Effects of comprehensive cardiac rehabilitation on functional capacity in a middle-income country: a randomized controlled trial

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ABSTRACT

Objective: Despite the growing epidemic of cardiovascular diseases in middle-income countries, there is insufficient evidence about cardiac rehabilitation (CR) in these countries. Thus, the effects of comprehensive CR on functional capacity and risk factors were investigated in Brazil, to test the hypothesis that it results in better outcomes than exercise-only or no CR.

Methods: Single-blinded, randomized controlled trial with three parallel arms: comprehensive CR (exercise + education) *vs* exercise-only CR *vs* wait-list control. Eligible coronary patients were randomized in blocks of four with 1:1:1 concealed allocation. Participants randomized to exercise-only CR received 36 exercise classes; comprehensive CR group also received 24 educational sessions. The primary outcome was Incremental Shuttle Walk Test (ISWT) distance; secondary outcomes were cardiovascular risk factors. All outcomes were assessed at baseline and 6 months later. Analysis of covariance was performed on the basis of intention-to-treat (ITT) and per-protocol.

Results: 115 (88.5%) patients were randomized; 93 (80.9%) were retained. There were improvements in ISWT distance from pre to post-test with comprehensive (from 358.4±132.6 to 464.8±121.6 meters; mean change=106.4; p<.001) and exercise-only (from 391.5±118.8 to 488.1±106.3 meters; mean change=96.5, p<.001) CR, with significantly greater functional capacity with comprehensive CR *vs* control (ITT: mean difference=75.6±30.7 meters, 95% confidence interval=1.4-150.2). There were also reductions in systolic blood pressure with comprehensive CR (ITT: reduction of 6.2±17.8 mmHg, p=.04). There were no significant differences for other outcomes.

Conclusion: Results showed clinically significant improvements in functional capacity and blood pressure with CR, and significantly greater functional capacity with comprehensive CR compared to usual care.

Keywords: coronary artery disease; cardiac rehabilitation; patient education; randomized controlled trials.

Key questions

What is already known about this subject?
Cardiac rehabilitation has been shown to reduce morbidity and mortality as well as improve functional capacity when compared to usual care (i.e.: no cardiac rehabilitation) in high-income countries.
What does this study add?
This study adds the importance of a comprehensive cardiac rehabilitation program (i.e.: includes the educational component) in low and middle-income countries.
How might this impact on clinical practice?
A comprehensive cardiac rehabilitation program in low and middle-income countries can improve the functional capacity and risk factors control, and these benefits likely translate to significant reductions in mortality.

Statement

INTRODUCTION

Cardiovascular diseases (CVD) are the leading cause of death globally, with >80% occurring in low and middle-income countries (LMICs).[1] Cardiac rehabilitation (CR) is an outpatient model of care designed to mitigate this burden, through comprehensive delivery of secondary prevention.[2,3] Participation in CR reduces morbidity and mortality by 20%.[4]

These benefits have been established in randomized controlled trials (RCTs) in high-income countries. A review of CR RCTs in LMICs identified only two,[5] in China and Turkey.[6,7] Oxygen consumption, walking performance, and lipids were improved. While it is assumed comparable benefits could be achieved in LMICs, clearly there is a dearth of evidence to demonstrate this, despite the fact that CR is available in 54 LMICs.[8] Given differences in socio-economic context, healthcare delivery, and in the nature of CR delivered in high versus LMICs (i.e., fewer core components[8]), more trials of CR in LMICs are warranted to understand the benefits that can be achieved.

Accordingly, we set out to undertake a pragmatic RCT of comprehensive (i.e., exercise with education) versus exercise-only versus no CR (wait-list control) in a LMIC, to determine whether comprehensive CR results in better functional capacity and cardiovascular risk factor control, when compared to exercise-only CR or no CR. It was hypothesized that participants randomized to comprehensive CR would have significantly better outcomes than those participating in exercise-only CR or not participating.

METHODS

The study was approved by the research ethics committees at Universidade Federal de Minas Gerais (UFMG), in Belo Horizonte, Brazil (#898.235) and York University, in Toronto, Canada (#e2015-172). The protocol was registered on clinicaltrials.gov (NCT02575976), and published.[9] Primary and secondary outcomes are reported here.

Study design

This was a single-blinded, single-site, pragmatic, superiority RCT with three parallel arms: comprehensive CR (education and exercise) *versus* exercise-only CR (no education, as delivered in Brazil) *versus* wait-list control. Assessments were undertaken pre-randomization and again six months later (in accordance with the end of CR).

Setting

Brazil was chosen as the LMIC for testing because of: (1) the great burden of CVD,[10] (2) the availability of country-specific CR guidelines ([11,12]; there are few national CR guidelines developed in LMICs), and (3) there has never been an RCT of CR (with any outcome) in South America to our knowledge.[5].

The trial was undertaken in a publicly-funded academic centre, Hospital das Clínicas da UFMG, in Belo Horizonte. The wait list control group received usual care, which consisted of follow-up appointments with their physician as deemed medically appropriate. The standard of care for Brazilian adults with CVD does not include access to CR, given the gross

lack of capacity.[13] Participants randomized to the wait-list control arm were offered CR after 6 months.

Participants

Coronary artery disease, post-myocardial infarction patients or those who had undergone percutaneous coronary intervention or coronary artery bypass graft surgery and had been referred to CR or were eligible to enroll, were invited to participate. The inclusion criteria were: ≥18 years old and living in the Belo Horizonte area. The exclusion criteria were: any comorbid physical or serious mental condition which could interfere with the ability to exercise according to CR clinical practice guidelines[10] (i.e., heart failure with ejection fraction less than 45%), or any visual or cognitive condition (e.g., advanced dementia) which could preclude the participant from completing the questionnaires. Sample size planned was 186 patients (62 per group); Calculations details were described elsewhere.[9]

Intervention arms

The CR program usually offers exercise only (not comprehensive). There is no charge to patients. It is delivered by physiotherapists and physicians. Participants undergo an assessment including functional capacity and risk factors at intake and again at end of the program.

CR participants received an individualized exercise prescription based on a graded exercise stress test. Participants were instructed to exercise between 50-80% of heart rate

reserve. The exercise program was six months, consisting of 36 supervised sessions offered in decreasing frequency (3 times to once/week).[9] The 1-hour exercise sessions were composed of 10 minutes of warm-up, 30 minutes of aerobic exercises (treadmill, bike and walking), 15 minutes of resistance training and 5 minutes for cool down. Patients were directed to exercise in their communities on the days they were not on site.

In the comprehensive CR arm, patients were additionally offered 24 education sessions, supported by a workbook (https://www.healtheuniversity.ca/en/cardiaccollege). These were delivered in a group setting, each for 30 minutes, just prior to or after an exercise session. The empirically-validated English version [14,15] was translated and culturally-adapted to Brazilian-Portuguese, using best practice methodologies.[16] Sessions covered diet, exercise, mental health and risk factor management, and were delivered mainly by a physiotherapist (GC) but also a cardiologist and dietitian.

Procedure

Consecutive patients were approached between March 2015 and April 2017 by a doctoral student (GC) at initial CR visit. With informed written consent and CR clearance from the physician (informed by intake stress test), potentially-eligible patients were scheduled to come on-site to complete pre-test assessments. This included the Incremental Shuttle Walk Test (ISWT; i.e., indicator of functional capacity),[17] blood pressure and adiposity. Participants were asked to bring their most recent laboratory test results for lipids

and glucose; They were provided a requisition to take for lipid and glucose assessment if not current or available. Participants were also asked to complete a sociodemographic questionnaire. Clinical data were extracted from medical charts.

Eligible participants were randomized to one of the three groups. The randomization sequence was generated by a professor not involved in the study using the randomization.com website in random blocks of four, with a 1:1:1 allocation ratio. To ensure allocation concealment, the principal investigator (RB) had the allocation sequence in a password-protected file, and only provided randomization information to the PhD student once it was confirmed the participant was eligible. Due to the nature of the intervention, participants and the doctoral student could not be blind to treatment allocation.

Six months post-randomization, participants were again invited to come to the study center for another shuttle walk test, and to undertake assessments of secondary outcomes. They were provided a requisition for laboratory testing for lipids and glucose. To minimize loss to follow-up, participants were reminded by phone to come on-site for these assessments. CR use was extracted from charts. A master's student blinded to random allocation was responsible for post-test assessments, outcome ascertainment, and data entry.

Measures

Primary outcome: functional capacity

At pre-test and 6 months later, the ISWT[17] was performed and the walked distance, in meters (primary outcome), was recorded. The test was terminated if participants felt too breathless or fatigued to maintain the required speed to complete a 10-meter shuttle interval in the time allowed.

Secondary outcomes: risk factors

The risk factors evaluated were blood pressure, body mass index, waist circumference, glucose and lipids. Blood pressure was assessed using the validated 7670-06 mobile stand (Welch Allyn Inc., Skaneateles Falls, NY, USA). Mean systolic and diastolic blood pressure values were recorded, and hypertension was considered where values exceed 140/90 mmHg and/or participant was taking a blood pressure-lowering medication.[11] A weight scale and measuring tape were used to assess anthropometrics. Those with body mass index above 30 kg/m^2 were considered obese.[11] Waist circumference was assessed at the superior border of the iliac crest.[11] Values greater than 102 cm in men and 88 cm in women were considered indicative of central obesity.[18] Glycaemia and lipid values were extracted from center charts. Dysglycemia was considered present where fasting blood glucose exceeded 126 mg/dl and/or participant was taking a glucose-lowering medication, and dyslipidemia was considered present where total cholesterol values exceeded 240 mg/dl and/or participant was on a lipid-lowering agent.[11]

Statistical analyses

First, session attendance of participants in the two CR arms was explored as a manipulation check, and to support per protocol analyses. Second, baseline sociodemographic and clinical characteristics were compared between groups to identify any chance differences that may have occurred despite random assignment, using chi-square and analysis of variance as appropriate. Third, retention for the post-test ISWT was considered, and differences in the sociodemographic and clinical characteristics of participants retained versus lost to follow-up were tested using chi-square and t-tests as appropriate.

Outcome analyses were performed on the basis of intention-to-treat (ITT) using last observation carried forward to mitigate bias, and per protocol (PP). Change in each outcome from pre to post-test was preliminarily considered by arm, and a paired t-test performed. To test the hypotheses, an analysis of covariance (ANCOVA) was performed for each outcome, with group (i.e., comprehensive CR *versus* exercise-only *versus* wait-list control) as the independent variable, and pre-test value as a covariate, and the post-test value as the dependent variable. PP analyses were run unadjusted, and then adjusting for any sociodemographic or clinical biases based on retention. A Bonferroni post-hoc test was performed where significant group differences were observed. SPSS version 24.0 was used (IBM Corp, 2016), and $p<.05$ was considered significant.

RESULTS

Respondent Characteristics

A flow diagram is shown in Figure 1. Of note, some participants were not eligible for the trial because they could not get an exercise stress test. There was a cardiopulmonary technician strike from June to October of 2015. As displayed, 115 patients were randomized.

Table 1 presents the sociodemographic and clinical characteristics of participants at pre-test. Overall, 62 (54.9%) achieved at least 7 metabolic equivalents of task (METs) on the stress test. Ninety-five (82.6%) were considered to have hypertension (i.e., blood pressure ≥ 140/90 or on a blood pressure-lowering medication), and 35 (30.4%) were obese (with 50 [45.0%] abdominally obese). Thirty (26.0%) had dysglycemia and 79 (69.9%) dyslipidemia.

Table 1 also presents the characteristics of participants by arm. Randomization was effective in ensuring equivalence across groups in most instances. Of note, there were no significant differences in any outcome at pre-test by arm, nor on the stress test.

As also shown in Figure 1, among those randomized to a CR arm, 57 (75%) initiated the program. Three (2.6%) participants in the exercise-only and five (4.3%) in the comprehensive arms had valid clinical reasons for missing sessions. None of these events were considered to be due to the CR intervention. There were no harms or adverse events related to exercise-only or comprehensive CR.

On average those in the exercise-only CR attended a mean of 23.6±8.5 of 36 prescribed exercise sessions (i.e., 65.5%); those in the comprehensive arm attended a mean of

24.4±7.2 prescribed exercise sessions (i.e., 67.8%), and a mean of 18.6±6.8 of 24 prescribed education sessions (i.e., 77.5%). Considering a threshold of 24 exercise sessions attended and 16 education sessions attended, overall 25 (80.6%) participants in the exercise only arm and 26 (81.2%) participants in the comprehensive arm were included in the PP analyses.

As shown in Figure 1, 93 (80.9%) participants were retained (i.e., completed the post-test ISWT). There were no deaths at 6 months. Table 2 compares the sociodemographic and clinical characteristics of those retained versus lost to follow up. There was minimal bias in the retained sample, except that those retained were significantly older and were less likely to be working and taking anti-platelets than those lost to follow-up. Therefore, sensitivity analysis were performed adjusting for these variables. Of note, there were no significant retention biases in relation to study outcomes.

Functional Capacity

Mean scores on the ISWT at pre and post-test are shown by arm on an ITT and PP basis in Figure 2. At pre-test, participants completed a mean of 37.3±12.8 shuttles and at post-test, participants completed a mean of 44.6±14.3 shuttles (significantly lower in women; $p<.001$). The main reason for ISWT termination at post-test was limb fatigue (n=73; 63.5%). There was a significant increase in ISWT distance from pre to post-test in both CR arms, but not in the wait-list control, whether examining change on an ITT or PP basis. When adjusting for the 3 variables where retention bias was observed, the significant difference persisted.

As also shown in Figure 2, there was a significant difference in the primary outcome by arm when examined via ITT and PP (unadjusted and adjusted). When adjusting for the 3 variables where retention bias was observed, the significant difference persisted. Post-hoc analyses showed ISWT distance at post-test was significantly greater in the comprehensive CR arm than in the control arm (ITT mean difference [MD]=75.6, 95% confidence interval [CI]=1.4-150.2; and PP_{adj} MD=94.1, 95% CI=3.3-184.3). No other differences were observed.

Exploratory analyses were undertaken to examine the impact of CR arm among women only. General linear model revealed a significant interaction of arm x time (ITT p=0.03; supplemental Figure 3), again supporting the benefits of CR on functional capacity.

Risk Factors

With regard to secondary outcomes, 81 (70.4%) completed the blood pressure and adiposity assessments (see Table 3). Due to the low number of participants that returned the lab work required, no inferences were made regarding glucose or lipids.

Mean risk factor scores at pre and post-test are also shown by arm on an ITT and PP basis in Table 3. As shown there was no significant change from pre to post-test in any risk factor in any arm, whether examined on the basis of ITT or PP, except for a significant reduction in systolic blood pressure in the comprehensive arm (PP). Moreover, there were no significant differences in post-test risk factor values by arm.

DISCUSSION

This first-ever RCT of CR in Latin America and third ever in a LMIC, has demonstrated that CR results in clinically meaningful improvements in functional capacity and reductions in blood pressure, and that comprehensive CR is superior to no CR in improving functional capacity. The magnitude of change found in walked distance in this study is greater than the clinically-important difference of 70 meters for better functional capacity.[9,19]. Given the association of functional capacity with mortality,[20,21] these results suggest that the benefits of CR are also substantive in LMICs. These results also support the importance of delivering comprehensive CR in LMICs to ensure patients achieve the benefits associated with CR.

The hypothesis of the trial was partially supported, based on ITT, and it is suspected that there was no significant difference in functional capacity between CR arms or between exercise-only and no CR because the target sample size for the trial was not reached. Thus, further adequately-powered research is needed to confirm. Results overall also suggest that comprehensive CR is effective in risk factor management, particularly hypertension. The lack of impact of CR on adiposity indices is not surprising, given lack of impact in many CR RCTs in HICs, except where specific focus on weight loss is a feature of a program.[22,23] The impact on lipids and glucose could not be properly assessed due to limited sample size. Again, further research is warranted.

Previous meta-analyses have shown equivalent or greater benefits of exercise-only CR when compared to comprehensive CR.[24,25] It is true that recommendations that CR be comprehensive are based on expert consensus (likely based on robust data showing the positive impact of each component delivered outside of the CR setting).[26] It is perceived that the impact of the exercise component may be greatest;[20,27] our group is currently testing this contention, comparing the impact of each core component head-to-head through network meta-analysis. Overall though, results of this trial point to the importance of delivering comprehensive CR in LMICs too. This has been the first trial comparing comprehensive to exercise-only CR in a LMIC, and clearly more adequately-powered, multi-centre trials are needed before drawing firm conclusions. However, as CR programs are developed in LMICs due to the shift of disease burden to non-communicable diseases such as CVD, it is recommended that programs be as comprehensive as resources allow.[2,3]

Caution is warranted in interpreting the findings of this study. First, generalizability of results is limited for several reasons. This was a single-site study (a public hospital), undertaken in one LMIC. There may have been selection bias, in that as shown with patients in high-income countries, patients who access CR are likely more advantaged than those who do not. Patients were recruited in a public system though and had quite low income.

Second, the sample size is small and the trial may have been under-powered for the secondary outcomes. It was under-powered for the primary outcome, there was also loss to

follow up, yet a significant effect was nevertheless observed both in ITT and PP analyses.

Because of recruitment challenges such as lack of CR referral and the strike of cardiopulmonary technicians who were responsible for stress testing, the target sample size was not reached. Moreover, because most of patients did not get their bloodwork done in a reasonable timeframe after the CR program, although retention for the primary outcome was quite high, there was a very low sample size for the secondary outcomes of lipids and glucose.

Finally, only proximal outcomes were tested in the current trial. It would be preferable to have tested for differences in mortality. This would have required a larger sample size, and longer follow-up (which would be contaminated because our control arm was to be offered CR at the end of the trial for ethical reasons). However, functional capacity is closely associated with mortality,[28] and given the magnitude of improvement achieved, it is probable that the benefits demonstrated herein would result in reduced mortality. On a related note, while walk tests are recommended in low-resource settings,[2,3] formal treadmill testing was not undertaken in the current trial, although it is a more robust way to establish functional capacity.

CONCLUSION

Clinically significant improvements in functional capacity and blood pressure are achieved with CR, as well as significantly greater functional capacity with comprehensive CR compared to usual care. These benefits likely translate to significant reductions in mortality,

although an adequately-powered trial to demonstrate this is needed. Thus, advocacy for greater implementation of comprehensive CR is needed,[29] with the aim of improving the care of cardiac patients in Brazil, as well as in other Latin American countries, and in LMICs more broadly.

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TABLE 1 Participants' baseline sociodemographic and clinical characteristics by randomized group

n (%) / *mean ± SD*	**Wait list control** (N=39)	**Exercise-only** (N=39)	**Comprehensive** (N=37)	**Total** (N=115)
Sociodemographic				
Sex (% male)	27 (69.2)	28 (71.8)	27 (73.0)	82 (71.3)
Age, *years*	58.7±9.6	59.0±9.9	60.7±8.8	59.5±9.4
Education (% low†)	28 (71.8)	33 (84.6)§	21 (56.8)§	82 (71.3)*
Marital status (% married or equiv.)	27 (69.2)	27 (69.2)	20 (54.1)	74 (64.3)
Work status (% employed)	17 (43.6)	14 (35.9)	15 (40.5)	46 (40.0)
Monthly income (% low#)	35 (89.7)	34 (87.2)	31 (83.8)	100 (87.0)
Clinical				
CR Indication (% yes)				
Myocardial infarction	35 (89.7)	37 (94.9)	35 (94.6)	107 (93.0)
Angina	27 (69.2)	21 (53.8)	21 (56.8)	69 (60.0)
PCI	23 (59.0)	23 (59.0)	22 (59.5)	68 (59.1)
Bypass surgery	10 (25.6)	7 (17.9)	12 (32.4)	29 (25.2)
First event (% no)	8 (21.1)	8 (21.1)	12 (32.4)	28 (24.8)
Comorbidities (% yes)				
Depression	7 (17.9)	7 (17.9)	6 (16.2)	20 (17.4)
Kidney disease	4 (10.3)	3 (7.7)	6 (16.2)	13 (11.3)
Liver disease	1 (2.6)	2 (5.1)	5 (13.5)	8 (7.0)

Rheumatic disease	4 (10.3)	1 (2.6)	2 (5.4)	7 (6.1)
Cancer	0§§	1 (2.6)	5 (13.5)§§	6 (5.2)*
Stroke	0	1 (2.6)	2 (5.4)	3 (2.6)
COPD	0	3 (7.7)	0	3 (2.6)
Functional Capacity				
Stress test (HR max, *bpm*)	119.0±20.3	124.8±21.4	120.4±24.2	121.4±21.9
Stress test (peak METs)	7.3±2.4	7.7±2.6	7.8±2.6	7.6±2.5
ISWT (meters)	376.4±145.6	361.0±119.4	381.1±120.9	372.7±128.5
Risk Factors				
BP systolic (*mmHg)*	117.9±17.6	117.3±24.7	123.8±15.1	119.6±19.6
BP diastolic (*mmHg)*	74.6±16.0	77.7±13.0	77.0±11.0	76.4±13.5
BMI (kg/m^2)	27.8±4.0	28.7±6.0	28.1±4.2	28.2±4.8
Waist circumference (*cm)*	94.9±9.8	96.7±10.6	96.0±11.5	95.9±10.6
Total Cholesterol (*mg/dl)*	152.8±34.6	148.7±39.4	165.0±61.9	155.7±46.9
LDL (*mg/dl)*	82.5±30.2	80.4±23.7	86.4±29.7	83.1±27.9
HDL (*mg/dl)*	42.0±7.0	40.4±14.3	39.5±7.9	40.7±10.1
Triglycerides (*mg/dl)*	141.3±51.3	137.7±75.2	166.0±117.0	148.6±85.6
Glucose (fasting, *mg/dl)*	109.9±38.3	107.2±35.3	104.6±20.2	107.3±32.0
Sleep apnea	5 (12.8)	4 (10.3)	4 (10.8)	13 (11.3)
Smoking (% current)	2 (5.1)	4 (10.3)	3 (8.1)	9 (7.8)
Medications				

Statins	38 (97.4)	37 (94.9)	36 (97.3)	111 (98.2)
ASA	36 (94.7)	35 (92.1)	35 (97.2)	106 (94.6)
Beta-blockers	37 (97.4)§§	30 (78.9)§§	33 (91.7)	100 (89.3)*
Anti-platelets	28 (73.7)	30 (78.9)	23 (63.9)	81 (72.3)
ACE-inhibitors	20 (52.6)	26 (68.4)	27 (75.0)	73 (65.2)
ARBs	12 (31.6)	8 (21.1)	6 (16.7)	26 (23.2)

SD: standard deviation; PCI: Percutaneous Coronary Intervention; COPD: chronic obstructive pulmonary disease; BP: blood pressure; LDL: low-density lipoprotein; HDL: high-density lipoprotein; BMI: body mass index; HR: heart rate; BPM: beats per minute; MET: metabolic equivalent of task; ISWT: incremental shuttle walk test; ASA: acetylsalicylic acid; ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blockers; CR: cardiac rehabilitation.
†did not complete high school;
#less than four minimum wages per month
Analysis of variance *p<.05
Bonferroni Post-hoc test §p<.05, §§p<.01

TABLE 2 Participants' baseline sociodemographic and clinical characteristics by retention status

n (%) / mean ± SD	**Retained** (N=93)	**Lost to follow-up** (N=22)	**Total** (N=115)
Sociodemographic			
Sex (% male)	65 (69.9)	17 (77.3)	82 (71.3)
Age, *years*	60.4±9.5*	55.6±8.3*	59.5±9.4
Education (% low†)	68 (73.1)	14 (63.6)	82 (71.3)
Marital status (% married or equiv.)	61 (65.6)	13 (59.1)	74 (64.3)
Work status (% employed)	30 (32.3)**	16 (72.7)**	46 (40.0)
Monthly income (% low#)	82 (88.2)	18 (81.8)	100 (87.0)
Clinical			
CR Indication (% yes)			
Myocardial infarction	85 (91.4)	22 (100.0)	107 (93.0)
Angina	57 (61.3)	12 (54.5)	69 (60.0)
PCI	55 (59.1)	13 (59.1)	68 (59.1)
Bypass surgery	26 (28.0)	3 (13.6)	29 (25.2)
First event (% no)	21 (23.1)	7 (31.8)	28 (24.8)
Comorbidities (% yes)			
Depression	14 (15.1)	6 (27.3)	20 (17.4)
Kidney disease	10 (10.8)	3 (14.3)	13 (11.3)

Liver disease	8 (8.6)	0	8 (7.0)
Rheumatic disease	6 (6.5)	1 (4.5)	7 (6.1)
Cancer	6 (6.5)	0	6 (5.2)
Stroke	3 (3.2)	0	3 (2.6)
COPD	3 (3.2)	0	3 (2.6)
Functional Capacity			
Stress test (HR max, *bpm*)	120.5±22.1	125.0±21.2	121.4±21.9
Stress test (peak METs)	7.6±2.6	7.6±2.2	7.6±2.5
ISWT (meters)	369.0±133.2	388.1±107.9	372.7±128.5
Risk Factors			
BP systolic (*mmHg)*	120.5±20.1	115.9±17.6	119.6±19.6
BP diastolic (*mmHg)*	76.2±13.7	77.3±13.2	76.4±13.5
BMI (kg/m^2)	28.3±5.0	27.7±4.4	28.2±4.8
Waist circumference (*cm)*	96.1±10.9	95.0±9.2	95.9±10.6
Total Cholesterol (*mg/dl)*	157.0±49.2	147.8±30.6	155.7±46.9
LDL (*mg/dl)*	83.8±28.2	79.3±27.2	83.1±27.9
HDL (*mg/dl)*	40.7±10.3	40.3±8.7	40.7±10.1
Triglycerides (*mg/dl)*	150.6±90.4	135.4±42.5	148.6±85.6
Glucose (fasting, *mg/dl)*	108.6±34.1	99.8±14.2	107.3±32.0
Sleep apnea	11 (11.8)	2 (9.1)	13 (11.3)
Smoking (% current)	7 (7.5)	2 (9.1)	9 (7.8)

Medications			
Statins	90 (97.8)	21 (100)	111 (98.2)
ASA	86 (94.5)	20 (95.2)	106 (94.6)
Beta-blockers	80 (87.9)	20 (95.2)	100 (89.3)
Anti-platelet	62 (68.1)*	19 (90.5)*	81 (72.3)
ACE-inhibitors	62 (68.1)	11 (52.4)	73 (65.2)
ARBs	23 (25.3)	3 (14.3)	26 (23.2)

SD: standard deviation; PCI: Percutaneous Coronary Intervention; COPD: chronic obstructive pulmonary disease; BP: blood pressure; LDL: low-density lipoprotein; HDL: high-density lipoprotein; BMI: body mass index; HR: heart rate; BPM: beats per minute; MET: metabolic equivalent; ISWT: incremental shuttle walk test; ASA: acetylsalicylic acid; ACE: angiotensin-converting-enzyme; ARB: angiotensin receptor blockers; CR: cardiac rehabilitation; ECR: exercise-only CR; CCR: comprehensive CR.
†did not complete high school;
#less than four minimum wages per month
Unpaired T Test *p<.05, **p<0.00

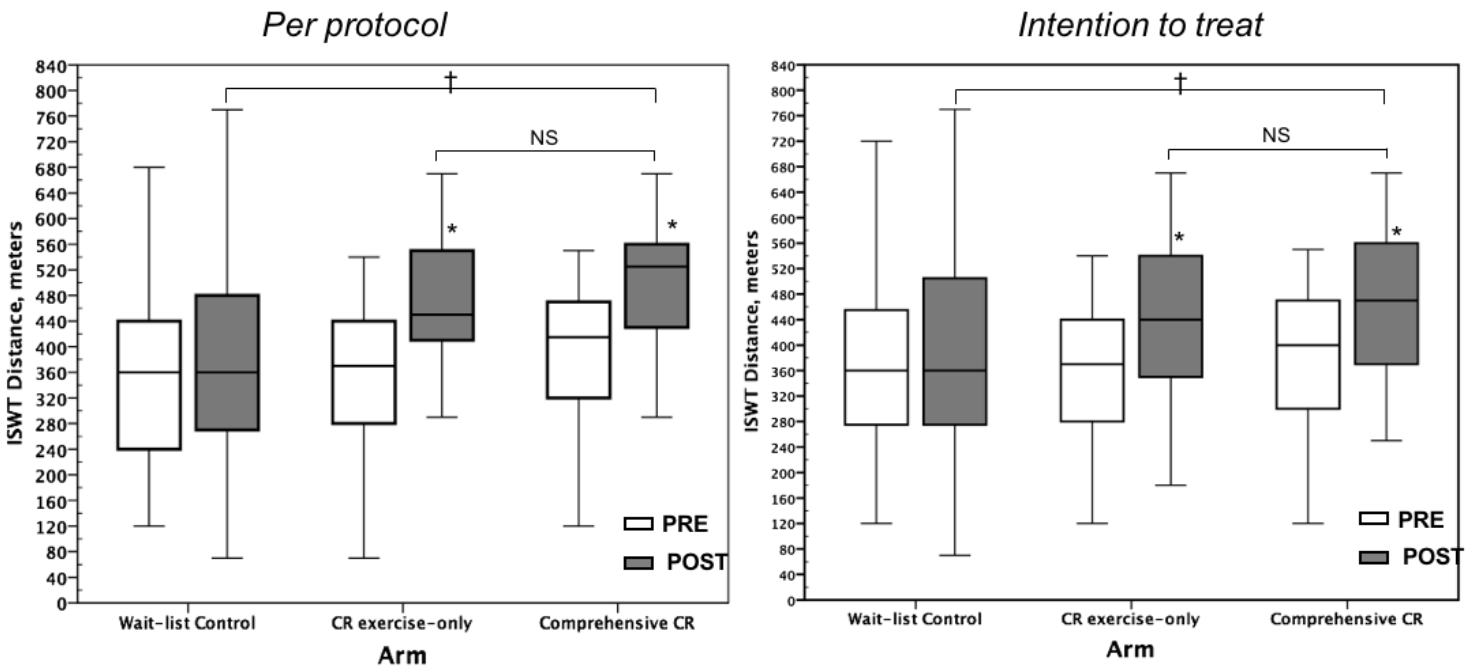
TABLE 3 Risk factors in participants completing assessments both pre and post-program

(Mean ± SD)		**Per Protocol** N=81				**Intention-to-treat** N=115		
	n	Pre-CR	Post-CR	Change†	n	Pre-CR	Post-CR	Change†
Risk Factors								
BP systolic,								
mmHg								
Wait-list control	30	120.3±16.3	120.0±18.4	0.3	39	117.9±17.6	117.7±19.1	0.2
ECR	25	120.0±18.0	114.4±16.3	5.6	39	117.3±24.7	117.4±17.0	0.18
CCR	26	121.3±14.8	114.6±19.2	6.7†	37	123.8±15.1	117.6±19.8	6.2†
Analysis of covariance		*F unadj=1.23, p=0.55; Fadj=1.16, p=0.32*				*F=1.14, p=0.32*		
BP diastolic,								
mmHg								
Wait-list control	30	75.3±16.3	77.0±15.3	1.7	39	74.6±16.0	75.9±15.3	1.3
ECR	25	76.0±14.4	74.2±11.9	1.8	39	77.7±13.0	77.8±12.6	0.1
CCR	26	75.7±12.0	73.7±12.7	2.0	37	77.0±11.0	75.3±12.6	1.7
Analysis of covariance		*F unadj=0.60, p=0.30; Fadj=0.55, p=0.58*				*F=0.50, p=0.60*		

BMI, *Kg/m²*								
Wait-list control	30	27.8±3.9	27.8±3.5	0.04	39	27.8±4.0	27.8±3.8	0.03
ECR	25	27.5±3.9	27.5±4.3	0.06	39	28.7±6.0	28.9±6.9	0.2
CCR	26	27.7±4.0	27.8±4.6	0.1	37	28.1±4.2	28.1±4.5	0.08
Analysis of covariance		*F unadj=0.10, p=0.90; F adj=0.02, p=0.98*				*F=0.15, p=0.86*		
Waist circumference, *cm*								
Wait-list control	28	95.0±9.2	94.9±9.4	0.1	37	94.9±9.8	94.8±9.9	0.05
ECR	24	94.8±9.4	93.0±10.0	1.8	38	96.7±10.6	95.6±10.9	1.0
CCR	25	95.8±12.5	95.5±13.4	0.3	36	96.0±11.5	95.6±11.9	0.4
Analysis of covariance		*F unadj=1.05, p=0.35; Fadj=0.94, p=.039*				*F=0.71, p=0.50*		

SD: standard deviation; SBP: systolic blood pressure; DBP: diastolic blood pressure; BMI: body mass index; CR: cardiac rehabilitation; ECR: exercise-only CR; CCR: comprehensive CR.
Difference between first and second assessment assessed using paired t-test; †p<.05
Fadj shows results of per protocol analysis, adjusting for age, work status and use of anti-platelets (as per retention bias in Table 2).

Figure 2 Distance walked on incremental shuttle walk test by arm and time



(Figure 2 legend)
Box plot of distance walked on incremental shuttle walk test (ISWT, meters) by arms and time (pre and post). The central rectangle spans the first quartile to the third quartile. The line inside the box shows the median, and the whiskers above and below the box show the minimum and maximum. * p<.05 within group, † p<0.05 between group, NS=no significant differences between groups. CR=cardiac rehabilitation

Figure 3 -Distance walked on incremental shutle walk test by arms, time and sex (supplemental)

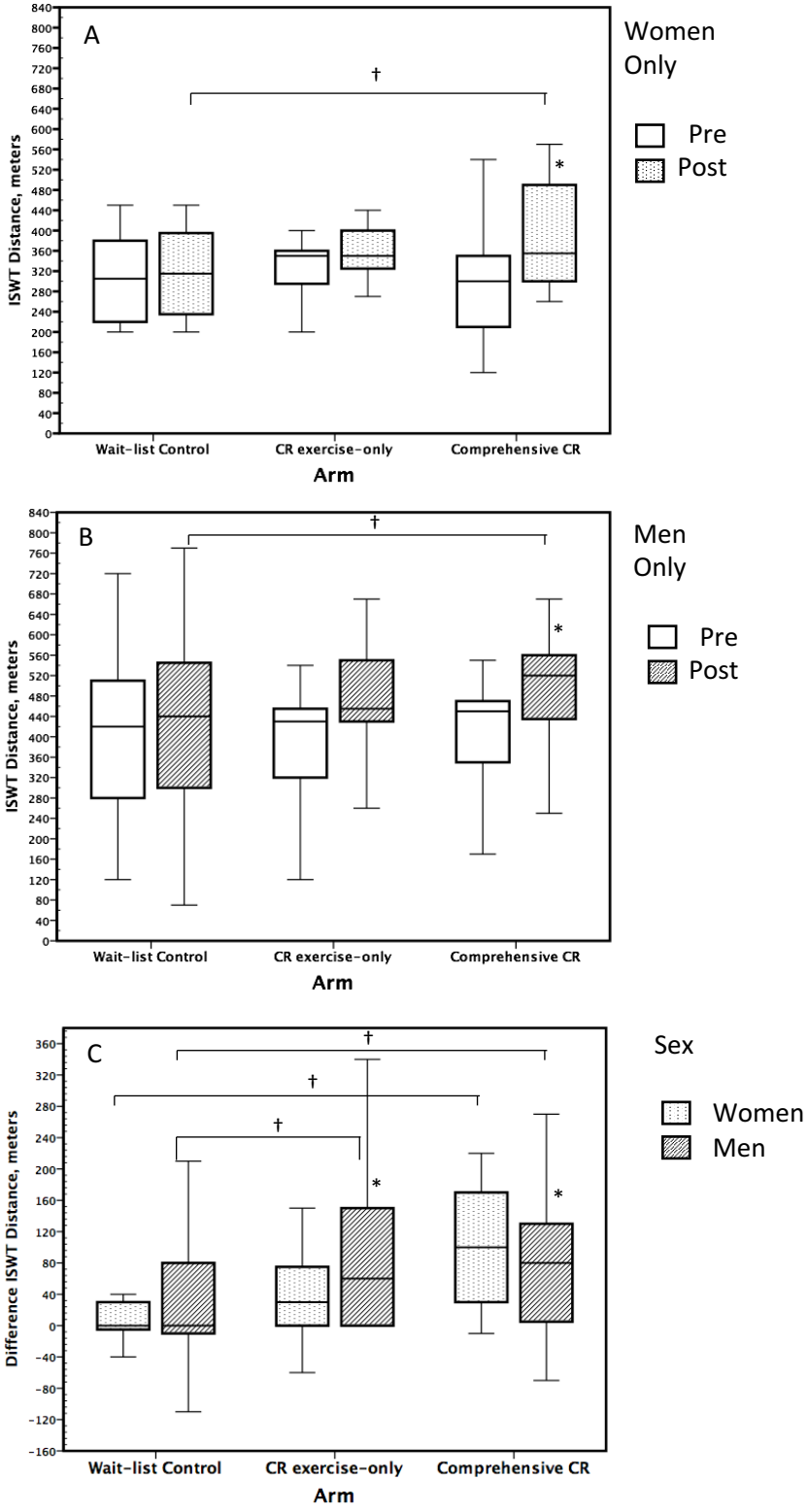


Figure 3 legend

Box blot of distance walked on incremental shutle walk test by arms and time. Panel A: intention to treat women only, panel B: intention to treat men only and panel C: difference of distance from pre to post-test according to sex. The central rectangle spans the first quartile to the third quartile. The line inside the box shows the median, and the whiskers above and below the box show the minimum and maximum. * p<.05 within group, † p<0.05 between group. ISWT=incremental shutle walk test. CR=cardiac rehabilitation