Title Page

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Title: Comprehensive Cardiac Rehabilitation Effectiveness in a Middle-income Setting: a Randomized Controlled Trial

Short title: Comprehensive CR in a Middle-Income Setting

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Conflict of interests

All authors declare no conflicts of interest

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Abstract

Purpose: The impact of comprehensive cardiac rehabilitation (CCR) in Latin America is not well-known. Herein, the pre-specified tertiary outcomes of a CR trial are reported: disease-related knowledge, depressive symptoms, and heart-healthy behaviors (exercise, diet, and smoking).

Methods: Single-blinded, single-centre (Brazil) randomized trial with three parallel arms: CCR (exercise + education) *vs* exercise-only CR *vs* wait-list control. Eligible patients were randomized in blocks of four with 1:1:1 concealed allocation. The CR program was six months long. Participants randomized to exercise-only CR received 36 exercise classes; the CCR group also received 24 educational sessions, including a workbook. All outcomes were assessed at pre-test and 6-months later (blinded). Analysis of covariance was performed by intention-to-treat (ITT) and per-protocol (PP).

Results: 115 (88.5%) patients were randomized; 93 (80.9%) were retained. There were significant improvements in knowledge from pre- to post-test with CCR (ITT [mean=51.2±11.9 [standard deviation] pre and 60.8±13.2 post] and PP $p<.01$), with significantly greater knowledge with CCR *vs* control (ITT mean difference [MD]=9.54, 95% confidence interval [CI]=2.31-16.77) and CCR vs exercise-only CR at post-test (ITT MD=6.84, 95% CI=0.34-14.02). There were also significant improvements in self-reported exercise from pre- to post-test with CCR (ITT [mean=13.7±15.8 pre and 32.1±25.7 post] and PP $p<.001$), with significantly greater exercise with CCR *vs* control at post-test (ITT MD=7.6, 95% CI=3.8-11.4). Also, there were significant improvements in diet from pre- to post-test with CCR (PP mean=3.4±7.5 pre and 8.0±7.0 post; $p<.05$).

Conclusions: In this first-ever randomized trial of CR for coronary artery disease in Latin America, the benefits of CCR have been supported.

Trial Registration: NCT, NCT02575976. Registered 15 October 2015

https://clinicaltrials.gov/show/NCT02575976

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

Condensed Abstract

Tertiary outcomes of this single-blinded, single-centre, randomized trial with three parallel arms (comprehensive cardiac rehabilitation [CCR; exercise + education] *vs* exercise-only CR *vs* wait-list control) showed that participation in CCR in a middle-income setting has benefits for knowledge about coronary artery disease, and health behaviors (self-reported exercise, diet).

INTRODUCTION

Cardiovascular diseases (CVDs) are among the leading burdens of disease and disability worldwide[1], particularly in low and middle-income countries (LMICs)[2]. Cardiac rehabilitation (CR) is an outpatient secondary prevention care model designed to mitigate this burden. Indeed, participation in CR has been shown to reduce morbidity and mortality by 20%, in a cost-effective manner[3,4]. Improved risk factor control, psychosocial well-being and health behaviors are also shown in LMICs with CR participation[5], however there are incredibly few randomized trials of CR in these settings (and none in Latin America to our knowledge)[6].

These benefits can be achieved as CR is comprised of several components, including not only structured exercise training but also education and counseling, to address all CVD guideline recommendations[7]. Indeed, meta-analyses of education for cardiac patients suggest it is associated with improvements in self-management behaviors[8-10], quality of life[11], decreased healthcare costs[11], and recurrence of cardiac events[8,11].

Unfortunately, however, many CR programs in LMICs are under-resourced, and hence do not have the capacity to offer comprehensive CR (CCR)[12,13]. In fact, while health literacy is often lower in LMICs[14], no CR educational program has been standardized or evaluated in LMICs to our knowledge. Accordingly, this trial investigated whether participation in CCR (i.e., exercise with education) in a Latin American MIC results in better knowledge, depressive symptoms, and health behaviors. It was hypothesized that participants randomized to CCR will have significantly better outcomes than those participating in exercise-only CR or not participating.

METHODS

This was a single-blinded, single-site, pragmatic, randomized controlled trial (RCT) with 3 parallel arms: CCR (education and exercise) versus exercise-only CR (no education) versus wait-list control. The protocol is available elsewhere[15]. Research ethics approval was obtained.

Patient assessments were undertaken pre-randomization and again 6 months later (in accordance with the end of CR). Primary (functional capacity) and secondary (risk factors) outcomes of the trial are reported elsewhere[16].

SETTING

This RCT was conducted in a Latin American city, in a publicly-funded academic centre. The wait-list control group received usual care which consists of follow-up appointments with their physician as deemed medically appropriate[17]. Participants randomized to the wait-list control were offered CR after 6 months. The usual wait time to start CR from referral at this centre is 4 weeks.

INTERVENTIONS

Participants undergo an initial assessment, including functional capacity and risk factors. at CR intake. Each CR participant received an individualized exercise prescription. The exercise program was six months in duration, consisting of 36 1-hour supervised sessions offered in decreasing frequency (three times to once/week)[15]. Aerobic and resistance training exercises were performed. Participants were instructed to exercise between 50 and 80% of heart rate reserve. They were also instructed to exercise in their communities on the days they were not on-

site, to accumulate 30 or more minutes of physical activity at a moderate to vigorous-intensity ≥ five days/week[18,19].

In the CCR arm, patients additionally had education sessions and received a workbook. The rigorously-developed and empirically-validated English patient education curriculum[20] was translated and culturally-adapted to the local language. The curriculum was theoretically-informed[21]. The translated workbook is available online at www.cardiaccollege.ca, but all participants of the study randomized to the CCR arm received a hard copy.

Education sessions were delivered weekly by a physiotherapist or graduate student. Education sessions were held in a classroom proximate to the CR program, with desks and a TV monitor, in groups of 2-4 patients. The education sessions were offered before or after the exercise sessions.

Twenty-four education sessions were offered from the beginning of the CR program, each 30 minutes in duration. The content of classes was reported elsewhere[15], but in brief covered all areas of secondary prevention recommended in guidelines[22].

PARTICIPANTS

Coronary artery disease, post-myocardial infarction patients or those who had undergone percutaneous coronary intervention or coronary artery bypass 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 region. The exclusion criteria were: any comorbid physical or serious mental condition which would interfere with the ability to exercise according to guidelines[19,22] or any visual or cognitive condition which would preclude questionnaire completion.

PROCEDURES

A doctoral student approached consecutive patients during the first physician consult after hospital discharge from March 2015-April 2017. With informed, written patient consent and physician CR clearance, eligible participants were scheduled to come on-site to complete pre-test assessments. This included completion of a survey. Follow-up assessments were performed between September 2015-October 2017.

RANDOMIZATION AND BLINDING

The randomization sequence was generated by a professor not involved in the study using the randomization.com website, in blocks of four. Eligible participants were randomized to one of 3 groups (1:1:1 allocation): control (no CR), exercise-only CR, and CCR (exercise + education). To ensure concealment, the local principal investigator had the allocation sequence in a password-protected file, and only provided randomization information to the 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.

Participants were invited to come back on site for their post-CR assessment, which again included a survey consisting of the below measures. A master's student blinded to random allocation undertook post-test assessments, outcome ascertainment and data entry.

MEASURES

Primary and secondary outcomes were reported elsewhere[16]. Herein, the pre-specified tertiary outcomes of the trial are reported, which were disease-related knowledge, depressive symptoms, and health behaviors, namely: exercise, diet, and smoking.

Knowledge: Patients' knowledge about their condition was assessed using the Portuguese version of the Coronary Artery Disease Education Questionnaire II (CADE-Q II)[23]. It is a 31-item scale that assesses cardiac patients' level of knowledge about their medical condition, risk factors, exercise, nutrition, and psychosocial risk. Each item has four response options, namely a fully correct answer (scored 3), a partially correct answer (scored 1), a wrong answer (scored 0), and 'I do not know' (which does not receive a value). Scores are summed; the maximum total CADE-Q II score is 93, with greater scores reflecting greater knowledge.

Depressive symptoms: Depressive symptoms were measured using the Portuguese version of the Patient Health Questionnaire-9 (PHQ-9)[24], which is a brief, valid[25] screening instrument. Frequencies of symptoms of major depression are solicited from patients, yielding scores ranging from 0 to 27, with higher scores indicating more severe symptoms. Severity categorizations are specified, with scores above 10 generally accepted as "elevated".

Exercise: Physical activity was assessed objectively and via self-report, as per best practices[26]. Participants received a Digi-Walker SW200 pedometer. Pedometers were worn on the belt, at the right hip. They were asked to wear this device for seven days at pre- (i.e., 7 consecutive days before CR intake) and at post-test, from the time they woke up until they went to bed. The SW-200, which is a body-borne spring-levered pedometer, has been shown to be valid and reliable in a wide range of settings[27-29], including CR[30]. Mean steps/day were computed, with 7,500 considered commensurate with guideline recommendations for ≥150 minutes/week in chronic disease populations[31].

Exercise was also assessed using the Portuguese version of the Godin-Shephard Leisure-Time Physical Activity Questionnaire[32], which is a self-administered survey that assesses the frequency and intensity of physical activity performed in a week. The respondents report the

number of times they engaged in vigorous, moderate and light intensity physical activity for at least 15 minutes bouts, considering a usual period of seven days. The frequency indicated by the participant is multiplied by a specific weight, which corresponds to the energy expenditure in metabolic equivalents of task (MET). Higher scores indicate higher levels of physical activity during leisure. Administration of this scale enabled consideration of exercise intensity, given recommendations that moderate to vigorous-intensity activity be accrued[33].

Diet: Diet was assessed using the 14-item Food Frequency Questionnaire (FFQ) for Cardiovascular Prevention[34], which was designed to assess the consumption of foods associated with an increase or decrease in coronary risk. A score was attributed to each food group, weighted according to their influence on coronary risk, ranging from –36 to +47 (higher scores reflect better diet).

Smoking: This was self-reported as current, never, or former.

Participants were also asked to complete a sociodemographic questionnaire. Clinical characteristics were extracted from medical charts. CR session attendance (both exercise and education sessions) was extracted from program charts at post-test for participants randomized to the CR arms.

STATISTICAL ANALYSIS

SPSS version 24.0 was used (IBM Corp, 2016). First, session attendance of participants in the two CR arms was explored to inform per-protocol (PP) analysis. Second, retention rate was computed, and differences in the sociodemographic and clinical characteristics of participants retained (i.e., completed post-test survey) versus lost to follow-up were compared using chi-square and t-tests as appropriate.

For the outcomes, analyses were performed on the basis of intention-to-treat (ITT; using last observation carried forward) and PP. Participants were included in the PP analysis if they met the threshold number of 24 or more exercise sessions in the exercise arm, and additionally 16 or more educational sessions in the CCR arm.

Change in outcome scores from pre to post-test in each arm were tested with paired t-tests (continuous variables only). Change in smoking was not tested due to the small cell sizes. Cohen's d was calculated by mean difference divided by standard deviation of the difference.

Finally, for the continuous outcomes (all but smoking), analysis of covariance (ANCOVA) was performed, with group (i.e., CCR *versus* exercise-only CR *versus* wait-list control) and pre-test score as the independent variables, and the post-test score as the dependent variable. The PP analysis adjusted for any clinical and sociodemographic biases based on retention. Post-hoc Bonferroni tests were performed where significant group differences were observed. Differences in smoking by arm were tested using Pearson's chi-square. A $p<.05$ was considered significant.

RESULTS

RESPONDENT CHARACTERISTICS

A flow diagram is shown in Figure 1. As displayed, 115 patients were randomized.

Table 1 presents the characteristics of participants at pre-test by arm (risk factors and medications reported elsewhere)[16]. Seventeen (15.5%) participants were engaging in guideline-recommended levels of activity.

As also shown in Figure 1, among those randomized to a CR arm, 57 (75.0%) 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. It was perceived that these events were unrelated to the CR intervention. There were no harms or adverse events related to exercise-only or CCR (no deaths at 6 months in any arm).

On average, those in exercise-only CR attended a mean of 23.6±8.5 (standard deviation) of 36 prescribed exercise sessions; those in the comprehensive arm attended a mean of 24.4±7.2 prescribed exercise sessions, and a mean of 18.6±6.8 of 24 prescribed education sessions. Considering a threshold of 24 exercise sessions attended and 16 education sessions attended, 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 surveys). Table 2 compares the sociodemographic and clinical characteristics as well as tertiary outcomes at pre-test in those retained versus lost to follow-up (additional clinical variables shown elsewhere[16]). There was minimal bias in the retained sample, except that those retained were significantly older and were less likely to be working than those lost to follow-up. Therefore, the PP analysis was adjusted by these variables. Of note, there were no significant retention biases in relation to clinical characteristics or study outcomes.

OUTCOMES

Descriptive statistics for all outcomes on an ITT and PP basis are shown in Table 3 (sample sizes shown in Table and Figure 1). Results showed that participants in the CCR arm only had significant increases in total knowledge from pre- to post-test (Table 3; finding held in

women as well; p=0.02); based on the PP sample, scores corresponded to 66% correct responses, and based on ITT, scores corresponded to 70% correct on the CADE-Q II.

As also shown in Table 3, total knowledge scores post-CR among participants in CCR were significantly higher than scores among participants in the other two arms (ITT mean difference [MD]=9.54, 95% confidence interval [CI]=2.31-16.77 for CCR vs control; and MD=6.84, 95% CI=0.34-14.02 for CCR vs exercise; and PP_{adj} MD=12.87, 95% CI=4.54-21.20 for CCR vs control; and MD=11.43, 95% CI=2.80-20.05 for CCR vs exercise).

As also shown in Table 3, the ITT analysis revealed that participants in the CCR arm increased their knowledge significantly in 4 of the 5 domains from pre to post-test, and that post-test knowledge scores related to exercise, nutrition and psychosocial risk were significantly higher in the CCR versus the other arms (trend for risk factors).

In regard to depressive symptoms, scores at pre-test were quite low. At post-test, 33 (28.7%) participants reported some depressive symptoms; of these, 8 (7.0%) reported major depressive symptoms. There were no significant changes in PHQ-9 scores from pre- to post-test in any arm, whether examined on the basis of ITT or PP, nor were there significant group differences at post-test.

At post-test, 16 (13.9%) participants were engaging in a mean of ≥7,500 steps/day. As shown in Table 3, while no differences were found in the pedometer values over time or by arm, there were significant effects for self-reported exercise. Similar to total knowledge, there was only a significant improvement in exercise in the CCR arm, on the basis of both ITT (Cohen's *d*=-0.27, effect size *r*=-0.13) and PP (Cohen's *d*=-0.24, effect size *r*=-0.12).

There was also a significant difference in the Godin total scores by arm at post-test when examined via ITT and PP. Post-hoc analyses showed Godin scores at post-test were significantly

greater in the CCR arm than in the control arm (ITT MD=7.6, 95% CI=3.8-11.4and PP_{adj} MD=11.6, 95% CI=7.4-18.9).

With regard to diet, there were significant differences in scores over time in the CCR arm, on the basis of PP (Cohen's *d*=- 0.63, effect size *r*=- 0.30; Table 3). With regard to smoking status, as shown in Table 1, there were few current smokers at pre-test. No differences were observed in smoking status by arm at post-test (Table 3).

DISCUSSION

Results from this first-ever RCT of CR for coronary artery disease patients in a Latin American country and third-ever in a LMIC[6,35] demonstrated that CCR significantly improves patients' CV knowledge, exercise (self-report) and dietary behaviors compared to no CR and exercise-only programs. There has been no trial of CR in a LMIC with knowledge as an outcome, but the other RCT did similarly demonstrate improvements in heart-health behaviors[36]. These results support not only the importance of CR as an integral part of the standard of care for cardiac patients in these settings, but coupled with the results from the primary outcomes of the trial establishing the benefits of CCR for functional capacity and risk factor control[16], outcomes which are closely associated with reduced mortality and morbidity[37], also support the importance of implementing CCR.

To our knowledge, there is no CCR program (i.e., with all components recommended by guidelines) in the Latin American country under study[12,13,17], particularly including a structured education program such as the one delivered for this study. It is recommended in international CR guidelines that programs be as comprehensive as resources allow[22], and these findings

certainly support those recommendations. From a patient perspective, no participants in the CCR arm dropped out for lack of interest, and indeed they attended 80% of prescribed education sessions, which is an indicator of acceptability of the comprehensive model. Patients were enthusiastic to learn, and very engaged in classes.

Results of this trial support proceeding to a multi-centre trial in LMICs, powered for so-called "hard" outcomes of mortality and morbidity, to establish such benefits as well as cost-effectiveness. While it is assumed benefits seen in higher-resource settings will be achieved, it is fathomed that the magnitude of benefit and cost-effectiveness will be greater in LMICs than higher-resource settings, given low CV risk factor identification and management rates, lower access to evidence-based medications[38], and higher CR adherence rates (such as observed in this trial). With such rigorous data in hand, advocacy to promote greater availability of CCR in MICs such as the Latin American one in this study (where there are only 75 programs, and 1 spot for every 98 incident ischemic heart disease patients)[39], and in other LMICs (1 spot for every 324 incident ischemic heart disease patient)[40] will be bolstered[41]. A stepped wedge and / or postponed information design should be used to avoid randomization to usual care.

STUDY LIMITATIONS

First, generalizability is limited. This was a single-centre study, undertaken in one LMIC. Moreover, there may have been selection bias, in that as shown with patients in high-income countries[42], patients who access CR are likely more advantaged than those who do not. However, patients were recruited in a public system, had low socioeconomic status and received CR at no cost. Also, while the consent rate was high, many patients were not enrolled in the trial as they did not attend the initial appointment (Figure 1), which may have introduced bias. Finally, there

was some retention bias. It appeared younger patients had to drop out to return-to-work, which is often seen in CR trials.

Second, while randomization was generally successful in ensuring equivalence between groups, participants in the CCR arm did have greater knowledge at pre-test than participants in the wait list control. This may have biased the trial towards confirming hypotheses. There was nevertheless a significant increase in knowledge in this domain in the CCR arm only, suggesting the benefits of CCR on knowledge in this domain are robust.

Third, the trial was not powered for these tertiary outcomes, and therefore it is unknown whether it was under-powered to test the hypotheses herein (i.e., lack of effect for depressive symptoms and smoking, however this was likely due to a floor effect). Finally, multiple comparisons were performed, which increases the chance of type 1 error.

CONCLUSION

Trial hypotheses were confirmed: participants randomized to CCR had significantly better disease-related knowledge, and self-reported exercise than those participating in exercise-only CR or not participating, and dietary behaviors improved with CCR alone. These results – together with results from the primary outcomes this trial demonstrating clinically-significant improvements in functional capacity and risk factor management with CR, and significantly greater functional capacity with CCR compared to usual care, confirm the need for advocacy for greater implementation of CCR in MICs.

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Table 1: Participants' sociodemographic and clinical characteristics, as well as outcome measures at pre-test by randomized group

n (%) / mean ± SD	**Wait-list control** (N=39)	**Exercise-only CR** (N=39)	**Comprehensive CR** (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[a])	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[b])	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)
Stable 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)
CABG	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)				
Elevated depressive symptoms	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)
Disease-related knowledge				
CADE-Q II total score (max=93)	45.39±14.80	48.24±13.30	51.24±11.90	48.32±13.46
Knowledge Domains				
Medical (max=24)	9.95±5.62	10.13±4.47	12.05±4.19	10.69±4.86
Risk factors (max=15)	5.97±3.44	6.49±3.42	7.43±3.20	6.62±3.37
Exercise (max=15)	8.64±4.87	10.41±5.15	12.70±4.64	10.55±5.13
Nutrition (max=24)	9.64±4.75	10.23±4.45	10.73±3.53	10.19±4.27
Psychosocial risk (max=15)	7.69±4.03	8.51±3.49	8.32±3.66	8.17±3.72
Depressive Symptoms				
PHQ-9 total score	4.41±5.07	5.38±5.71	4.95±4.53	4.91±5.11
PHQ-9 classification				
Minimal (1-4)	26 (66.7)	22 (56.4)	22 (59.5)	70 (60.9)
Mild (5-9)	7 (17.9)	7 (17.9)	9 (24.3)	23 (20.0)
Moderate (10-14)	3 (7.7)	6 (15.4)	4 (10.8)	13 (11.3)
Moderately severe (15-19)	3 (7.7)	3 (7.7)	2 (5.4)	8 (7.0)
Severe (20-27)	0 (0.0)	1 (0.9)	0 (0.0)	1 (0.9)
Health Behaviors				

Exercise				
Godin total scores	11.15±12.96	14.38±16.78	13.73±15.81	13.08±15.19
Godin Classification				
Insufficiently active (<14)	24 (61.5)	19 (48.7)	22 (59.5)	65 (56.5)
Moderately active (14-23)	9 (23.1)	13 (33.3)	7 (18.9)	29 (25.2)
Active (>=24)	6 (15.4)	7 (17.9)	8 (21.6)	21 (18.3)
Pedometer (daily mean steps)	4426.52±2399.05	4736.15±3948.09	4487.86±3416.91	4550.73±3289.64
Diet				
FFQ total score	7.90±6.89	5.92±7.36	4.65±7.72	6.18±7.38
Smoking Status				
Current	2 (5.1)	4 (10.3)	3 (8.1)	9 (7.8)
Never	16 (41.0)	11 (28.2)	12 (32.4)	39 (33.9)
Former	21 (53.8)	24 (61.5)	22 (59.5)	67 (58.3)

SD: standard deviation; CR: cardiac rehabilitation; PCI: Percutaneous Coronary Intervention; CABG: Coronary Artery Bypass Graft; COPD: chronic obstructive pulmonary disease; CADE-Q II: Coronary Artery Disease Education Questionnaire; PHQ-9: Patient Health Questionnaire-9; FFQ: Food Frequency Questionnaire.
Abbrev. Max=maximum
[a]did not complete high school
[b]less than four minimum wages per month

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Table 2: Participants' sociodemographic and clinical characteristics, as well as outcome measures at pre-test by retention status

n (%) / mean ± SD	**Retained** (N=93; 80.9%)	**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[a])	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[b])	82 (88.2)	18 (81.8)	100 (87.0)
Clinical			
Indication (% yes)			
Myocardial infarction	85 (91.4)	22 (100.0)	107 (93.0)
Stable angina	57 (61.3)	12 (54.5)	69 (60.0)
PCI	55 (59.1)	13 (59.1)	68 (59.1)
Bypass	26 (28.0)	3 (13.6)	29 (25.2)
First event (% no)	21 (23.1)	7 (31.8)	28 (24.8)
Comorbidities (% yes)			
Elevated depressive symptoms	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)
Disease-related knowledge			
CADE-Q II Total Scores (max=93)	48.10±13.40	48.44±14.11	48.32±13.46
Knowledge Domains			
Medical (max=24)	10.91±4.60	9.73±5.87	10.69±4.86
Risk factors (max=15)	6.62±3.08	6.59±4.47	6.62±3.37
Exercise(max=15)	10.92±4.85	8.95±6.03	10.55±5.13
Nutrition(max=24)	10.65±3.87	8.27±5.34	10.19±4.27
Psychosocial risk(max=15)	8.47±3.45	6.91±4.58	8.17±3.72
Depressive Symptoms			
PHQ-9 Total Scores	4.89±5.09	5.00±5.29	4.91±5.11
PHQ-9 Classification			
Minimal (1-4)	57 (49.6)	13 (59.1)	70 (60.9)
Mild (5-9)	19 (20.4)	4 (18.2)	23 (20.0)
Moderate (10-14)	9 (9.7)	4 (18.2)	13 (11.3)
Moderately severe (15-19)	7 (7.5)	1 (4.5)	8 (7.0)
Severe (20-27)	1 (1.1)	0 (0.0)	1 (0.9)
Health Behaviors			

Exercise			
Godin Total Scores	13.30±15.76	12.14±12.81	13.08±15.19
Godin Classification			
Insufficiently active (<14)	53 (57.0)	12 (54.5)	65 (56.5)
Moderately active (14-23)	23 (24.7)	6 (27.3)	29 (25.2)
Active (>=24)	17 (18.3)	4 (12.2)	21 (18.3)
7-day Pedometer use, daily mean	4342.90±2960.27	5461.22±4433.98	4550.73±3289.64
Diet			
FFQ Total Scores	5.70±7.60	8.23±6.11	6.18±7.38
Smoking Status			
Current	7 (7.5)	2 (9.1)	9 (7.8)
Never	33 (35.5)	6 (27.3)	39 (33.9)
Former	53 (57.0)	14 (63.6)	67 (58.3)

SD: standard deviation; PCI: Percutaneous Coronary Intervention; CABG: Coronary Artery Bypass Graft; COPD: chronic obstructive pulmonary disease; CADE-Q II: Coronary Artery Disease Education Questionnaire; PHQ-9: Patient Health Questionnaire-9; FFQ: Food Frequency Questionnaire.
[a]did not complete high school;
[b]less than four minimum wages per month
Analysis of variance *p<.05 **p<.01

Table 3: Outcomes by arm and assessment point

		Per Protocol N=81				**Intention-to-treat** N=115		
(Mean ± SD)	n	Pre-test	Post-test	Change	n	Pre-test	Post-test	Change
Disease-related								
Knowledge								
CADE-Q II Total Scores								
Wait-list control	30	44.5±15.9	48.0±15.0**	3.5	37	45.4±14.8	47.6±14.5**	2.2
Exercise-only CR	25	46.1±13.4	49.3±14.4§§	3.2	37	48.2±13.3	50.1±14.0§	1.9
Comprehensive CR	26	53.0±10.3	65.3±8.9**§§	12.5†††	37	51.2±11.9	60.8±13.2**§	9.6††
Analysis of covariance [c]		*F =5.97 p=0.004*; 95% CI (48.26-53.84)				*F=6.95 p=0.001*; 95% CI (48.17-52.92)		
Medical Domain								
Wait-list control	30	9.7±5.4	11.0±4.9	1.3	37	10.5±5.2	11.5±4.6	1.0
Exercise-only CR	25	10.0±3.7	11.28±4.8	1.2	37	10.7±3.9	11.1±4.8	0.4
Comprehensive CR	26	12.8±4.0	12.4±5.0	0.3	37	12.1±4.2	12.9±4.2	0.8
Analysis of covariance [c]		*F =1.11 p=0.3;* 95% CI (10.31-12.13)				*F=0.26 p=0.77;* 95% CI (10.67-12.22)		
Risk Factors Domain								

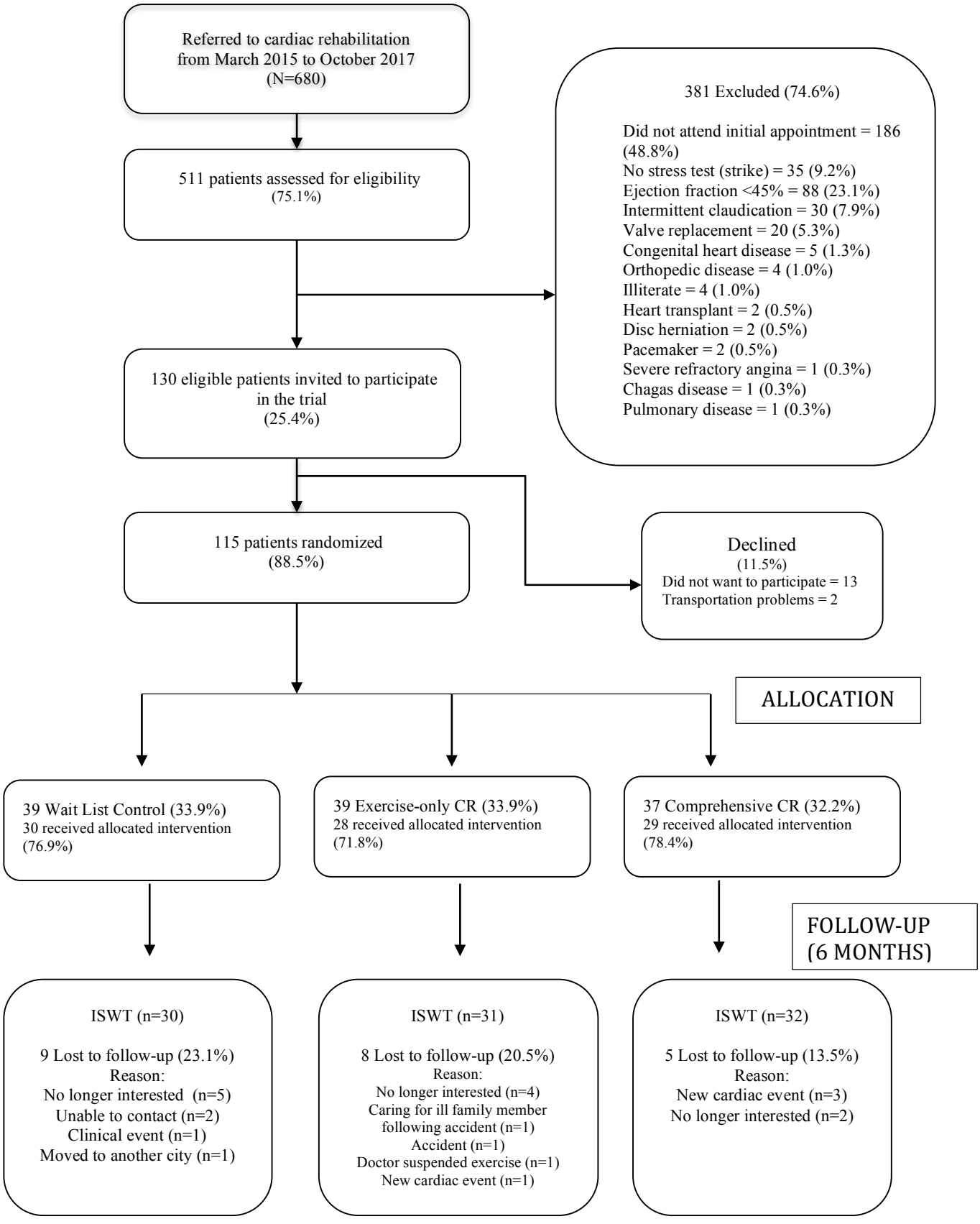
Wait-list control	30	6.1±3.3	7.0±2.3	0.9	37	6.3±3.2	6.9±2.4	0.6
Exercise-only CR	25	6.2±2.9	7.4±2.7	1.2	37	6.8±3.1	7.2±3.5	0.4
Comprehensive CR	26	7.2±3.0	9.3±3.7	2.0†	37	7.4±3.2	9.6±3.0	2.2††
Analysis of covariance [c]		*F =0.61 p=0.54;* 95% CI (6.68-7.71)				*F=2.84 p=0.06;* 95% CI (6.90-7.87)		
Exercise Domain								
Wait-list control	30	9.0±4.6	10.1±4.8	1.7	37	9.1±4.5	9.9±4.8***	0.8
Exercise-only CR	25	10.5±4.9	11.4±5.2	0.9	37	11.0±4.7	11.5±4.9§§	0.5
Comprehensive CR	26	13.6±4.8	15.4±5.5	1.8	37	12.8±4.7	15.7±4.3***§§	2.9†††
Analysis of covariance [c]		*F =0.21 p=0.81;* 95% CI (10.73-12.58)				*F=3.23 p=0.04;* 95% CI (10.87-12.45)		
Nutrition Domain								
Wait-list control	30	9.9±4.5	11.6±3.7	1.7	37	10.2±4.3	11.4±3.5*****	1.2
Exercise-only CR	25	10.9±4.2	11.1±4.2	0.2	37	10.8±3.8	11.2±3.9 §	0.4
Comprehensive CR	26	11.3±2.8	13.4±4.5	2.1	37	10.7±3.5	13.3±3.6*****§	2.6†††
Analysis of covariance [c]		*F =1.42 p=0.25;* 95% CI (10.59-12.11)				*F=4.42 p=0.01;* 95% CI (10.62-11.91)		
Psychosocial Risk Domain								
Wait-list control	30	8.3±4.0	8.0±3.6	0.3	37	8.1±3.7	7.7±3.6*	-0.4
Exercise-only CR	25	8.5±3.1	8.2±3.5	0.3	37	9.0±2.9	8.5±3.3*§	-0.5
Comprehensive CR	26	9.0±2.9	9.8±3.8	0.8	37	8.3±3.7	9.7±3.3§	1.4†
Analysis of covariance [c]		*F =0.67 p=0.52;* 95% CI (7.99-9.30)				*F=3.85 p=0.02*; 95% CI (7.98-9.12)		
Depressive Symptoms								
PHQ-9 Total Scores								
Wait-list control	30	4.0±4.5	3.8±3.9	-0.2	39	4.4±5.1	4.3±4.7	-0.1

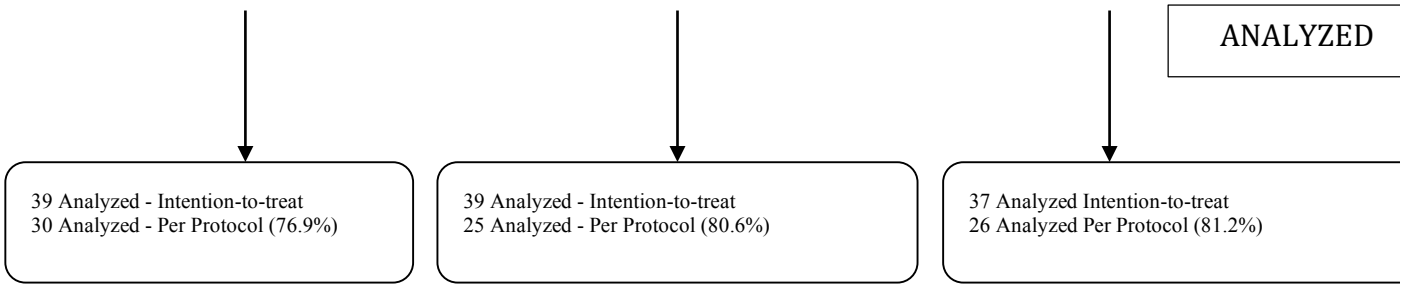
Exercise-only CR	25	5.3±5.9	4.9±5.9	-0.4	39	5.4±5.7	5.2±5.0	-0.2
Comprehensive CR	26	4.8±4.7	4.2±4.8	-0.6	37	5.0±4.5	4.5±5.0	-0.5
Analysis of covariance [c]		*F=0.06 p=0.94;* 95% CI (3.54-5.50)				*F=0.08 p=0.93;* 95% CI (3.88-5.66)		
Health Behaviors								
Exercise – Godin Total Scores								
Wait-list control	30	11.4±13.9	13.4±11.8**	1.9	39	11.2±13.0	11.8±11.9**	0.6
Exercise-only CR	25	16.6±18.4	21.8±19.8	5.2	39	14.4±16.8	18.2±18.3	3.8
Comprehensive CR	26	11.3±13.6	39.0±25.3**	27.7†††	37	13.7±15.8	32.1±25.7**	18.4†††
Analysis of covariance [c]		*F=14.3 p<.001;* 95% CI (15.66-22.16)				*F=7.92 p=0.001;* 95% CI (14.29-19.49)		
Exercise – 7-day Pedometer use, daily mean								
Wait-list control	28	4388.98±2458.68	3709.65±2646.48	-679.33	38	4426.5±2399.0	3922.3±2571.1	-504.2
Exercise-only CR	25	4550.99±3085.60	4853.76±4155.54	302.77	38	4736.2±3948.1	4996.8±4504.4	260.6
Comprehensive CR	25	4758.33±3658.49	5796.00±3982.90	1037.67	37	4487.9±3416.9	5422.0±4284.7	934.1
Analysis of covariance [c]		*F=1.14 p=0.33;* 95% CI (4030.00-5322.57)				*F=1.61 p=0.21;* 95% CI (4075.91–5254.94)		

Diet - FFQ Total Scores								
Wait-list control	30	7.5±7.3	6.0±5.7	-1.4	39	7.9±6.9	6.9±5.9	-1.0
Exercise-only CR	25	5.9±7.3	5.8±6.7	-0.04	39	5.9±7.4	6.5±6.9	0.6
Comprehensive CR	26	3.4±7.5	8.0±7.0	4.6†	37	4.7±7.7	7.8±7.1	3.1
Analysis of covariance [c]		*F=3.93 p=0.02;* 95% CI (4.87-7.33)				*F=3.02 p=0.05;* 95% CI (5.50-7.71)		
Smoking Status (n,% current)								
Wait-list control	30	1 (3.3)	2 (6.7)	1	39	1 (2.6)	2 (5.2)	1
Exercise-only CR	25	4 (16.0)	4 (16.0)	0	39	4 (10.4)	4 (10.4)	0
Comprehensive CR	26	2 (7.7)	2 (7.7)	0	37	2 (5.4)	2 (5.4)	0
X^2 *analysis*		X^2 *= 3.14 p=0.50;* 95% CI (0.28-0.30)				X^2 *= 2.07 p=0.61;* 95% CI (0.77-0.80)		

CR: cardiac rehabilitation; CI: confidence interval.
Difference between first and second assessment compared using paired t-test; †p<.05, ††p<0.01, †††p<.001
[c] testing differences in outcomes at post-test by arm, adjusting for pre-test values.
Analysis of Covariance, Bonferroni post-hoc test *p<.05, **p<0.01, ***p<.001; §p<.05, §§p<0.01, §§§p<.001

FIGURE 1 Study flow diagram





*The threshold sessions was a minimum of 24 exercise sessions and 16 education classes