ORIGINAL INVESTIGATION

# Effect of High-Intensity Interval Versus Continuous Exercise Training on Functional Capacity and Quality of Life in Patients With Coronary Artery Disease

## A RANDOMIZED CLINICAL TRIAL

[AQ01]

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■ **PURPOSE:** There is strong evidence that exercise training has beneficial health effects in patients with cardiovascular disease. Most studies have focused on moderate continuous training (MCT); however, a body of evidence has begun to emerge demonstrating that high-intensity interval training (HIIT) has significantly better results in terms of morbidity and mortality. The aim of this study was to compare the effects of MCT versus HIIT on functional capacity and quality of life and to assess safety.

■ **METHODS:** Seventy-two patients with ischemic heart disease were assigned to either HITT or MCT for 8 weeks. We analyzed cardiopulmonary exercise stress test data, quality of life, and adverse events.

■ **RESULTS:** High-intensity interval training resulted in a significantly greater increase in $\dot{V}O_{2peak}$ ($4.5 \pm 4.7$ mL·kg$^{-1}$·min$^{-1}$) compared with MCT ($2.5 \pm 3.6$ mL·kg$^{-1}$·min$^{-1}$) ($P < .05$). The aerobic threshold ($VT_1$) increased by 21% in HIIT and 14% in MCT. Furthermore, there was a significant ($P < .05$) increase in the distance covered in the 6-minute walk distance test in the HIIT group ($49.6 \pm 6.3$ m) when compared with the MCT group ($29.6 \pm 12.0$ m). Both training protocols improved quality of life. No adverse events were reported in either of the groups.

■ **CONCLUSIONS:** On the basis of the results of this study, HIIT should be considered for use in cardiac rehabilitation as it resulted in a greater increase in functional capacity compared with MCT. We also observed greater improvement in quality of life without any increase in cardiovascular risk.

K E Y  W O R D S

coronary artery disease

functional capacity

high-intensity interval training

quality of life

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All authors have approved the final manuscript.

The authors declare no conflicts of interest.

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DOI: 10.1097/HCR.0000000000000156

In Europe, cardiovascular diseases cause 1.8 million deaths per year.[1] Exercise has a class I recommendation[2] for the management of these patients and results in a 15% to 31% reduction in mortality because of cardiac causes.[3]

Physical exercise increases functional capacity such as peak oxygen uptake ($\dot{V}O_{2peak}$), which is considered to be the best predictor of survival in cardiovascular disease.[4,5] In their meta-analysis of 33 studies involving 84 323 individuals, Kodama et al[6] concluded that a 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$ increase in $\dot{V}O_{2peak}$ (1 metabolic equivalent or MET) is associated with a 13% reduction in the risk of all-cause mortality and a 15% reduction in cardiovascular events. Similarly, Gullati et al[7] confirmed in their study with 5721 asymptomatic women that, for every increase in exercise capacity of 1 MET, the risk of death was reduced by 17%. In addition, patients with myocardial infarction who were followed up for 19 years, an increase of 1 MET was associated with an 8% to 14% reduction in mortality.[8]

The majority of studies published on the benefits of exercise in cardiovascular disease use moderate continuous training (MCT) at 60% to 80% of $\dot{V}O_{2peak}$. These studies have shown a significant improvement in functional capacity between 12% and 31% of $\dot{V}O_{2peak}$.[9]

Over the past decade, high-intensity interval training (HIIT) has raised great interest in the context of cardiac rehabilitation because of excellent results with regard to morbidity and mortality outcomes.[10,11] High-intensity interval training consists of a repeating series of high-intensity (peak interval) exercises, alternating with periods of low-intensity exercise (recovery interval). These brief recovery intervals require the patient to perform aerobic exercise practically without requiring energy production by the lactate-producing glycolytic system for energy. This avoids prolonged acidosis and prevents the sympathoadrenergic system from increasing cardiovascular effort, as the heart is already overworked.[12] Therefore, patients can comfortably maintain these high-intensity workloads, for a prolonged period and without any significant risk of cardiovascular complications.[12,13] Recent reviews and meta-analyses have shown that using HIIT better results are obtained for certain prognostic variables related to morbidity and mortality, such as aerobic capacity, left ventricular function, endothelial function, and quality of life, without any additional cardiovascular risk.[10,11]

The principal objective of this study was to compare the effect of 2 exercise training protocols (MCT vs HIIT) on functional capacity and quality-of-life variables. Our hypothesis was that HIIT would increase $\dot{V}O_{2peak}$ more than MCT in stable patients with coronary artery disease. The secondary outcome was to determine the impact of the type of exercise on quality of life and to verify the safety of following these 2 exercise programs.

## METHODS

### Participants

A prospective, randomized clinical trial (NCT02168712) was conducted with patients referred by the Cardiac Rehabilitation Department who were diagnosed with stable New York Heart Association functional class I or II coronary artery disease with angina pectoris or myocardial infarction and no heart failure. To be included in the study, patients had to achieve a respiratory exchange ratio ≥1.10 during the initial cardiopulmonary exercise test (CPET). This respiratory exchange ratio value is often used as a criterion for achieving a maximum exercise effort.[14] Patients who had residual ischemia (by electrocardiogram [ECG] criteria or angina symptoms), severe ventricular arrhythmias, uncontrolled hypertension, permanent pacemakers, or implanted cardiac defibrillators were excluded.

After signing an informed consent form, patients were randomized on a one-to-one basis to either the MCT or the HIIT group. The mode of exercise training was a cycle ergometer with 40 minutes per sessions, 3 days per week (total of 24 sessions over 2 months).

Patients entered the study within 6 weeks from the revascularization procedure. Clinical variables including the 6-minute walk test (6MWT) distance, selected CPET variables, and variables related to quality of life were recorded before and after the exercise training. Cardiopulmonary exercise tests were administered by staff blinded as to which exercise training group the patients were assigned.

### CPET

All patients underwent exercise testing with a cycle ergometer (Ergoline900S, Ergoline GmbH, Bitz, Germany) including analysis of exhaled gases (UltimaCardi$O_2$, Medical Graphics Corporation, St Paul, Minnesota). The exercise test protocol was tailored to each patient's physical condition, with gradual increments of 10, 15, or 20 W/min. The same protocol was applied before and after the exercise training program. The objective of the exercise tests was to achieve a sustained effort for 8 to 12 minutes, with the aim of proper oxygen uptake ($\dot{V}O_2$) kinetics and maintaining a linear relationship between $\dot{V}O_2$, exercise workload, and heart rate (HR).

A 12-lead ECG was continuously monitored, and blood pressure was measured every 3 minutes during the exercise tests. Exercise workloads in watts and metabolic, cardiac, ventilatory, and electrocardiographic parameters were analyzed. The ECG was continuously monitored during the first 5 minutes of recovery. Recorded HR was determined from the computerized test reports and was the average of the last 5 RR intervals.

The first ($VT_1$) and second ($VT_2$) ventilatory thresholds were considered to be indicators of the aerobic and anaerobic thresholds, respectively, and were determined after the ventilatory equivalent method described by Skinner et al.[14] The $\dot{V}O_2$ in $mL{\cdot}kg^{-1}{\cdot}min^{-1}$ and HR in beats$\cdot$min$^{-1}$ at $VT_1$ were the parameters used to determine the MCT exercise intensity.

## 6MWT

We performed 2 consecutive 6MWT using a standardized protocol[15] with the better of the 2 results being recorded. This process was used before and after the exercise training programs.

## Steep Ramp Test

To design the HIIT program, we used the steep ramp test (SRT) protocol, according to the methodology described by Meyer et al.[16] This exercise test protocol is composed of 2 minutes of free pedaling at 25 W followed by progressive 25-W increments every 10 seconds, maintaining a constant pedal cadence of between 50 and 60 rpm. The test was stopped when the patient could not maintain continuous pedal cadence for >40 rpm after encouragement to increase to 50 rpm and/or experienced hemodynamic and/or electrical alterations. The maximum exercise load achieved, as measured in watts, was the exercise parameter that was used to design the HIIT program for each patient.

## MCT and HIIT Program Designs

The metabolic parameters obtained during the pretraining CPET were used to design the MCT program. Patients were asked to keep their training HR below an HR corresponding to the HR at $VT_1$ during the first month. During the second month, the intensity of the exercise was adjusted, increasing to a training HR that corresponded to $VT_1$ plus 10%.

The HIIT protocol used the methodology initially described by Meyer et al[16] and which was recently published by our group.[17] In this type of exercise, the intensity was established using workload (watts), without taking HR into consideration as a measure for regulating the intensity of the exercise. The training workloads depended on the maximum workload achieved during the SRT. The intervals were designed as follows. In the first month of training, 20-second repetitions at an intensity corresponding to 50% of the maximum load reached with the SRT (peak intervals) were followed by 40-second recovery periods at 10%. In the second month of training, the intensity of exercise was adjusted using the results of a new SRT (Figure 1).

The total duration of both types of training was 40 minutes per session throughout the exercise program (including warm-up and cool-down). Table 1 summarizes the exercise time and intensity progression for both MCT and HIIT. Patients rated the peak level of exertion during each training session using the Borg Rating of Perceived Exertion Scale.[18]

Both types of exercise were reviewed and approved by the local Research Ethics Committee. Patients enrolled in the study participated in other activities established in our cardiac rehabilitation program that were aimed at managing psychological stress and learning about cardiac health habits. They were also taught to devise a home walking program for the days on which they did not have to attend sessions in

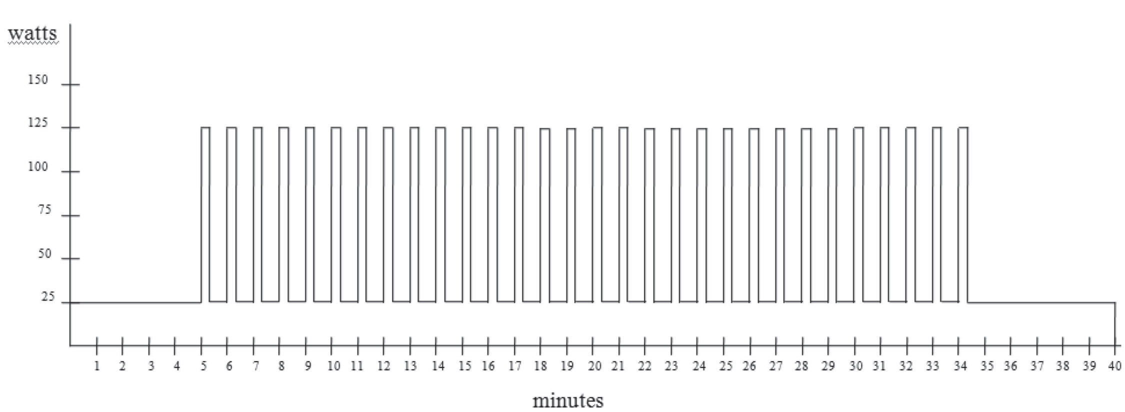


**Figure 1.** Interval training: 20-second repetitions at an intensity corresponding to 50% of the maximum workload reached with the steep ramp test, followed by 40-second intervals at 10%.

**Table 1 • Program Designs for MCT and HIIT Groups**

| Week | Warm-Up Time and Intensity (MCT and HIIT) | Exercise Time and Intensity (MCT/HIIT) | Cool-Down Time and Intensity (MCT and HIIT) |
|---|---|---|---|
| 1 | 12 min (25 W) | MCT: 15 min at $VT_1$ | 13 min (25 W) |
| | | HITT: 15 repetitions[a] | |
| 2 | 10 min (25 W) | MCT: 20 min at $VT_1$ | 10 min (25 W) |
| | | HITT: 20 repetitions[a] | |
| 3 | 7 min (25 W) | MCT: 25 min at $VT_1$ | 8 min (25 W) |
| | | HITT: 25 repetitions[a] | |
| 4 | 5 min (25 W) | MCT: 30 min at $VT_1$ | 5 min (25 W) |
| | | HITT: 30 repetitions[a] | |
| 5-8 | 5 min (25 W) | MCT: 30 min at ($VT_1$+ 10%) | 5 min (25 W) |
| | | HITT: 30 repetitions[b] | |

Abbreviations: HIIT, high-intensity interval training; MCT, moderate continuous training; SRT, steep ramp test.
[a]Intervals of 50% (20 seconds) to 10% (40 seconds) of the maximum load reached in the first SRT.
[b]Intervals of 50% (20 seconds) to 10% (40 seconds) of the maximum load reached in the second SRT.

hospital. The recommended intensity of walking was a perceived exertion of 11 to 13 on the Borg scale.

### Safety of the Exercise Training Programs

To verify the safety of using this kind of aerobic exercise training, we made a daily record of any incidents or adverse effects that could limit the planned exercise. An incident was considered low if there were no repercussions and it was possible to start and/or restart training (eg, muscle overload, fatigue, muscular pain, and dyspnea without oxygen desaturation). A moderate incident was defined as one that limited the planned training (dyspnea with des aturation <94%, muscle injury, vasovagal conditions), and an incident was defined as severe if it was potentially life-threatening (ischemia, ventricular arrhythmia, hypertensive emergencies).

### Quality-of-Life Questionnaires

A general quality-of-life (QOL) questionnaire (36-Item Short Form Health Survey [SF-36]) was given to the patients before and after the exercise training program. A disease-specific health-related QOL questionnaire, MacNew Heart Disease Health-related Quality of Life, was also administered before and after the exercise program.[19]

### Statistical Analysis

Quantitative variables were described using means and standard deviations, and the qualitative variables were reported using frequency distributions. To evaluate the effect of each exercise protocol on the quantitative variables, pre- and postprogram values were compared using Student's dependent samples *t* test. The effect was measured in absolute terms via the difference between the postprogram values and those obtained before training. These changes were described with the mean and standard deviation. Comparisons between the 2 training programs were made using Student's *t* test in the case of quantitative variables and using the $\chi^2$ test of association or Fisher exact test for qualitative variables. All the comparisons were made using 2-tailed tests, and the level of significance was set at $P < .05$. The statistical analyses were done using R-3.0.1 for Windows (Microsoft Corporation, Redmond, Washington).

## RESULTS

A total of 72 patients were included and studied (36 patients per group). At the start of the study, there were no significant differences between the groups with regard to clinical characteristics and medication use (Table 2).

### Training Data

The intensity of exercise in the MCT group in the first month was 64.2% ± 8.5% of the $\dot{V}O_{2peak}$ reached during the initial CPET (corresponding to the $VT_1$) and 69.5% ± 8.7% in the second month (corresponding to $VT_1$ + 10%). The exercise workload applied at the peak intervals in the HIIT group after the Meyer et al methodology[16] was 104.5% ± 22.2% (first month) and 134.5% ± 29.7% (second month) of the maximum load reached in the initial CPET corresponding to 50%

**Table 2 • Patient Characteristics and Medication Use[a]**

| | MCT (n = 36) | HIIT (n = 36) | *P* Value |
|---|---|---|---|
| Age, y | 58 ± 11 | 58 ± 11 | .82 |
| Men | 92 | 78 | .21 |
| Body mass index, kg/m$^2$ | 29.5 ± 4.1 | 29.6 ± 4.4 | 1.00 |
| Waist circumference, cm | 104 ± 9 | 104 ± 11 | 1.00 |
| Hip circumference, cm | 105 ± 8 | 104 ± 9 | .88 |
| Waist-to-hip ratio | 0.99 ± 0.05 | 1.00 ± 0.07 | .90 |
| Cardiovascular risk factors | | | |
| Family history | 47 | 46 | 1.00 |
| Hypertension | 57 | 65 | .67 |
| Diabetes mellitus | 31 | 27 | .88 |
| Dyslipidemia | 66 | 43 | .09 |
| History of smoking | 81 | 73 | .74 |
| Active smoker | 10 | 14 | .64 |
| Medical history | | | |
| Angina pectoris | 50 | 43 | .36 |
| Myocardial infarction | 50 | 57 | .45 |
| LVEF, % | 59 ± 14 | 62 ± 11 | .29 |
| PCI | 73 | 59 | .35 |
| CABG | 15 | 22 | .53 |
| Conservative medical management | 12 | 19 | .44 |
| Time from procedure to start of exercise program, d | 54 ± 6 | 50 ± 4 | .35 |
| Medications | | | |
| β-Blockers | 89 | 86 | 1.00 |
| Calcium channel blockers | 14 | 27 | .27 |
| ACE inhibitors | 71 | 54 | .20 |
| Angiotensin receptor antagonists | 20 | 19 | 1.00 |
| Nitrates | 11 | 11 | 1.00 |
| Antiplatelet agents | 97 | 97 | 1.00 |
| Statins | 94 | 100 | .23 |
| Antidiabetics | 22 | 22 | 1.00 |

Abbreviations: ACE, angiotensin-converting enzyme; CABG, coronary artery bypass graft; HIIT, high-intensity interval training; LVEF, left ventricular ejection fraction; MCT, moderate continuous training; PCI, percutaneous coronary intervention.
[a]Continuous data were reported as mean ± standard deviation; categorical data were reported as percentage.

of the SRT in both months. The resulting HR during the first and second months in the HIIT group was between $V_{T_1}$ and $V_{T_2}$.

No significant differences were observed in perception of exercise between the HIIT and MCT groups during the first (RPE 11-13) and second (RPE 14-16) months of training. Adherence to the treatment sessions (the number of sessions attended compared with the number of sessions scheduled) was 87.5% in the MCT group and 92% in the HIIT group. There was no significant difference between groups for adherence.

[AQ02]

## CPET and 6MWT

Results of testing for both groups before and after exercise training are summarized in Table 3. After 8 weeks of exercise training, both exercise programs significantly increased $\dot{V}O_{2peak}$, with a greater increase

**Table 3 • CPET Variables and 6MWT Distance in Both Study Groups**

| | MCT Group | | | HIIT Group | | |
|---|---|---|---|---|---|---|
| | Pretraining | Posttraining | Change | Pretraining | Posttraining | Change |
| CPET results | | | | | | |
| Total exercise time, min | 9.00 ± 2.02 | 10.1 ± 2.59 | 1.1 ± 1.8[c] | 7.80 ± 1.75 | 9.55 ± 2.26 | 1.7 ± 1.9[c] |
| $\dot{V}O_2$ peak, mL·kg$^{-1}$·min$^{-1}$ | 20.3 ± 5.0 | 22.8 ± 6.5 | 2.5 ± 3.6[c] | 19.4 ± 4.7 | 24.0 ± 4.8 | 4.5 ± 4.7[c,d] |
| $\dot{V}O_2$, % predicted | 80 ± 17 | 89 ± 20 | 9.0 ± 13.2[c] | 80 ± 21 | 96 ± 19 | 16.5 ± 17.8[c,d] |
| Resting HR, beats·min$^{-1}$ | 61 ± 9 | 59 ± 8 | −1.6 ± 8.2 | 66 ± 14 | 64 ± 10 | −2.2 ± 10.0 |
| Resting SBP, mm Hg | 122 ± 18 | 116 ± 15 | −5.6 ± 18.3 | 126 ± 15 | 123 ± 15 | −3.1 ± 17.7 |
| Resting DBP, mm Hg | 74 ± 10 | 73 ± 9 | −0.4 ± 11.3 | 76 ± 10 | 74 ± 8 | −1.8 ± 11.0 |
| Resting DP | 7 368 ± 1 746 | 6 783 ± 1 388 | −585 ± 1 614[a] | 8 333 ± 1 945 | 7 794 ± 1 421 | −539 ± 1 727 |
| Maximum HR, beats·min$^{-1}$ | 118 ± 20 | 119 ± 21 | 1.0 ± 11.6 | 115 ± 14 | 126 ± 14 | 10.6 ± 11.7[c,e] |
| Maximum SBP, mm Hg | 171 ± 23 | 165 ± 26 | −6.1 ± 22 | 171 ± 21 | 178 ± 23 | 7.2 ± 23.9[d] |
| Maximum DBP, mm Hg | 92 ± 12 | 89 ± 8 | −3.0 ± 12.4 | 90 ± 11 | 92 ± 11 | 1.6 ± 10.9 |
| Maximum DP | 20 205 ± 4 880 | 20 098 ± 5 044 | −107 ± 4 111 | 19 973 ± 4 099 | 22 312 ± 4 572 | 2 339 ± 4 386[b,d] |
| Maximum HR, % | 73 ± 14 | 73 ± 11 | −0.2 ± 10.0 | 72 ± 10 | 77 ± 8 | 5.5 ± 8.7[c,d] |
| Recovery HR at 1 min, beat·min$^{-1}$ | 20 ± 9 | 21 ± 8 | 1.3 ± 8.0 | 15 ± 7 | 21 ± 7 | 5.8 ± 8.1[c,d] |
| Maximum RER | 1.12 ± 0.09 | 1.15 ± 0.10 | 0.03 ± 0.1 | 1.15 ± 0.09 | 1.19 ± 0.12 | 0.04 ± 0.1[a] |
| Peak workload, W | 109 ± 37 | 123 ± 41 | 13.1 ± 19.3[c] | 103 ± 38 | 129 ± 46 | 26.3 ± 23.5[c,d] |
| HR at $VT_1$, beats·min$^{-1}$ | 90 ± 14 | 89 ± 14 | −0.9 ± 7.0 | 90 ± 11 | 93 ± 11 | 3.5 ± 9.2[a,d] |
| $\dot{V}O_2$ at $VT_1$, mL·kg$^{-1}$·min$^{-1}$ | 12.6 ± 2.9 | 14.4 ± 3.5 | 1.8 ± 2.1[c] | 12.0 ± 2.6 | 14.5 ± 2.7 | 2.5 ± 3.0[c] |
| Power at $VT_1$, W | 55 ± 24 | 62 ± 27 | 7.9 ± 17[b] | 49 ± 22 | 65 ± 22 | 15.3 ± 16.1[c] |
| HR at $VT_2$, beats·min$^{-1}$ | 106 ± 17 | 107 ± 18 | 0.1 ± 7.0 | 102 ± 14 | 109 ± 14 | 6.9 ± 11.8[a,d] |
| $\dot{V}O_2$ at $VT_2$, mL·kg$^{-1}$·min$^{-1}$ | 17.2 ± 4 | 19.1 ± 4.1 | 1.9 ± 2.9[b] | 17.0 ± 3.8 | 19.9 ± 3.9 | 2.9 ± 3.7[b] |
| Power at $VT_2$, W | 92 ± 38 | 106 ± 33 | 14.0 ±15.5[c] | 88 ± 30 | 106 ± 28 | 17.2 ± 19.0[b] |
| 6MWT | | | | | | |
| Distance, m | 528 ± 96 | 558 ± 109 | 29.6 ± 12.0[c] | 531 ± 74 | 580 ± 80 | 49.6 ± 6.3[c,d] |

Abbreviations: BP, blood pressure; CPET, cardiopulmonary exercise test; DBP, diastolic blood pressure; DP, double product; HIIT, high-intensity interval training; HR, heart rate; MCT, moderate continuous training; RER, respiratory exchange ratio; SBP, systolic blood pressure; $V\cdot O_2$, oxygen uptake; $VT_1$, first ventilatory threshold; $VT_2$, second ventilatory threshold; 6MWT, 6-minute walk test.
Within-group differences: [a]$P < .05$; [b]$P < .01$; [c]$P < .001$.
Between-group differences: [d]$P < .05$; [e]$P < .001$.

noted in the HIIT group (4.5 ± 4.7 mL·kg$^{-1}$·min$^{-1}$ vs 2.5 ± 3.6 mL·kg$^{-1}$·min$^{-1}$, for patients in the HIIT and MCT groups, respectively; $P < .05$). Both groups also showed a significant increase in the peak exercise workload achieved (MCT 13.1 ± 19.3 W vs HIIT 26.3 ± 23.5 W), with a significantly higher increase in the HIIT group ($P < .001$). A significant increase was observed in maximal HR in the HIIT group only (10.6 ± 11.7 beats·min$^{-1}$; $P < .001$). The $V\cdot O_2$ and exercise workload at $VT_1$ and $VT_2$ significantly increased in both groups, but HR only increased in the HIIT group.

Thirty-two HIIT and 34 MCT patients, respectively, achieved $VT_1$ on the first CPET, and 35 and 34 patients, respectively, achieved it on the second, posttraining CPET. Concerning the achievement of $VT_2$, 20 HIIT and 25 MCT patients, respectively, achieved it on the initial CPET. On the CPET after the training programs, 29 HIIT and 32 MCT patients, respectively, achieved $VT_2$.

With regard to the HR recovery in the first minute after the exercise test, the only significant change was observed in the HIIT group (5.8 ± 8.1; $P < .001$).

Both groups showed significant ($P < .001$) increases in 6MWT distance (Table 4) after training, with a

**Table 4 • Quality-of-Life Results in MCT and HIIT Groups[a]**

| | MCT Group | | | HIIT Group | | |
|---|---|---|---|---|---|---|
| | Pretraining | Posttraining | Change | Pretraining | Posttraining | Change |
| SF-36[a] | | | | | | |
| Physical functioning | 73 ± 24 | 77 ± 23 | 4.3 ± 13.6 | 78 ± 15 | 83 ± 16 | 4.6 ± 13.3 |
| Role—physical | 51 ± 43 | 59 ± 44 | 8.1 ± 51.4 | 49 ± 42 | 54 ± 45 | 4.4 ± 49.4 |
| Body pain | 67 ± 30 | 73 ± 25 | 5.8 ± 28.2 | 72 ± 23 | 74 ± 25 | 2.4 ± 26.2 |
| General health | 58 ± 19 | 62 ± 22 | 3.9 ± 14.8 | 58 ± 18 | 63 ± 19 | 5.0 ± 17.4 |
| Vitality | 62 ± 18 | 67 ± 18 | 4.1 ± 14.7 | 57 ± 19 | 63 ± 23 | 6.2 ± 22.4 |
| Social functioning | 83 ± 22 | 83 ± 22 | 0.6 ± 23.4 | 82 ± 19 | 89 ± 17 | 7.7 ± 24.0 |
| Role—emotional | 73 ± 38 | 75 ± 40 | 2.9 ± 45.2 | 48 ± 44 | 73 ± 36 | 25.5 ± 47.9[c] |
| Mental health | 70 ± 20 | 73 ± 22 | 3.3 ± 14.6 | 64 ± 17 | 73 ± 18 | 9.3 ± 19.0[c] |
| Self-reported health status | 3 ± 1 | 2 ± 1 | −0.6 ± 0.9[c] | 3 ± 1 | 2 ± 1 | −0.9 ± 1.2[d] |
| Physical health index | 43 ± 11 | 46 ± 12 | 2.6 ± 7.3[b] | 47 ± 8 | 47 ± 7 | −0.5 ± 7.6 |
| Mental health index | 48 ± 12 | 50 ± 14 | 1.6 ± 11.8 | 41.0 ± 12.4 | 49 ± 11 | 7.8 ± 14.0[c] |
| MacNew | | | | | | |
| Emotional domain | 5.5 ± 1.1 | 5.7 ± 1.1 | 0.3 ± 0.8 | 5.3 ± 0.9 | 5.8 ± 0.9 | 0.5 ± 0.9[c] |
| Physical domain | 5.6 ± 0.9 | 5.9 ± 0.9 | 0.3 ± 0.7[b] | 5.5 ± 1.0 | 5.9 ± 1.0 | 0.4 ± 0.7[c] |
| Social domain | 5.7 ± 0.9 | 6.0 ± 0.8 | 0.4 ± 0.8[b] | 5.6 ± 0.9 | 6.0 ± 0.9 | 0.4 ± 0.7[c] |
| Global domain | 5.5 ± 0.9 | 5.8 ± 0.9 | 0.3 ± 0.7[b] | 5.3 ± 0.9 | 5.8 ± 0.9 | 0.5 ± 0.7[c] |

Abbreviations: HIIT, high-intensity interval training; MacNew, MacNew Heart Disease Health-related Quality of Life questionnaire; MCT, moderate continuous training; SF-36, 36-Item Short Form Health Survey.
[a]All data reported as mean ± standard deviation.
Within-group differences: [b]$P < .05$; [c]$P < .01$; [d]$P < .001$.

greater increase in distance for the HIIT group compared with the MCT group ($P < .05$).

## Quality of Life

After the training program, scores in all domains of the MacNew questionnaire significantly improved in both groups except for the emotional domain in the MCT group. With regard to the SF-36 QOL questionnaire, significant increases in the role—emotional, metal health, and self-reported health status scales—and the mental health index were observed in the HIIT group (Table 4).

## Safety of the Training Intervention

No incidents or adverse events were recorded that limited the ability of patients to perform the prescribed exercise in either of the training programs.

# DISCUSSION

Recent studies have revealed that HIIT is more effective than MCT for improving functional capacity and other variables predictive of cardiovascular risk.[10,11,20-22] In our study, despite the increase in $\dot{V}O_{2peak}$ in both groups after 8 weeks of aerobic training, the improvement was significantly greater in the HIIT group. The mean increase in $\dot{V}O_{2peak}$ was 4.5 ± 4.7 mL·kg$^{-1}$·min$^{-1}$ in the HIIT group and 2.5 ± 3.6 mL·kg$^{-1}$·min$^{-1}$ in the MCT group. These results are important not only for the improved $\dot{V}O_{2peak}$ but also for the benefit that increased functional capacity has on survival. Before $\dot{V}O_{2peak}$ is considered to be the best predictor of survival in patients with cardiovascular diseases, HIIT may potentially contribute to the reduction of morbidity and mortality because its effect on increasing $\dot{V}O_2$.

The 24% increase (HIIT group) and the 12% increase (MCT group) in $\dot{V}O_{2peak}$ are similar to those reported by other authors,[21] but are far from the results obtained by Wisloff et al,[20] who reported improvements in $\dot{V}O_{2peak}$ of 46% with HIIT and 15% with MCT. These greater differences in favor of the HIIT group could possibly be due to the fact that Wisloff's study was conducted on patients with heart failure and severe left ventricular dysfunction (average left ventricular ejection fraction ≈29%), with a lower baseline functional capacity ($\dot{V}O_{2peak}$= 13 mL·kg$^{-1}$·min$^{-1}$) and the use of a different interval protocol compared with this study.

$VT_1$ expressed in mL·kg$^{-1}$·min$^{-1}$ increased in both groups after the exercise program, but the HR at $VT_1$ in the HIIT group was significantly higher than in the MCT group. This finding reflects important peripheral and central adaptations to the exercise training as it allows patients to exercise longer at submaximal levels before the onset of fatigue and represents an improved aerobic capacity without increasing cardiovascular work.[23,24] This shift in the $VT_1$ toward increased $\dot{V}O_2$ could account for the increase ($P < .05$) in meters walked during the 6MWT after training in the HIIT group (49.6 ± 6.3 m) compared with the MCT group (29.6 ± 12 m).

On the other hand, an improvement in acidosis tolerance was observed in both training groups, with a shift of the $VT_2$ closer to the $\dot{V}O_{2peak}$. This trend in the HIIT group could be due to a higher metabolic rate during exercise and a greater capacity of for eliminating or buffering the lactate accumulated during incremental exercise.[25] This change in the anaerobic threshold provides a possibility of training at higher intensity without producing undesirable metabolic changes when exceeding the $VT_2$.[26]

It is interesting to note that the maximum HR reached in the CPET after completing the exercise programs was significantly greater than at baseline testing in the HIIT group with no change in the MCT group. These findings in the HIIT group could be due to the fact that higher workloads were obtained after completing the program in the HIIT group (103 ± 38 W vs 129 ± 46 W) and were due to a significant increase in the exercise time on the second CPET (7.80 ± 1.75 minutes vs 9.55 ± 2.26 minutes; $P < .001$) and to an improved cardiovascular adaptation to exercise.

HR recovery in the first minute after maximum effort is considered by many to be predictive for future morbidity and mortality. A decrease in HR of ≤12 beats·min$^{-1}$ during the first minute of recovery is considered abnormal.[27-29] Improved HR recovery was observed only in the HIIT group, and this could be due to an increase in the vagal tone in patients in the HIIT group, as has been previously demonstrated.[28] These results suggest a greater contribution of the autonomic nervous system because of an increase in vagal tone that occurs after HIIT.[28] However, both the short- and long-term effects of HIIT on the autonomic nervous system are still unclear because of diversity in the results obtained in different studies.

Many of our results are similar to those reported by other authors, but it is difficult to compare them because of the different designs used for interval training programs. Different methods for determining the exercise intensity used during the peak and the recovery intervals include percentage of $\dot{V}O_{2peak}$[20]; percentage of $\dot{V}O_2$ reserve[30]; percentage of $HR_{max}$[20,31]; percentage HR reserve[32]; or, as used in this study, percentage of workload.[16,17] There are also differences between studies in the duration of the intervals, the number of peak and recovery periods per session, and the number of sessions per week.[10,11,22] All of the above constitute important limitations because these variables significantly alter the total volume of training.[10,11,22]

Our workgroup established the intensity of interval training exercise using exercise workload in watts as a percentage of the maximum workload achieved on the SRT. Our results show that the workloads applied in the peak intervals in this study were of high intensity and ranged between 104% and 134% of the maximum workload achieved during the initial CPET. Meyers et al[25] reported that using this methodology for the HIIT design, the exercise times during training at an intensity greater than 85% of the $\dot{V}O_{2peak}$ were prolonged and safe. This methodology described by Meyers et al[25] has been suggested as an alternative method for establishing the intensity of the short intervals,[25,33] but we are aware that using it could be a limitation in our study because the SRT is not fully validated and is not a widely used test in cardiac rehabilitation.

Physiological improvement with both types of exercise training was accompanied by an improvement in QOL as measured by the MacNew and SF-36 questionnaires. Although no significant differences were observed between the 2 groups, the most analyzed domains in both questionnaires showed greater improvements in the HIIT group. All 3 domains in the MacNew questionnaire (emotional, physical, and social) improved demonstrated greater improvement in the HIIT group. This is a very important fact because it is related to adherence to exercise programs[34-37] and it reflects good tolerance for and acceptability of the HIIT protocol.

In general, HIIT programs have been shown to be safe, although the number of studies is limited. As described in other studies,[10,11,22,38] we observed good acceptability and tolerability by all of the patients in the HIIT group and no incidents or complications were recorded during the training program.

Although the absence of incidents in our study suggests that HIIT is safe way to prescribe exercise and the data are reassuring, we cannot draw a clear conclusion that HIIT is safe. Further long-term studies are necessary in order for HITT to be accepted as a standard methodology for exercise training in cardiac rehabilitation. We recommend that large-scale, randomized clinical trials be conducted to investigate the impact of

HIIT on morbidity and mortality in patients with cardiovascular diseases. Fortunately, 2 multicenter, randomized studies are already underway in Europe: the SAINTEX-CAD coronary artery disease study[39] and the SMARTEX-HF heart failure study.[40] The results from these studies will be an important advance in being able to make definitive recommendations regarding HITT and the previously mentioned problems of patient safety and future morbidity and mortality risk.

## CONCLUSIONS

The results of our study documented that HIIT in low-risk patients diagnosed with chronic ischemic heart disease resulted in a greater increase in functional capacity compared with MCT and favored the HIIT group in both maximal ($\dot{V}O_{2peak}$) and submaximal ($VT_1$ and $VT_2$) values. The acceptance and tolerability by patients, absence of adverse incidents, and its positive impact on the quality of life justify the use of HITT as an alternative to standard exercise training protocols used in cardiac rehabilitation programs.

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JCRP-D-14-00122_LR 9 24/09/15 5:05 PM

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