Canadian Journal of Cardiology 38 (2022) 1235–1243

Clinical Research

Sustained Effects of Different Exercise Modalities on Physical and Mental Health in Patients With Coronary Artery Disease: A Randomized Clinical Trial

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See editorial by Taylor et al., pages 1135–1137 of this issue.

ABSTRACT

Background: Twelve-week high-intensity interval training (HIIT), moderate-to-vigorousintensity continuous training (MICT), and Nordic walking (NW) have been shown to improve functional capacity, quality of life (QoL), and depression symptoms in patients with coronary artery disease. However, their prolonged effects or whether the improvements can be sustained remains unknown. In this study we compared the effects of 12 weeks of HIIT, MICT, and NW on functional capacity, QoL, and depression symptoms at week 26.

Methods: Patients with coronary artery disease were randomized to a 12-week HIIT, MICT, or NW program followed by a 14-week observation

RÉSUMÉ

Contexte : Il a été démontré que l'entraînement fractionné de haute intensité (EFHI), l'entraînement continu d'intensité modérée à élevée (ECIME) et la marche nordique (MN) pratiqués durant 12 semaines améliorent la capacité fonctionnelle et la qualité de vie (QdV), en plus d'atténuer les symptômes de dépression chez les patients atteints de coronaropathie. Toutefois, leurs effets à long terme et la persistance de leurs bienfaits restent à confirmer. Notre étude nous a permis de comparer les effets que l'EFHI, l'ECIME et la MN pratiqués durant 12 semaines avaient au bout de 26 semaines sur la capacité fonctionnelle, la QdV et les symptômes de dépression.

Patients with coronary artery disease (CAD) frequently show diminished functional capacity,[1] low quality of life (QoL),[2] and high rates of depression[3]—all increasing the risk of subsequent cardiovascular events and mortality.[4-6] Cardiovascular rehabilitation (CR) including moderate-to-vigorous intensity continuous exercise training (MICT) after coronary revascularization is a class IA[7,8] recommendation to improve functional capacity,[9,10] QoL,[10,11] and depression symptoms,[10,12,13] and to reduce risk of myocardial infarction, all-cause hospitalization, and mortality.[11]

The health benefits of exercise-based CR[14,15] including MICT[16] are well established. However, compared with MICT, growing evidence suggests that nonconventional exercise interventions, such as high-intensity interval training (HIIT) and Nordic walking (NW) are more effective in improving functional capacity measured using a 6-minute walk test (6MWT),[10,17,18] an important predictor of cardiovascular events in patients with CAD.[4] Studies have also shown that HIIT, MICT, and NW are equally effective in improving QoL,[10,18,19] and depression severity[19] in patients with CAD. In our randomized clinical trial (RCT) in which 12 weeks of supervised HIIT, MICT, and NW were simultaneously compared in a CR setting, NW was statistically and clinically superior in increasing functional capacity whereas all exercise modalities similarly improved QoL and depression symptoms.[10]

Patients with CAD are encouraged to maintain an active lifestyle after the completion of exercise-based CR. However, during the observation phase after the completion of CR,

Received for publication February 1, 2022. Accepted March 28, 2022.

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See page 1241 for disclosure information.

https://doi.org/10.1016/j.cjca.2022.03.017

phase. At baseline, and at weeks 12 and 26, functional capacity was measured with a 6-minute walk test (6MWT); QoL was assessed using the HeartQoL and Short Form-36; and depression severity using the Beck Depression Inventory-II. Prolonged (between baseline and week 26) and sustained (between weeks 12 and 26) effects were assessed using linear mixed models with repeated measures.

Results: Of 130 participants randomized, 86 (HIIT: n = 29; MICT: n = 27; NW: n = 30) completed week 26 assessments. There were significant improvements in 6MWT distance, QoL, and depression symptoms from baseline to week 26 ($P < 0.05$); NW increased 6MWT distance (+94.2 ± 65.4 m) more than HIIT (+59.9 ± 52.6 m; interaction effect $P = 0.025$) or MICT (+55.6 ± 48.5 m; interaction effect $P = 0.010$). Between weeks 12 and 26, 6MWT distance and physical QoL increased significantly ($P < 0.05$).

Conclusions: Twelve weeks of HIIT, MICT, and NW have positive prolonged effects on functional capacity, QoL, and depression symptoms. However, NW conferred additional benefits in increasing functional capacity. The effects of the 12-week exercise programs were sustained at week 26.

Méthodologie : Des patients atteints de coronaropathie ont été répartis de façon aléatoire pour suivre un programme d'EFHI, d'ECIME ou de MN de 12 semaines, suivi d'une phase d'observation de 14 semaines. Au début de l'étude et aux semaines 12 et 26, la capacité fonctionnelle a été mesurée au moyen d'un test de marche de six minutes (TDM6); la QdV a été évaluée à l'aide des questionnaires *HeartQoL* et *Short Form-36*; la gravité de la dépression a été établie à l'aide de l'inventaire de dépression de Beck II. Les effets à long terme (entre le début de l'étude et la semaine 26) et la persistance des effets (entre les semaines 12 et 26) ont été évalués à l'aide de modèles linéaires mixtes à mesures répétées.

Résultats : Sur les 130 participants répartis de façon aléatoire, 86 (EFHI : n = 29; ECIME : n = 27; MN : n = 30) ont terminé les évaluations de la semaine 26. Des améliorations significatives de la distance parcourue au TDM6, de la QdV et des symptômes de dépression ont été observées entre le début de l'étude et la semaine 26 ($P < 0{,}05$); la MN a permis d'augmenter davantage la distance parcourue au TDM6 (+94,2 ± 65,4 m) que l'EFHI (+59,9 ± 52,6 m; valeur P de l'effet d'interaction = 0,025) ou que l'ECIME (+55,6 ± 48,5 m; valeur P de l'effet d'interaction = 0,010). Entre les semaines 12 et 26, la distance parcourue au TDM6 et la QdV physique ont augmenté de façon significative ($P < 0{,}05$).

Conclusions : L'EFHI, l'ECIME et la MN pratiqués durant 12 semaines ont des effets positifs prolongés sur la capacité fonctionnelle, la QdV et les symptômes de dépression. Toutefois, la MN s'est révélée plus bénéfique en matière d'augmentation de la capacité fonctionnelle. Les effets des programmes d'exercices de 12 semaines persistaient à la semaine 26.

adherence to structured exercise remains low[20,21] and physical activity engagement decreases significantly.[22] Although functional capacity,[23] QoL, and depression[24] remain significantly above baseline measures at 1 year after 6-12 weeks of HIIT and MICT, improvements observed at the end of the exercise intervention diminished over the year.[23,25,26] Strategies to improve functional capacity, QoL, and depression over a prolonged period (ie, over intervention and observation phases) and to sustain the improvements induced by CR (ie, during the observation phase) are warranted.

Studies that examined the effects of different exercise modalities in CR have predominantly focused on their short-term efficacy (eg, CR enrollment to completion). In our recent 12-week RCT we compared the efficacy of HIIT, MICT, and NW on functional capacity, QoL, and depression.[10] However, the prolonged effects (eg, over intervention and observation phases) of such exercise modalities were not investigated. Further, it was unknown whether the improvements induced by HIIT, MICT, and NW could be sustained during the observation phase. In this study we followed participants randomized to 12 weeks of HIIT, MICT, and NW programs[10] and examined changes in functional capacity, QoL, and depression symptoms 14 weeks after the completion of the exercise programs. The primary purpose of the study was to compare the prolonged effects of 12 weeks of HIIT, MICT, and NW on functional capacity. The secondary purposes were to assess: (1) the prolonged effects of 12 weeks of HIIT, MICT, and NW on QoL and depression symptoms; (2) the sustained effects of 12 weeks of HIIT, MICT, and NW on functional capacity, QoL, and depression; and, (3) physical activity levels after 12 weeks of HIIT, MICT, and NW. It was hypothesized that NW would be superior to HIIT and MICT in improving functional capacity over a prolonged period and sustaining the improvements.

Methods

Design

This was a single-centre, prospective RCT with repeated measures (ie, baseline, week 12, and week 26) to compare the prolonged (ie, changes between baseline and week 26) and sustained (ie, changes between week 12 and week 26) effects of 12 weeks of HIIT, MICT, and NW on functional capacity, QoL, and depression in patients with CAD. The efficacy of these CR programs (between baseline and week 12) has been published.[10] We chose a 14-week observation phase to examine if the effects of a 12-week exercise intervention would diminish, remain, or amplify over the follow-up phase similar in length to the exercise intervention. This study was registered with ClinicalTrials.gov (NCT02765568) and the study protocol was approved by the Ottawa Health Science Network Research Ethics Board (protocol 20160127-01H). The study is reported in accordance with the **Con**solidated **S**tandards **o**f **R**eporting **T**rials (CONSORT) and Template for Intervention Description and Replication (TIDieR) checklist.[27]

Participants

Eligible patients were those with documented CAD (40-74 years of age) who were referred to a CR program. We excluded

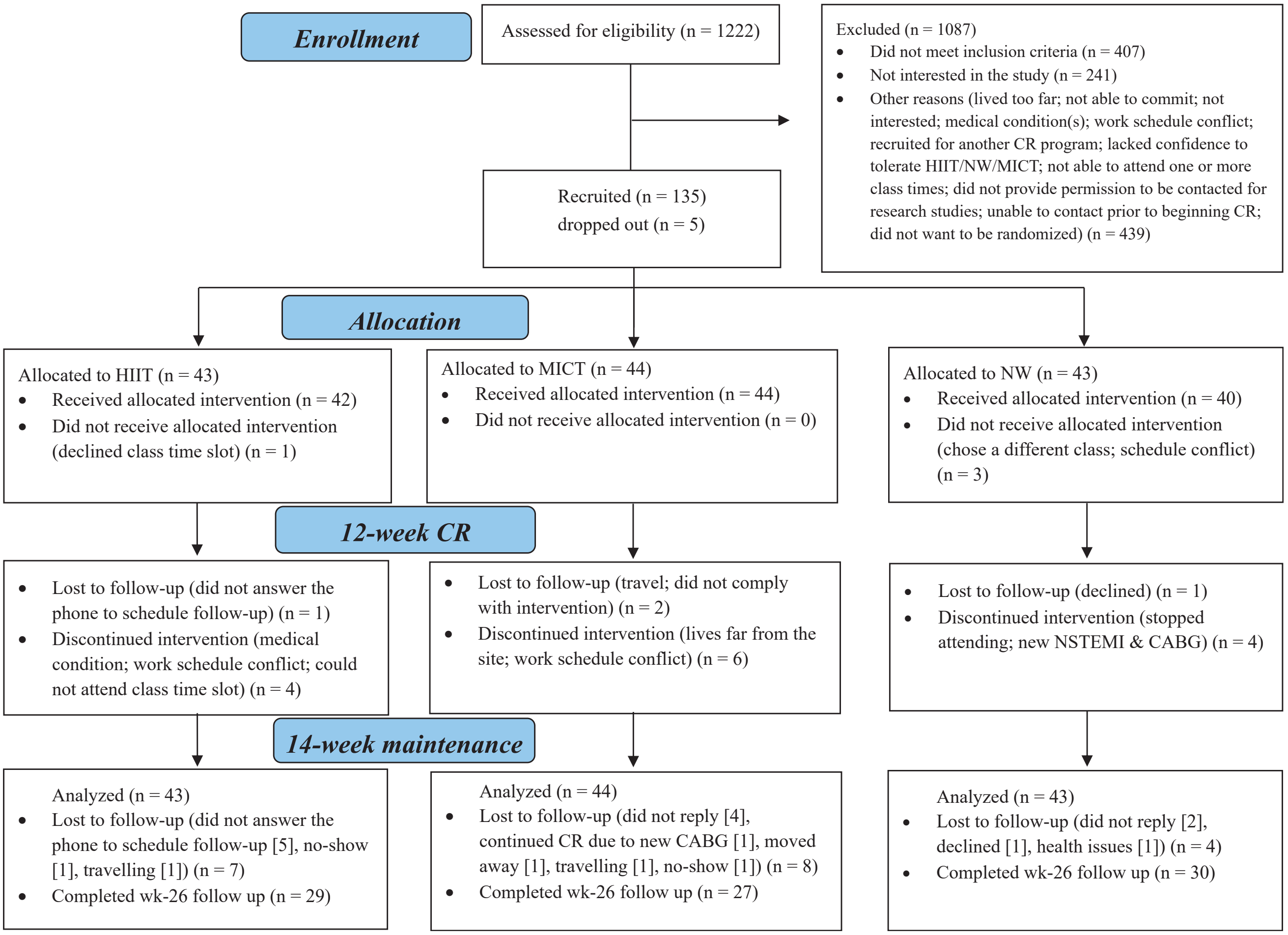

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram of participants recruited and reasons for withdrawals. CABG, coronary artery bypass graft surgery; CR, cardiac rehabilitation; HIIT, high-intensity interval training; MICT; moderate-to-vigorous intensity continuous training; NSTEMI, non-ST segment elevation myocardial infarction; NW, Nordic walking.

patients who: (1) were exercising > 2 times per week and/or using NW poles; (2) were unable to walk independently; (3) were pregnant or lactating; (4) were unwilling or unable to return for a follow-up visit at 12 weeks; (5) were unable to read and understand English or French; or, (6) had the following conditions: an active infection or inflammatory condition; persistent or permanent atrial fibrillation; unstable angina; established diagnosis of chronic obstructive pulmonary disease; severe mitral or aortic stenosis; or, hypertrophic obstructive cardiomyopathy. All patients provided written informed consent.

Randomization

Participants were randomized in a 1:1:1 ratio to 12 weeks of HIIT, MICT, or NW using a computer-generated blocked, stratified (according to sex [male vs female] and age [< 60 vs ≥ 60 years], and random sequence. Treatment assignments were placed in sealed envelopes to ensure concealment until baseline data were collected.

Exercise interventions

Details of the 12-week twice weekly exercise programs have been described elsewhere.[10] Briefly, participants in the HIIT arm followed a modified Norwegian HIIT protocol[28] (ie, 4 × 4 minutes of high-intensity work periods at 85%-95% peak heart rate [HR] interspersed with 3 minutes of lower-intensity work periods at 60%-70% peak HR). Each HIIT session was 45 minutes in duration. Patients could complete HIIT using either aerobic exercise equipment or dance/movement-based routines. Participants in the MICT and NW arms were instructed to maintain their HR within +20 to +40 beats per minute above resting HR and a rating of perceived exertion of 12 to 16 points (somewhat hard to hard). MICT participants performed continuous aerobic exercise. NW participants performed continuous or intermittent walking with Nordic poles. The MICT and NW sessions were each 60 minutes in duration. After 12 weeks of exercise interventions, self-management tools (eg, Heart Wise Exercise)[29] were provided to participants to encourage active lifestyle. However, no supervised exercise sessions were provided.

Outcome measures

Anthropometrics and hemodynamics. Height, body mass, percent fat mass, waist circumference, resting systolic and diastolic blood pressure (BP) and resting HR were measured as previously described[10] at baseline, week 12, and week 26.

Functional capacity. Functional capacity was assessed at baseline, week 12, and week 26 using a 6MWT on a measured indoor track. Participants were instructed to walk as far as possible for 6 minutes without running or jogging. To account for a possible learning effect,[30] 2 6MWTs were completed on separate days at each time point and the average distance was used in the statistical analyses. The test is a valid method for assessing functional capacity with strong test-retest reliability (intraclass correlation = 0.97).[31]

Disease-specific and general QoL. The **Heart Quality of Life** (HeartQoL) is a 14-item ischemic heart disease-specific questionnaire. The HeartQoL is used to assess the influence of heart disease during the preceding 4 weeks on patients' daily functioning and yields a global health-related QoL score and physical and emotional subscales.[32] Each item is rated on a 4-point scale (0-3 points) and higher scores indicate better QoL. The HeartQoL is a valid and reliable questionnaire with high internal consistency for the global health-related QoL physical and emotional subscales (Cronbach α are 0.92, 0.91, and 0.87, respectively).[33]

General QoL was measured using the Short Form-36 (SF-36),[34] a multipurpose, short-form health survey with 36 questions. The SF-36 yields an 8-scale profile of functional health and well-being scores as well as psychometrically based physical and mental health summary (ie, physical component summary [PCS] and mental component summary [MCS]) scores. Higher scores reflect better QoL. In patients with CAD, the SF-36 subscales show high internal consistency (Cronbach α ranging from 0.72 to 0.94).[35]

Depression. Depression symptoms were assessed using the Beck Depression Inventory-II (BDI-II), a widely used instrument for measuring depression symptoms and severity in patients after myocardial infarction.[36] Higher BDI-II scores reflect greater depression severity. The BDI-II has high internal consistency (Cronbach α, 0.91).[37]

Physical activity levels. Physical activity levels of participants were measured using an accelerometer, ActiGraph GT3X (ActiGraph, Pensacola, FL), over 7 days at baseline, and at weeks 12 and 26. A valid day was defined as $\geq$ 10 hours of wear time, and participants were required to have a minimum of 4 valid days to be retained in the analyses.[38] Sasaki cut points: 150-2689 counts per minute for "light" intensity, and $\geq$ 2690 counts per minute for "moderate-to-vigorous" intensity[39] were used to compute daily average time (minutes per day) spent in light and moderate-to-vigorous intensity physical activity.

Sample size calculation

As described previously,[10] with a 2-sided 5% significance level and 80% power, a sample size of 108 (36 per group) was needed to detect clinically meaningful differences in our primary outcomes measure (ie, 6MWT distance) for the 3 exercise modalities. With an expected 20% dropout rate, we planned to recruit 135 patients in this trial.

Statistical analysis

Data were analyzed using IBM SPSS for Windows (version 27; IBM Corp, Armonk, NY). Categorical variables are presented as frequencies and percentages, and continuous variables as mean $\pm$ standard deviation (SD). Statistical significance was set at $P < 0.05$.

Intention-to-treat analysis was used in assessment of all variables. A linear mixed-effects model for repeated measures with unstructured covariate matrix was used to compare the prolonged (ie, between baseline and week 26) and sustained (ie, between week 12 and week 26) effects of 12 weeks of HIIT, MICT, and NW. A missing value analysis showed outcome variables were missing at random. Using the maximum likelihood estimation method, the main effects for time and time $\times$ exercise modality interaction effects for anthropometrics, hemodynamics, 6MWT distance, QoL, and depression scores were examined. The residuals were tested for normality using Kolmogorov-Smirnov tests of normality. Fat mass, waist circumference, resting HR, systolic and diastolic BP, HeartQoL, and general QoL scores violated the normality assumption. These data were normalized using a 2-step approach.[40] Because the transformed data showed consistent results with nontransformed data, outputs using the nontransformed data are reported. The same analytical approach was used to assess physical activity levels. Changes in time spent in light and moderate-to-vigorous intensity physical activity from baseline to week 12 (not included in the previous publication[10]), from baseline to week 26, and from week 12 to week 26 were analyzed.

Results

Of the 1222 patients initially screened, 135 were recruited. Five participants dropped out before randomization and 130 (15.4% female) were randomized. The reasons for not participating in the study are summarized in the CONSORT flow diagram (Figure 1). Participants' baseline characteristics are summarized in Table 1. At baseline, no significant differences were observed for the HIIT, MICT, and NW groups in their demographic characteristics, anthropometrics, medical conditions, functional capacity, or QoL. Prescribed medications did not differ significantly at baseline between the groups except for antiplatelet medication; clopidogrel was more frequently prescribed in the NW group (n = 7) compared with the HIIT group (n = 0; $P = 0.030$). The depression score was significantly higher in the MICT group compared with the HIIT group at baseline ($P < 0.05$). Detailed data on medical conditions and medications have previously been published.[10] There were no diffrences in prescribed medications between the groups at week 26.

Functional capacity

The effect of the exercise modality on functional capacity is presented in Figure 2. A main effect of time showed a significant increase in 6MWT distance from baseline to week 26 (573 $\pm$ 78 vs 656 $\pm$ 95 m; $P < 0.001$). There was a significant time $\times$ exercise modality interaction effect ($P = 0.014$), with a greater improvement in 6MWT distance over 26 weeks for NW participants (586 $\pm$ 88 vs 695 $\pm$ 104) compared with HIIT participants (571 $\pm$ 70 vs 645 $\pm$ 83;

Table 1. Demographic and outcome measures at BL, Wk12, and Wk26

	HIIT			MICT			NW			Prolonged effect (BL to Wk26) *P*			Sustained effects (Wk12 to Wk26) P		
	BL (n = 43)	Wk12 (n = 38)	Wk26 (n = 31)	BL (n = 44)	Wk12 (n = 36)	Wk26 (n = 30)	BL (n = 43)	Wk12 (n = 36)	Wk26 (n = 30)	Time	Group	Time × Group	Time	Group	Time × Group
Demographic characteristics															
Age, years	61 (7)			60 (7)			61(8)								
Female sex, n (%)	7 (16.3)			6 (13.6)			7 (16.3)								
Ethnicity, n (%)															
White	32 (74.4)			39 (90.7)			34 (81.0)								
Asian	0 (0)			1 (2.3)			4 (9.5)								
Other	11 (26.6)			3 (7.0)			4 (9.5)								
Marital status, n (%)															
Single	9 (20.9)			4 (9.3)			4 (9.3)								
Married/common law	32 (74.4)			34 (79.1)			35 (81.4)								
Divorced/widowed	2 (4.7)			5 (11.7)			4 (9.3)								
Other	11 (26.6)			3 (7.0)			4 (9.5)								
Anthropometrics and hemodynamics															
Body mass, kg	85.6 (20.1)	86.0 (17.4)	86.2 (22.9)	91.1 (20.4)	88.6 (16.5)	86.6 (12.4)	86.0 (16.7)	84.6 (16.7)	80.8 (14.1)	0.481	0.365	0.657	0.926	0.559	0.846
BMI	29.0 (5.8)	29.0 (5.5)	28.2 (5.1)	30.1 (6.4)	29.5 (5.4)	29.0 (4.2)	29.3 (4.9)	28.4 (4.4)	27.6 (3.8)	0.619	0.674	0.721	0.875	0.748	0.843
Waist circumference, cm	100.9 (15.2)	100.7 (13.7)	98.8 (12.7)	104.5 (15.6)	105.3 (18.7)	100.4 (11.2)	100.4 (12.5)	97.0 (12.5)	96.2 (9.6)	0.192	0.524	0.233	0.158	0.185	0.086
Fat mass, %	28.9 (7.2)	27.3 (5.2)	26.8 (5.4)	30.5 (7.6)	28.9 (7.4)	29.6 (7.4)	28.5 (8.7)	27.3 (7.0)	26.5 (6.1)	0.434	0.319	0.897	0.627	0.508	0.998
Systolic BP, mm Hg	121 (15)	127 (18)	126 (14)	124 (14)	125 (15)	127 (14)	122 (14)	121 (161)	124 (13)	**0.043**	0.836	0.897	0.118	0.516	0.673
Diastolic BP, mm Hg	77 (9)	82 (9)	81 (7)	79 (10)	80 (10)	82 (11)	78 (10)	78 (10)	80 (9)	**0.005**	0.491	0.946	0.120	0.638	0.326
Resting heart rate, bpm	60 (10)	59 (9)	59 (9)	66 (10)	58 (8)	62 (10)	62 (11)	58 (11)	60 (10)	0.250	0.098	0.693	**0.002**	0.858	0.266
Heart QoL															
Global, points	2.1 (0.5)	2.6 (0.4)	2.7 (0.3)	1.9 (0.6)	2.5 (0.4)	2.4 (0.6)	2.0 (0.6)	2.5 (0.5)	2.5 (0.7)	**< 0.001**	0.074	0.932	0.437	0.096	0.239
Physical, points	2.1 (0.6)	2.6 (0.5)	2.7 (0.3)	1.9 (0.6)	2.5 (0.4)	2.4 (0.7)	2.0 (0.6)	2.5 (0.5)	2.6 (0.6)	**< 0.001**	0.135	0.798	0.409	0.166	0.217
Emotional, points	2.3 (0.7)	2.6 (0.5)	2.7 (0.5)	1.9 (0.9)	2.4 (0.6)	2.4 (0.8)	2.2 (0.8)	2.5 (0.5)	2.5 (0.8)	**< 0.001**	0.160	0.357	0.744	0.182	0.590
General QoL															
MCS, points	51.9 (9.6)	55.7 (7.1)	52.6 (9.6)	46.4 (12.2)	52.4 (8.3)	50.9 (10.1)	49.9 (11.1)	54.4 (7.0)	52.6 (49.9)	**0.038**	0.161	0.286	**0.047**	0.321	0.671
PCS, points	41.8 (8.8)	49.7 (6.8)	51.4 (7.0)	41.9 (9.4)	47.0 (8.1)	50.6 (6.8)	41.9 (6.6)	50.0 (7.3)	49.9 (8.1)	**< 0.001**	0.959	0.827	**0.047**	0.418	0.282
Depression, points	5.9 (5.8)*	3.5 (4.3)	4.5 (5.3)	9.9 (7.9)	6.1 (6.0)	6.4 (6.9)	7.5 (6.6)	4.8 (4.5)	5.6 (6.4)	**0.021**	**0.031**	0.480	0.273	0.261	0.917
Accelerometry measures															
Light-intensity PA, min/d	57.6 (32.8)	80.3 (49.7)	78.3 (33.74)	53.2 (34.7)	73.9 (48.2)	86.6 (64.3)	63.7 (40.4)	79.8 (40.0)	83.2 (41.0)	**< 0.001**	0.750	0.598	0.663	0.958	0.746
MVPA, min/d	16.2 (13.4)	23.6 (19.2)	21.0 (10.9)	15.9 (14.6)	17.5 (12.5)	21.6 (20.8)	18.5 (18.4)	24.4 (20.3)	27.9 (21.8)	**0.011**	0.481	0.715	0.662	0.262	0.422

Demographic characteristics did not differ between groups at BL.

Values in boldface represent statistical significance ($P < 0.05$).

BL, baseline; BMI, body mass index; BP, blood pressure; bpm, beats per minute; HIIT, high-intensity interval training; MCS, mental component summary; MICT, moderate- to vigorous-intensity continuous training; MVPA, moderate-to-vigorous intensity physical activity; NW, Nordic walking; PA, physical activity; PCS, physical component summary; QoL, quality of life; Wk12, week 12; Wk26, week 26.

*Significantly lower than MICT ($P < 0.05$).

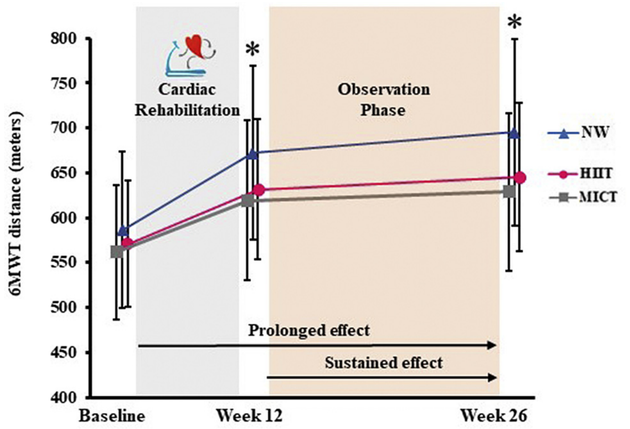

Figure 2. Changes in 6-minute walk test (6MWT) distance over time. Data are shown as mean ± SD. * Represents a significantly greater improvements from baseline in Nordic walking (NW) compared with high-intensity interval training (HIIT) and moderate-to-vigorous intensity continuous training (MICT).

interaction effect: $P = 0.025$) or MICT participants (562 ± 75 vs 628 ± 88; interaction effect: $P = 0.010$). The changes in 6MWT distance over 26 weeks did not differ significantly between HIIT and MICT groups ($P = 0.717$). Between week 12 and week 26, the 6MWT distance increased significantly from 641 ± 90 to 656 ± 95 m (main effect time: $P = 0.001$) with no significant time × exercise modality interaction effect ($P = 0.598$).

QoL

HeartQoL and general QoL scores are summarized in Table 1. Between baseline and week 26, there were significant increases in HeartQoL global (2.0 ± 0.6 vs 2.6 ± 0.5 points; $P < 0.001$), physical (2.0 ± 0.6 vs 2.6 ± 0.6 points; $P < 0.001$) and emotional (2.1 ± 0.8 vs 2.5 ± 0.7 points; $P < 0.001$) scores with no time × exercise modality interaction effect. Between week 12 and week 26, no main effect of time or no time × exercise modality interaction effects were observed for HeartQoL scores.

Between baseline and week 26, there were significant increases in MCS (49.4 ± 11.1 vs 52.1 ± 9.6 points; $P = 0.038$) and PCS (41.9 ± 8.3 vs 50.6 ± 7.3 points; $P < 0.001$) scores with no time × exercise modality interaction effects. Between week 12 and week 26, the PCS scores increased significantly (48.9 ± 7.5 vs 50.6 ± 7.3 points; $P = 0.047$), whereas the MCS scores significantly decreased (54.1 ± 7.5 vs 52.1 ± 9.6 points; $P = 0.047$). No time × exercise modality interaction effects were observed.

Depression symptoms

BDI-II scores are summarized in Table 1. Between baseline and week 26, BDI-II scores decreased significantly from 7.7 ± 7.0 to 5.5 ± 6.2 points (main effect of time, $P = 0.021$). There was no time × exercise modality interaction effect. Between week 12 and week 26, there was no significant effect of time or time × exercise modality interaction effect.

Physical activity levels

Accelerometry was completed by 118 participants at baseline (HIIT: n = 37; MICT: n = 40; NW: n = 41), 98 participants at week 12 (HIIT: n = 33; MICT: n = 33; NW: n = 32), and 82 participants at week 26 (HIIT: n = 28; MICT: n = 26; NW: n = 28). Daily light physical activity and moderate-to-vigorous physical activity minutes are summarized in Table 1. Between baseline and week 12, light (58 ± 36 vs 78 ± 46 min/d; $P < 0.001$) and moderate-to-vigorous (17 ± 16 vs 22 ± 18 min/d; $P = 0.029$) physical activity minutes increased. Between baseline and week 26, significant increases in time spent in light (58.0 ± 36.2 vs 82.6 ± 47.2 min/d; $P < 0.001$) and moderate-to-vigorous (16.9 ± 15.5 vs 26.6 ± 18.5 min/d; $P = 0.011$) physical activity were observed. There were no time × exercise modality interaction effects. Between week 12 and week 26, no changes in light or moderate-to-vigorous physical activity were observed.

Anthropometrics and hemodynamics

Anthropometrics and hemodynamic measures are summarized in Table 1. Body mass, body mass index, waist circumference, percent fat mass, and resting HR did not change significantly between baseline and week 26. There were significant increases in systolic BP (122 ± 14 vs 126 ± 14 mm Hg; $P = 0.043$) and diastolic BP (78 ± 10 vs 81 ± 14 mm Hg; $P = 0.005$). However, there were no time × exercise modality interaction effects.

From week 12 to week 26, resting HR increased significantly (59 ± 8 vs 61 ± 10 beats per minute; $P = 0.002$). Body mass, body mass index, waist circumference, percent fat mass, and systolic and diastolic BP did not change. There were no time × exercise modality interaction effects.

Discussion

This is the first RCT to simultaneously compare the prolonged effects of HIIT, MICT, and NW after coronary revascularization procedures. The primary finding was that, between baseline and week 26, NW had a significantly greater effect on increasing functional capacity measured using the 6MWT compared with HIIT and MICT. We previously showed that NW had a superior effect on increasing 6MWT distance compared with HIIT and MICT at the end of the 12-week supervised exercise program.[10] Our results add to this finding by showing that NW has a greater prolonged effect on improving functional capacity (ie, at 26 weeks) compared with HIIT and MICT. The mean changes from baseline to 26 weeks in 6MWT distance were 94.2 ± 65.4, 59.9 ± 52.6, and 55.6 ± 48.5 m for NW, HIIT, and MICT, respectively. Thus, although the NW group showed significantly greater improvements, all groups met the minimal clinical important difference of 54 m[41] at week 26. Our results also showed that: (1) HIIT, MICT, and NW had significantly positive prolonged effects on disease-specific and general QoL and depression symptoms with no differences in the degree of improvements between exercise modalities; (2) functional capacity continued to improve significantly after the completion of CR (ie, during the observation phase); (3) PCS continued to improve whereas MCS significantly deteriorated during the observation phase; and, (4) physical activity levels significantly increased from baseline to week 12, which was maintained during the observation phase.

Functional capacity assessed using the 6MWT is an important predictor of cardiovascular events in patients with stable CAD; its ability to predict cardiovascular events is similar to that of exercise capacity measured using treadmill testing with stress echocardiograms.[4] The significantly greater increase in 6MWT distance after NW than HIIT and MICT is largely attributable to the greater increase at week 12 (ie, at the end of supervised exercise-based CR).[10] As previously described, this significantly greater increase by NW might reflect an alignment of testing and training modalities (ie, walking) and improvements in postural control and gait parameters.[10] Although functional capacity continued to increase during the observation phase, the increase was smaller compared with the intervention phase (ie, baseline to week 12).

We also found significant prolonged improvements in disease-specific and general QoL and depression symptoms, with no differences in the degree of changes between exercise modalities. Such improvements are important because patients in CR have many psychosocial concerns[12] and depression increases risk of cardiovascular complications and death in patients with CAD.[13] The prolonged improvements were largely supported by significant positive changes during supervised exercise sessions because there were no further improvements after the completion of CR during the observation phase, except for the PCS score of general QoL, which increased significantly. Conversely, the MCS score of general QoL significantly worsened during the observation phase, highlighting the need for additional strategies to sustain the positive changes in mental QoL. Although there were statistically significant increases in systolic and diastolic BP from baseline to week 26 and resting HR between weeks 12 and 26, such changes are unlikely clinically meaningful.

The sustained increase in functional capacity and PCS scores during the observation phase might be explained by increased physical activity levels. Between baseline and week 12, daily time spent in light and moderate-to-vigorous intensity physical activity significantly increased, whereas daily activity minutes did not change between week 12 and week 26. Consequently, adherence to physically active behaviours after the completion of CR might explain the continued increases in functional capacity and physical QoL between week 12 and week 26. Considering that a large proportion of patients (> 80%) engage in either no or insufficient physical activity after acute coronary syndrome,[42] our results support the benefits of exercise-based CR to promote physical activity after graduating from CR programs. However, our results suggest this was not sufficient to sustain the CR-induced improvement in the MCS score of general QoL.

Our study has strengths and limitations. To date, most studies have focused on immediate changes induced by CR. Our RCT was the first to simultaneously compare the prolonged effects of HIIT, MICT, and NW, addressing an important gap in the literature. One of the limitations of the study was its relatively short follow up duration (ie, 14 weeks after CR completion). Because many studies have shown diminished effects of CR on physical and psychological health at 1 year,[23,24,26,43] it was important to assess changes at an earlier time point. Although our study showed that physical activity level was maintained for 14 weeks after the completion of CR, a recent study showed that physical activity levels decreased over 26 weeks after the completion of CR.[44] Future studies with follow-up measures at multiple time points during an extended observation phase will further clarify the prolonged benefits of different exercise modalities. Additionally, participants were recruited from a single centre and there were a small number of females. This limits the generalizability of our findings. The small proportion of female participants randomized in our study represents the smaller number of female patients referred to CR. We screened 1223 patients referred to CR, of whom 228 (18.6%) were female. This is consistent with a meta-analysis in which it was reported that females are significantly less likely to be referred to CR compared with men.[45]

Conclusion

In conclusion, when prescribing exercise for patients with CAD, patients' preference should be considered.[16] This study showed that HIIT, MICT, and NW have similar prolonged effects on disease-specific and general QoL and depression symptoms, providing patients with CAD different exercise modalities to improve such important patient-rated outcomes. These prolonged benefits might be perpetuated by the continuation of physically active behaviours after CR. For increasing functional capacity, our study showed that NW is superior to HIIT and MICT. Considering that functional capacity is an important predictor of future cardiovascular events in patients with CAD, NW might offer important prolonged benefits for patients with CAD after completing on-site CR.

Acknowledgements

The authors thank the patients, CR staff, and Anna Clarke, Christie Cole, Dr Daniele Chirico, Kyle Scott, Brenna Czajkowski, Rachelle Beanlands, Janet Wilson, Aaron Brautigam, and Yannick MacMillan for their contributions to this research.

Funding Sources

This investigator-initiated research was supported by the Innovations Fund of the Alternate Funding Plan for the Academic Health Sciences Centres of the Ministry of Ontario (PIs: A.P., J.L.R.) and Heart and Stroke Foundation of Canada (PI: R.D.R.). T.T. was supported by a Canadian Institutes of Health Research Postdoctoral Fellowship and Jan and Ian Craig Cardiac Prevention and Rehabilitation Endowed Fellowship from the University of Ottawa Heart Institute.

Disclosures

The authors have no conflicts of interest to disclose.

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