHg; p=0.77).

In the PP analyses, the PI values of SBP were lower in the MICT group compared to the HIIT group [MICT: 117.2 mmHg (IQR 115.5–121.0) vs. HIIT: 125.7 mmHg (IQR 120.0–129.5); p < 0.001], whereas for the DBP, the differences did not achieve statistical or practical difference [MICT: 79.2 mmHg (IQR 71.5–83.0) vs. HIIT: 79.2 mmHg (IQR 75.0–85.0); p=0.26]. In the intra–group analysis of the PP analyses, no statistically significant differences were found in the SBP and DBP values (table 2).

Training intensities were individually monitored and controlled by trained personnel, who continuously supervised the heart–rate monitor of each participant during the exercise sessions in order to guarantee compliance with the intensities for each load. The mean heart rate was determined to be 169.6 beats per minute, equivalent to 91.2% HR_{max}.

In total, five adverse events (three in the MICT group and two in the HIIT group) occurred during the interventions period, all of which affected the musculoskeletal system. The three events in the MICT group included one event of Hoffitis in the right knee that was not associated with training in this study, as this originated from lifting a heavy object at home. The second event included muscle fatigue in the gastrocnemius associated with running on the treadmill, which improved by reducing the training load. The third event was a right medial ankle contusion, not associated with the interventions, which occurred while the participant played soccer one day after finishing the training sessions, forcing the final evaluations to be postponed for 12 days. In the HIIT group there were two adverse events associated with the intervention. The first was right pes anserine bursitis due to training and associated with the inclination of the treadmill. The participant abandoned the intervention after 15 sessions due to the non–improvement of the symptoms, despite treatment with oral non–steroidal anti-inflammatories. The second event was a tendinitis in the vastus medialis oblique, in its insertion in the patella, which was associated with training on the treadmill. The participant partially improved with a reduced training load and non–steroidal anti–inflammatory drugs.

In regards to adherence, 18 individuals in the HIIT group and 19 in the MICT group (81.8% vs. 86.4%, respectively; p=0.71) completed ≥70% of the planned sessions. It should be noted that 13 subjects in the HIIT group completed ≥ 90% of the sessions, while 10 volunteers in the MICT group completed ≥ 90% of the sessions.

Discussion

The main finding of this study suggests that after adjusting for confounding variables, such as age, BMI, weight, height, and baseline VO_{2max}, a HIIT protocol was not superior to the MICT protocol in improving the VO_{2max} of this group of apparently healthy young men who engage in physical activity for less than 150 minutes/week. This finding is congruent with recent meta–analysis results from apparently healthy young adults, in which it was reported that HIIT–based interventions (regardless of their characteristics) did not have significant improvements in CRF compared to MICT protocols (17,28,29). Conversely, from the practical and statistical points of view, those with health impairments, such as classic cardiovascular risk factors (i.e. obesity, hypertension, blood glucose disorders, and among others), coronary heart disease, and heart failure, the HIIT protocols have shown to be more advantageous than MICT to increase VO_{2max}, (15,30-34). It is noteworthy to mention that in these individuals, an increase of 1.0 ml/kg/min in VO_{2max} is associated with reduction in overall mortality, which is considered a clinically significant and relevant change. However, in apparently healthy individuals, an increase of at least 3.5 ml/kg/min in VO_{2max} (1 MET) is required for long–term reductions in mortality and morbidity (4,35,36).

As it is well known, the randomization process attempts to balance and account for known and unknown factors that could affect the dependent variables; however, randomization cannot fully guarantee the identification of these factors, especially when sample sizes are small. Therefore, when there are differences between groups in some of the variables as happened in this case, these variables should be adjusted in the final analyzes (37), which justifies the use of an ANCOVA for our VO_{2max} analyses. It should be noted that the HIIT group presented a VO_{2max} that was 3.0 ml/kg/min lower at baseline compared to the MICT group, which could explain the higher gain obtained by this group (+3.5 ml / kg / min) compared to the increase in MICT group (+1.9 ml / kg / min).

This finding is congruent with previous findings revealing that HIIT has an apparent adaptive effect on VO_{2max} in favor of less trained subjects (30). In addition, we should mention that individuals in the HIIT group were about six-years-older than those in the MICT group; yet, despite these differences, participants in the HIIT group were still able to improve VO_{2max} values, even though it is well established that VO_{2max} decreases about 10% per decade, regardless of physical activity (38). These findings support the notion that HIIT is beneficial to improve aerobic capacity regardless of age and initial fitness levels.

In the intra–group analyses, the VO_{2max} increase was clinically significant in the participants undergoing HIIT, as it changed from 39.2 ml/kg/min at baseline to 42.7 ml/kg/min at the end of the intervention. This finding is similar to that of other studies, which show that a HIIT program provides improvement in aerobic power in young, sedentary adults after two and eight weeks of training (39) compared to those who do not exercise. Moreover, it is important to note that the intra–group gains in VO_{2max} observed in HIIT averaged 9.4%, reaching proportions up to 28.9%. Meanwhile, the MICT group only averaged a VO_{2max} increase of 5.9%, with increases up to 43.1%. Improvements in VO_{2max} for those who complete HIIT could be explained by central adaptations. These adaptations include increases in systolic volume and cardiac output, as well as peripheral changes (40). In addition, peripheral changes, increases in the number of mitochondria and their increased size, increased mitochondrial enzyme activity, arterial vasodilation, increased nitric oxide bioavailability, and reduced oxidative stress may provide significant improvements in CRF. It should be noted that although no differences were found in changes in VO_{2max}

when comparing HIIT vs. MICT, interval training achieved a clinically significant increase in this variable. This benefit occurred with a 7.5-minute stimulus, which represented 19% of the continuous protocol stimulus and 56% of the total effective exercise time. These finding suggests that important beneficial physiological adaptations could be generated in a shorter amount of time. In addition, it should be noted that previous studies (9,10,14,18,19) performed HIIT interventions with longer load periods and recovery times with fewer or equal intervals, in comparison to this RCT.

In regards to the secondary outcome, a lower SBP was found in individuals who received the MICT intervention, a difference that achieved statistical and clinical significance. It is worth noting that SBP in the HIIT group increased by 3.8 mmHg in relation to its initial value, whereas the MICT group SBP was reduced by 1.7 mmHg from baseline. These changes explain the difference in blood pressures between the groups. Our findings disagree with previous data regarding the benefits attributed to aerobic exercise, as both HIIT and MICT contribute to the reduction of SBP and BPD, with higher decreases in hypertensive individuals (21). Nonetheless, no physiological explanations can be provided by the authors to support the increase in SBP in the HIIT group other than coincidental, as all the evaluations were performed at the same time of day, under equal conditions, and following equal protocols. This finding differs from that reported in two meta–analyses involving people with cardiovascular risk factors, in which no differences in SBP were found in those trained with HIIT vs. MICT (15,40). On the other hand, there is evidence that indicates that in order to improve vascular function, long–duration HIIT is more effective compared to short–duration HIIT (40). This could explain the reduction in SBP in those receiving the MICT as the HIIT stimulus only lasted little over seven-minutes. For DBP, no PI differences were found between the groups, nor when comparing the baseline and PI values within each of the groups. These results are partially consistent with those found in the meta–analysis by Ramos et al. (40), which found that postmenopausal women with cardiovascular risk factors achieved a reduction in this blood–pressure component. Also, these results coincide with the meta analysis findings of Hwang et al. (15), which included individuals with cardio–metabolic alterations, reporting no differences in the SBP and DBP values.

While the stimulus with the strength protocol that both groups received was applied as a non–differential co–intervention, it is possible that this intervention had some influence on the effect of VO_{2max}, as well as SBP and DBP. However, according to the results presented by Buckley et al. (41) in their RCT, when comparing a HIIT protocol against a protocol that included HIIT and strength exercises in recreationally active women, no statistically significant differences were found between the groups for VO_{2max} (38.3 ± 4.6 vs. 38.5 ± 5.4 ml/kg/min; $p=0.99$). Similarly, a recent study among patients with cardiovascular disease compared the effects of a six-months program of HIIT or MICT, which included resistance training during the last three-months, and reported no significant improvements in VO_{2peak} for either of the two groups between three and six months of training (HIIT: 28 ± 17 % vs. MICT: 26 ± 29 %; $p = 0.824$) or SBP and DBP ($p \geq 0.05$) (42). Therefore, we believe our “secondary intervention”, as designed, did not have a significant role in altering VO_{2max} for anyone in the groups.

The practical justification for including the strength component in both intervention protocols lies in the need to include strength exercises as a fundamental part of any holistically oriented physical activity (PA) program. It is important that different components of physical fitness, cardiorespiratory endurance, muscular strength and endurance, are incorporated in exercise intervention programs. Thus, our study focused on improving not only cardiovascular health, but also musculoskeletal health for apparently healthy adults (22). The results obtained with this study may have a greater practical applicability, given that recommendations for PA are aimed to develop the different components of physical fitness, especially the cardiorespiratory and musculoskeletal components.

A familiarization period before the intervention protocol may be beneficial in reducing adverse effects of exercise training. Although our study only reported five incidents total between the HIIT and MICT groups, a reduction of these aversive events could be beneficial in completion of these specific exercise interventions. The familiarization period could help individuals adjust to demand of the different loads specific training, given the subjects low level of physical activity.

In addition to the methodological design used (RCT), a main strength of this study was having the ability to conduct the training sessions in an individualized manner and under the constant supervision of a qualified trainer. Nevertheless, we believe this study is not without limitations, which could affect its findings. Most significantly, we believe not being able to control the participants PA levels outside of the research interventions may have affected the variations in VO_{2max} from baseline values, which may have hindered the detection of possible differences between the two groups. Although the volunteers were given a pedometer as an instrument to monitor PA, it was not possible to record the steps in all of the participants. Another limitation was not having the VO_{2max} values in baseline as an inclusion criterion for the volunteers. Although the level of physical activity was used as an inclusion criteria through the Global Physical Activity Questionnaire (GPAQ), some of the individuals who were randomly assigned to the MICT group had VO_{2max} baseline values above the average for subjects with low physical activity levels according to age. Given the characteristics of the interventions in both arms of this RCT, which are based on exercise sessions that demanded a group of volunteers to exercise at moderate intensity and another group at high intensity, it is complex to blind participants to the interventions. Finally, it should be noted that this sample size was calculated with a power of 80%.

In summary, the results of this RCT do not allow us to affirm that HIIT is superior to MICT to increase VO_{2max} in healthy men 18 to 44 years old or vice versa. It is prudent, however, to assert, as stated in the meta–analysis of Milanovic et al. (17), that both methods increase VO_{2max}, even though that when compared, neither shows a more beneficial response. As suggested by Gist et al. (28) and Weston et al. (30), additional studies are required to not only test the effectiveness of HIIT on VO_{2max}, but also its viability related to musculoskeletal limitations, exercise tolerance, and adherence to the protocol. Finally, since most exercise intervention studies have been developed and completed in controlled environments and under constant supervision, it would be very practical to carry out further investigations under less–controlled conditions in relation to the daily life of the participants.

Acknowledgments

The authors are indebted to everyone in the Laboratory for Physical Activity and Sports Sciences, University of Antioquia for their help and support through this project.

Conflicts of interest

The authors report no conflicts of interest.

Funding

The study was partially funded by The Epidemiology Group of the National Faculty of Public Health, University of Antioquia, who financed compensation for the trainers.

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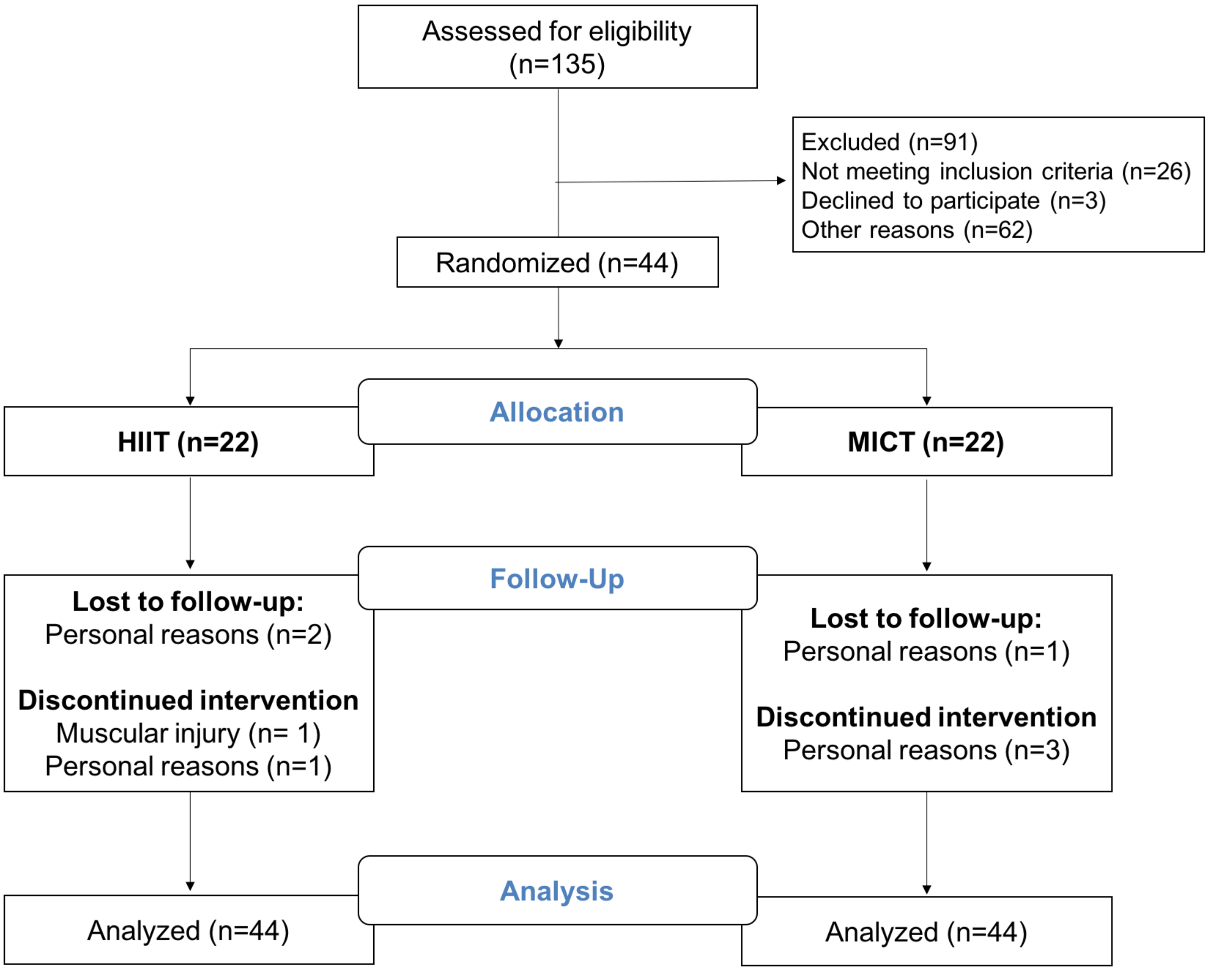

Figure 1. Participant enrollment flow diagram

Table 1. Baseline characteristics of study subjects

	HIIT (n=22)	**MICT** (n=22)	***p***
Age (years)**	29.5 (25-38)	23.5 (20-34)	0.03‡
Height (cm)*	173.5 (5.79)	171.9 (5.69)	0.36
Weight (kg)**	79.1 (74.6-85.9)	69.3 (63.2-77.4)	0.008‡
BMI (kg/m^2)**	26.2 (24.6–27.3)	23.5 (22.0–26.8)	0.03‡
WC (cm)**	87.9 (83.0–91.7)	79.2 (74.7–87.0)	0.006‡
FM (%)*	26.2 (5.6)	20.7 (7.4)	0.008‡
FFM (%)*	35.9 (3.5)	39.7 (5.0)	0.006‡
PAL (Mets/min/week)**	880.0 (540.0-1440.0)	960.0 (360.0-1280.0)	0.91
$VO_{2máx}$ (mL/kg/min)*	39.2 (6.0)	42.2 (9.1)	0.20
SBP(mmHg)**	120.7 (116.0-133.5)	118.2 (116.0-126.0)	0.40
DBP(mmHg)**	79.2 (76.0-85.0)	77.7 (70.5-87.5)	0.72

Body mass index (BMI), Waist circumference (WC), Fat mass (FM), Fat-free mass (FFM), Physical activity level (PAL), Maximum oxygen consumption ($VO_{2máx}$), Systolic blood pressure (SBP), Diastolic blood pressure (DBP). *Values are given as mean ± SD. **Values are given as medians and interquartile ranges. ‡Differences between groups at base line p<0.05.

Table 2. Effects of HIIT versus MICT on $VO_{2máx}$ and SBP/DBP after eight weeks: A) Intention-to-treat analysis, and B) per-protocol analysis

A. Intention to Treat Analysis				
Variables	**HIIT** (n=22)	**MICT** (n=22)	**Differences between groups (post-intervention)**	***p***
$VO_{2máx}$ (mL/kg/min)*	42.7 (6.0)	44.1 (8.7)	0.98 (-2.26 to 4.23)	0.54
SBP(mmHg)**	124.5 (120.0-129.5)	116.5 (115.0-119.0)	8.0	<0.001‡
DBP(mmHg)**	79.2 (76.0-85.0)	79.0 (71.5-83.0)	0.2	0.15
B. Subjects who completed the protocol				
Variables	**HIIT** (n=18)	**MICT** (n=18)	**Differences between groups (post-intervention)**	***p***
$VO_{2máx}$ (mL/kg/min)*	44.0 (5.8)	45.1 (8.9)	0.50 (-2.64 to 3.63)	0.75
SBP(mmHg)**	125.7 (120.0-129.5)	117.2 (115.5-121.0)	8.5	0.0005‡
DBP(mmHg)**	79.2 (75.0-85.0)	79.2 (71.5-83.0)	0.0	0.26

For maximum oxygen consumption ($VO_{2máx}$), values adjusted for base line and confounding variables (age, body mass index, weight and height). Systolic blood pressure (SBP), Diastolic blood pressure (DBP). *Values are given as mean ± SD. **Values are given as medians and interquartile ranges. ‡Differences between groups post-intervention p<0.05. ANCOVA (95 % confidence interval) for $VO_{2máx}$. Mann-Whitney U Test for SBP and DBP.