TIME-TO-REFERRAL, USE AND EFFICACY OF CARDIAC REHABILITATION FOLLOWING HEART TRANSPLANTATION

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ABBREVIATIONS

AT=aerobic training

CPET=cardiopulmonary exercise test

CRP=cardiac rehabilitation program

HT=heart transplant

RT=resistance training

VAT=ventilator anaerobic threshold

$\dot{V}O_{2peak}$ =peak oxygen uptake

ABSTRACT

Background: Timely access, adherence, and efficacy of cardiac rehabilitation programs (CRP) are important given the potential to mitigate/reverse the side-effects of immunosuppressive medications, weight gain, and cardiovascular deconditioning that place heart transplant (HT) recipients at increased cardiovascular risk. However, there is a dearth of information on use and efficacy of CRPs. Therefore, we examined process indicators (time-to-referral and correlates, program adherence) and clinical outcome indicators (functional capacity (VO_{2peak}), anthropometrics) of CR post-HT compared to post-coronary artery bypass graft (CABG).

Methods: Baseline and 6 month exercise stress test results, and anthropometrics were examined retrospectively among consecutively enrolled post-HT and age- and sex-matched CABG patients. Time-to-referral/program entry, attendance and completion rates were also measured.

Results: HT (n=43) and CABG patients were referred 24.9 ± 48.9 and 2.1 ± 3.6 months respectively, following surgery ($p=0.003$). Once referred, there was no difference in elapsed-time to program entry ($p=0.2$). There was a positive relationship between time-to-referral and baseline waist circumference ($r=0.5, p=0.001$), body mass index ($r=0.5, p=0.002$), hip circumference ($r=0.4, p=0.008$), and body fat percentage ($r=0.4, p=0.03$) in HT. HT and CABG patients had similar rates of CRP dropout (27.9% vs. 37.2% respectively, $p=0.4$). There was improvement in VO_{2peak} for HT ($2.4 \pm 4.2 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}, p=0.02$) and CABG ($5.5 \pm 5.4 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}, p<0.001$), but was greater for CABG ($p=0.04$). Anthropometric measures remained stable for both cohorts ($p>0.05$).

Conclusions: There is a lengthy delay in time-from-HT to CRP referral, though once referred, gain significant benefit in functional capacity. The appropriateness of this wait needs to be elucidated, however it appears that longer wait times are associated with adverse effects on body composition.

INTRODUCTION

Comprehensive cardiac rehabilitation (CR) programs are recommended in many major guidelines as a standard of care for individuals recovering from cardiac disease(1). CR programs have been clearly shown to improve fitness, psychosocial well-being, and to significantly reduce morbidity and mortality in persons recovering from acute cardiac illness(2-4). Cardiac rehabilitation and secondary prevention programs are also recommended for people recovering from heart transplant (HT) surgery by major health associations including the American Heart Association and the American College of Cardiology Foundation(1). Timely referral to CR treatment is recognized as important to patient enrolment(5, 6), and may result in greater improvement in functional capacity(7, 8) and greater beneficial effects on left ventricular remodeling following myocardial infarction(9). Timely access to CR may be particularly critical for the person with a transplanted heart. Exercise may ameliorate some of the side-effects of immunosuppressive medications that develop in early recovery including weight gain, peripheral muscle atrophy, bone demineralization, cardiovascular deconditioning, and metabolic syndrome(10-16). These changes place the HT recipient at increased risk for secondary disease such as stroke, coronary artery disease, renal insufficiency, osteoporosis, hypertension, diabetes, and dyslipidemia(10, 11, 17-19). Indeed, Canadian recommendations suggest 4-10 days as a “preferable” wait following transplantation to initiate a CR program, with 10-60 day as the “acceptable” benchmark(20). Nevertheless, the elapsed time from HT to commencement of aerobic or resistance exercise has exceeded one year in most(21-25), but not all(26-28) randomized controlled studies. There may be barriers to timely access to CR programs after HT that are unique when compared to other chronic disease populations. For example, people post HT may have infection, rejection, side-effects of immunosuppressant medication, as well as psychosocial issues related to organ transplant.

Despite the importance of timely exercise training and risk factor modification interventions, the length of time from surgery to commencement of CR in HT recipients in the “real-world” has not been reported. Moreover, HT patient adherence (attendance and program completion), in this group has been scantily investigated. Change in cardiovascular fitness has received more attention in the literature. Results of a recent meta-analysis showed that exercise training following HT resulted in significantly greater gains in peak oxygen uptake ($\dot{V}O_{2peak}$) than standard of care treatment in 6 prospective studies(29).

Accordingly, the aims of this study were to determine process and clinical outcome indicators for persons with HT participating in CR including: (1) the timing of CR initiation, and the relationship to anthropometrics and functional capacity at program entry, (2) the degree of program completion/attendance, and (3) efficacy (i.e., anthropometrics and functional capacity). A cohort of age-and sex-matched post-coronary artery bypass graft (CABG) patients was used as a comparison group. It was hypothesized that the elapsed time from surgery to commencement of a CR program would be greater following HT than CABG, but that there would be no differences in program adherence rates or change in anthropometrics. Also, because the denervated heart functions differently, we hypothesized that a CR program would yield mitigated gains in parameters of cardiovascular fitness in HT compared to CABG.

MATERIAL AND METHODS

Study Design and Procedure

This was a retrospective analysis of HT and CABG patient assessments pre-program and following 6 months of CR. The study was approved by the institution’s Research Ethics Board.

Consecutive patients who had undergone a HT and enrolled in a single cardiac rehabilitation program (CRP) in Toronto, Canada from January 1996 to October 2013 were identified for this

study (see figure 1). Consecutively-enrolled age- and sex-matched patients with a documented history of CABG surgery (primary diagnosis) and no prior history of HT were identified for comparison. They were matched to year and month of CR referral for consistency in medical care and CR program delivery. Data were extracted from the institution's database.

CR Intervention

Participants were referred to the CR program by their family physicians, surgeon, or other health care professional. The program was led by an interprofessional team of physicians, physiotherapists, nurses, kinesiologists, psychologists, and dietitians. The program delivery model was the same for CABG and HT patients. Patients attended 90-minute exercise classes once per week for 6-12 months and monthly classes for 4 to 12 months (duration varied depending on date of CR entry), and were offered baseline and 6 month cardiopulmonary exercise tests (CPETs).

Exercise classes included aerobic training (AT), education sessions as well as psychosocial and dietary counselling. Each patient was assigned to a case manager and patients were required to complete 5 AT and 2-3 resistance training (RT) sessions per week, which were tracked via an exercise diary. One exercise session was conducted in the facility, with the balance of the exercise being completed in the home/community. The initial walking prescription was set at a distance of approximately 1.6 km per day and an intensity equivalent to the ventilatory anaerobic threshold (VAT) and/or 60-80% of $\dot{V}O_{2peak}$ with a longer warm-up and cool-down period for HT than CABG. Prescriptions were progressed every 2 weeks, increasing distance to a maximum of 6.4 km and then increasing intensity to a maximum of 80% of $\dot{V}O_{2peak}$ (maximum duration of 60 minutes). Thereafter, training intensity was adjusted to maintain a pace equivalent to 80% of $\dot{V}O_{2peak}$. RT exercises were initiated 8 weeks after AT, and included 3 lower body (2 with

dumbbells one with exercise bands), 5 upper body (dumbbells) and 2 trunk-stabilizing exercises (patients' body weight). Patients were advised to gradually progress from 10 to 15 repetitions and then to increase resistance by 5 kg or one band level and reduce repetitions to 10.

Participants

Patients were eligible for the program if they did not have contraindications to exercise(30) such as acute systemic illness or fever, uncontrolled resting severe hypertension, or uncontrolled metabolic disease such as diabetes.

Measures

Time to Referral and Program Initiation, and CR Adherence

Three wait time intervals were considered. First, *time from cardiac surgery to program initiation*, was calculated as the elapsed number of days from the date of surgery to the date that the patient attended the first exercise session. Within this period, *time from cardiac surgery to referral* was calculated as elapsed number of days from surgery to the date on the physician referral document, and *time from referral to program initiation* was measured as the elapsed number of days from the date of physician referral to the date that the patient attended the first exercise session. The CPET was conducted in the interval between referral and program initiation.

Proportion of pre-scheduled on-site weekly attendance was one of the adherence variables of interest. Subjects attended a maximum of 24 classes over 6 months and monthly classes for 4 to 12 months (duration varied depending on date of CR entry). Patients were coded as “dropout” when there was confirmation by a patient that he/she no longer wished to or was unable to participate, and/or when three or more consecutive on-site visits were missed, and/or if the patient was unreachable by telephone on repeated (minimum of three) attempts over a 2-month period. Reasons for withdrawal were categorized as medical or non-medical.

Anthropometrics

Percent body fat was assessed by bioelectrical impedance for patients referred after 1999, (Tanita TBF-300A, Tokyo, Japan), and prior to this by skin fold measurements(31). Waist circumference was measured at the narrowest part of the torso between the iliac crest and xiphoid process or at the level of the iliac crest after normal exhalation(30). Hip circumference was measured at the maximal circumference of the buttocks(30). Abdominal obesity was considered for waist circumference >88 cm and >102 cm for women and men respectively(32).

Functional Capacity

CPETs were conducted in all patients at baseline and 6 months, except in those who prematurely discontinued the CR program or when program completion coincided with a CPET conducted elsewhere with the transplant team. A CPET on either an upright cycle ergometer (Ergoselect 200P, Germany), or a treadmill (same modality pre- and post-training) was performed depending on patient balance and comfort. On the cycle, work load was increased by either 8.3 or 16.7 Watts every minute maintaining a pedaling rate of 60 RPM. On the treadmill, the Bruce or Modified Bruce protocol was selected(30). Gas samples were collected via calibrated metabolic cart (SensorMedics Vmax Encore, California) with continuous monitoring of 12-lead ECG (Marquette Case 80), and blood pressure. The test was terminated at peak volitional effort (i.e., unable to maintain treadmill speed or pedaling rate), if a physiological maximum was achieved, or if the patient had adverse clinical signs or symptoms. VAT was determined by a combination of the V-slope and ventilatory equivalents methods(33, 34) by agreement between the supervising physician and technologist. The expected $\dot{V}O_{2peak}$ ($\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) was calculated from established age and sex norms(35).

Statistical Analysis

A descriptive examination of the variables of interest was performed, including sociodemographic and clinical characteristics, wait times, program use, as well as anthropometrics and functional capacity indicators. Differences between the groups pre-program were assessed using independent samples Student's *t* tests for continuous variables and X^2 tests for categorical variables.

Student's *t* test for paired samples was used to determine within-group differences from pre-program to 6 months later. Between-group differences were analyzed by independent-samples *t* test and categorical variables by X^2 or Fisher exact tests. The time-from-transplant to start of CR data was positively skewed and was log transformed to approximate normal distribution. The relationship between time-from-HT to referral and baseline anthropometric measures were determined using the Pearson correlation coefficient. Probability values <0.05 were considered significant. All analyses were performed in SPSS (version 21.0, SPSS, Inc., Chicago, IL).

RESULTS

Participant Characteristics

Forty-three men and women were referred to the CR program following HT surgery from January 1996 to October 2013. Table 1 displays their sociodemographic and clinical characteristics. The prescribed immunosuppressant medications at baseline were prednisone (n=32, 74.4%), mycophenolate mofetil (n=22, 51.2%), cyclosporine (n=19, 44.2%), tacrolimus (n=14, 32.6%), sirolimus (n=7, 16.3%), azathioprine (n=3, 7.0%) and everolimus (n=2, 4.7%). At baseline, there was no between-group difference in employment status but a greater proportion of the CABG participants had a diagnosis of CAD and hypertension than HT participants, with expected differences in use of standard cardiovascular medications.

Wait Times, Attendance and Completion Rate

As shown in Table 1, the elapsed time from surgery to program initiation was over 6 times longer ($p=0.004$), and time from surgery to referral was 12 times longer ($p=0.003$) for HT when compared to CABG patients. Once referred, there was no significant difference in elapsed time to the initiation of the first exercise session ($p=0.2$). Among HT patients, 29.3% ($n=9$) were referred to CR within 60 days following HT, in contrast to 74.4 % ($n=32$) of those post-CABG ($p<0.001$). Only 11.6% ($n=5$) of the post-CABG cohort started the program within 60 days, while none of the HT patients met this benchmark.

The longer the time from HT to referral, the greater the baseline waist circumference ($r=0.5$, $p=0.001$), body mass index ($r=0.4$, $p=0.03$), hip circumference ($r=0.4$, $p=0.008$), and body fat % ($r=0.4$, $p=0.03$) at the time of entry. There was no significant relationship between wait time and functional capacity indicators pre-program ($r=0.04$, $p=0.8$). There was no significant correlation between time from CABG to referral and anthropometrics or functional capacity.

The HT and CABG patients had similar rates of program completion (72.1% and 62.8% respectively, $p=0.4$), attending a mean of 19.4 ± 18.9 and 15.7 ± 11.8 pre-scheduled visits, respectively ($p=0.3$; Table 1). Among HT and CABG dropouts, 50% and 18.8%, discontinued CR for medical reasons, respectively ($p=0.1$).

Within the HT cohort, non-completers were more likely to have a diabetes diagnosis (58.3%; $n=7/12$ vs. 19.4%; $n=6/31$, $p=0.04$), have abdominal obesity (72.2%; $n=8/11$, vs. 35.5%; $n=11/31$, $p=0.04$; Figure 2), and a lower peak diastolic blood pressure (73.8 ± 9.6 vs. 82.5 ± 11.4 mmHg,

p=0.03) compared to completers. Non-completers were referred a mean of 50.0 ± 79.7 vs. 15.2 ± 25.9 months post-HT surgery compared to completers (p=0.2).

Anthropometric and Cardiorespiratory Outcomes

Table 2 displays the outcomes and change from pre-program values among the HT and CABG patients who completed the program. There was no significant change in any of the anthropometric measures within both cohorts. With regard to functional capacity indicators, there was significant improvement in $\dot{V}O_{2peak}$ for HT ($\Delta 2.4 \pm 4.2 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$; $16.0 \pm 28\%$, p=0.02) and CABG ($\Delta 5.5 \pm 5.4 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$; $28.6 \pm 30.2\%$, p<0.001) participants, but the change was greater for CABG patients (p=0.04). Within group changes revealed a significant improvement in VAT for the CABG group only, with a trend for greater improvement in the CABG than HT cohort (p=0.05). Elapsed time from HT surgery to CR referral did not correlated with change in any outcome measure (p>0.05).

DISCUSSION

Results of this retrospective analysis demonstrate that a CR program yields significant gains in cardiovascular fitness, and acceptable adherence and completion rates in consecutively enrolled HT patients. However, when compared to a matched group of CABG patients, there is a markedly longer delay in referral time and mitigated gains in cardiovascular fitness parameters.

The person with a transplanted heart has a profile that may include episodes of rejection, and diastolic dysfunction as well as years of pre-transplant physical inactivity and disability(36, 37). These factors may have contributed to the marked deconditioning in HT patients at CR entry, measuring 51% of age- and sex-normative values. In fact, $\dot{V}O_{2peak}$ was significantly lower in HT than the post-CABG group despite the same relative effort on the baseline CPET as determined

by the respiratory exchange ratio. Generally, the oxygen requirements for carrying out activities of daily living fall within the range of 10 to 18 mL·kg·min⁻¹ (activities such as dressing, walking 4.3 kilometers per hour)(38). Thus, with the $\dot{V}O_{2peak}$ of only 15 mL·kg·min⁻¹ that was observed in the HT group, some routine activities may be prohibitive due to the maximal strain that may be imposed on the cardiovascular system. Therefore, the documented magnitude of gain in exercise capacity post CR program (16%) would have positive implications for activity of daily living function. Moreover a higher $\dot{V}O_{2peak}$ may proffer a mortality benefit in patients with CAD and HT(39-41). Despite a greater proportion of women, the magnitude of change in the current study is similar to that reported in other HT studies (10.2 to 27%)(13, 29, 39).

There is a dearth of studies examining the underlying mechanisms that determine change in cardiovascular fitness in HT patients. Kavanagh et al. were among the first to suggest that the exercise related change in $\dot{V}O_{2peak}$ was likely related in large part to peripheral adaptations in view of the absence of change to submaximal stroke volume or cardiac output(13). Similarly, other studies have failed to show central changes in response to exercise training (21, 42) and most (22, 24, 43, 44) but not all (45) have reported that endothelial function improves with exercise training. Moreover, reversal of muscle myopathy induced by corticosteroids and calcineurin inhibitors, may be other peripheral mechanisms contributing to improved functional capacity (46-48).

In the current study there was a trend for greater improvement in VAT in the CABG group compared to HT. While improvements in $\dot{V}O_{2peak}$ are important for prognostic outcome(40), delaying lactate accumulation may be more clinically relevant to submaximal endurance performance(49) given that many activities of daily living are performed below or near the VAT.

Research is required to elucidate optimal exercise prescription strategies such as high intensity interval training to improve the VAT in an HT population attending CR.

The elapsed time from HT surgery to CR program initiation was markedly longer than the time elapsed in a matched cohort following CABG surgery (mean of 2.2 years vs. 4.1 months respectively). Both groups exceeded the acceptable benchmark of 60 days established for both HT and CABG patients by the Canadian Cardiovascular Society(20) with only 11.6% of CABG patients starting the program within the acceptable time delay. This is not unexpected, as an examination of the elapsed time from HT to commencement of the exercise intervention exceeded 1 year in most(21-25), but not all(26-28) published randomized controlled studies. The greatest difference in delay between cohorts in the current study was related to referral initiation. Once patients were referred, wait time to program entry was similar between patient groups.

The underlying reasons for referral initiation taking approximately 23 months longer for HT patients may be multifactorial. Early post-HT, patients may have more medical issues requiring more intense medical follow up (i.e. major rejection episodes, side effects of immunosuppressant therapy) leaving less time and motivation to attend further ‘medical’ appointments required of a CR program. However, it is unlikely that these reasons would fully account for the lengthy delay revealed in the current study. In earlier studies, health system, patient, and physician factors have also been identified as barriers to referral in patients with mixed cardiac diagnoses eligible for CR(50, 51). For example, delayed referral may be related to the amount and strength of physician support and endorsement, the type of referral strategy utilized by the acute care hospital (automatic vs. patient initiated referral), lack of awareness of CR, and/or lack of motivation for exercise (52-54). These factors may be intensified in people following HT. Yet, despite exercise being an important component of rehabilitation, no study has examined the barriers to timely referral specific to HT patients. Research is needed to understand the causes of referral delay

including intercurrent clinical issues, and to educate physicians on the importance of timely referral.

A compelling observation from this study is that the greater the delay in CR referral from the time of HT surgery, the more unfavorable the waist and hip circumference, percent body fat, and BMI measures. This is in congruence with previous studies showing that adverse body composition changes develop following HT surgery including a weight gain of up to 10.3 kg within the first year post-transplant, an increase in trunk fat, waist circumference, and a decrease in peripheral lean mass(11). While further research comparing these parameters in post-HT patients referred within the “preferred” benchmark versus later is required, the association between elapsed time to referral and deterioration in anthropometric measures has important clinical implications for optimal timing of a CR intervention and long-term disease burden. Generally, obesity is associated with numerous adverse effects such as CAD, stroke, dyslipidemia, hypertension, sleep-disordered breathing, systolic and diastolic dysfunction and some cancers(55-59). It is also related to metabolic abnormalities including type II diabetes, insulin resistance, and glucose intolerance(19, 60). Obesity has been associated with greater risk of rejection episodes, failed allografts, and a survival disadvantage in HT patients(15, 61-65). In the current study, abdominal obesity was highly prevalent, occurring in 45.2% of the HT cohort. Although abdominal obesity also occurred in a large proportion of the CABG patients (39.5%), there is growing evidence that abdominal obesity may be a particularly powerful risk factor for the development of the metabolic syndrome in HT patients(10, 65).

We also observed that patients with abdominal obesity and those with a diabetes diagnosis were significantly over-represented in the HT group that did not complete CR compared to those who completed CR. This is similar to previous studies reporting that obesity and diabetes are significant predictors of dropout in CR programs(66, 67). This may also explain why the elapsed

time to referral in those who dropped out was 4 times longer than time to referral in the completers (albeit the difference did not reach statistical significance). While the underpinnings of this relationship have not been fully explored, overweight and obesity can have an adverse effect on joint health that can affect participation in exercise programs and increase health service utilization(68, 69). This may in part explain the greater proportion of medical dropouts in the HT group. Yet, the association of these conditions with CR completion did not occur in the CABG group despite similar baseline anthropometric measures and prevalence of diabetes. This suggests that a more complex relationship exists and requires further exploration.

Collectively, these findings suggest that the longer the time to referral, the greater the risk of secondary disease and risk of non-compliance with CR treatments. While there were no significant changes in any anthropometric measure following CR, earlier referral may help to halt these unfavorable body composition changes that occur with time and promote compliance to heart-healthy behaviors. In an early study, Kobashigawa et al. randomized 27 patients within 2 weeks after HT to either a 6 month exercise intervention or a nonexercise control group(28).

While there was a significantly greater improvement in $\dot{V}O_{2peak}$ for the exercise vs control group, there was a mean weight gain of 8 kg in both cohorts. Despite this finding and the well-documented deterioration in anthropometric and body composition parameters within the first year post-transplant (11, 15), the current study demonstrated stability of these measures over 6 months of exercise training regardless of length of time from HT in those who completed CR.

This may be owing to the CR program being a comprehensive risk factor modification intervention that offers dietary education and counseling by a registered dietitian. Therefore, although the established benchmarks for acceptable wait times for accessing CR programs were not evidence based but developed through consensus, it appears that earlier referral may be beneficial. However, the appropriateness of this recommendation requires further investigation.

STUDY LIMITATIONS

This was a retrospective study conducted in a single centre located in a large city centre and may lack generalizability to other programs, including those where CR services are not publicly funded. It is also possible that the sample was not large enough to detect significant differences between cohorts in certain variables. We did not have access to information regarding length of stay in hospital or rejection episodes following surgery, which may have impeded CR referral. The lack of non-CR and early referral post-HT comparison groups also poses a limitation, however there is a dearth of knowledge in this area of research and as CR programs for HT expand, and patients are living longer post-transplant, further research to build on these findings will be required to investigate the efficacy of CR interventions known to extend life in other populations.

CONCLUSIONS

Patients were referred to the CR program a mean of 2.1 years post-HRT. This is of concern as the longer the elapsed time to CR referral, the greater the deterioration in patients' body composition. These data strongly support further research to provide evidence regarding the appropriate wait for HT patients to prevent or reverse the development of the well-documented atherogenic profile and to examine barriers to early referral. The marked deconditioning of HT patients compared to patients early post-CABG surgery suggests that CR should be initiated earlier than observed. However, while participation in the CR program yielded gains in VO_{2peak} , the magnitude of change was less than that observed in CABG patients, and there was only a trend towards improvement in anaerobic threshold for HT patients. Therefore, research is also required to elucidate optimal exercise prescription strategies for HT patients, who should ideally access programs earlier.

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Figure 1. Flow Diagram

CABG=coronary artery bypass graft

CR=cardiac rehabilitation

AT=aerobic training

RT=resistance training

Figure 2. Pre-Program Characteristics of Cardiac Rehabilitation Completers versus Non-Completers among Heart Transplant Recipients

*p<0.05

Table 1. Sociodemographic and Pre-Program Clinical Characteristics, and Adherence to Cardiac Rehabilitation, by Clinical Indication

Characteristics	HT n=43	CABG n=43
Sociodemographic		
Male, n (%)	22 (51.2)	22 (51.2)
Age, yrs (range)	51.6±10.7(25-67)	51.8±10.4(27-67)
Partnered, n (%)	27/39 (69.2)	24/41 (58.5)
Not Employed, n(%)	30/39 (76.9)	27/42 (64.3)
Clinical		
Body Mass Index, kg·m ²	26.8±6.1	27.2±4.5
Waist Circumference, cm	93.7±14.2	93.2±11.9
Abdominal Obesity, Waist >88 cm >102 cm, n(%)	19/42 (45.2)	17/43 (39.5)
Hip Circumference, cm	101.3±14.9	102.4±9.3
Waist-to-Hip Ratio	0.93±0.11	0.91±0.08
Body Fat, %	27.6±8.7	28.5±8.1
CAD Diagnosis, n(%)	8 (18.6)	43(100)†
Diabetes diagnosis, n(%)	13(30.2)	16(37.2)
Hypertension, n(%)	8 (18.6)	17 (39.5)*
Medications, n(%)		
β-blockers	5 (11.6)	36 (83.7)*
Ca ²⁺ -channel antagonists	11 (25.6)	6 (14.0)
Diuretic	11 (25.6)	5 (11.6)
Other Antihypertensives	16 (37.2)	18 (41.9)
Lipid-lowering agents	35 (81.4)	38 (88.4)

Platelet Inhibitor	20 (46.5)	42 (97.7)*
Antidiabetic agents	11 (25.6)	15 (34.9)
Antidepressants/anxiolytics	12 (27.9)	11 (25.6)
Vasodilator	0 (0)	11 (25.6)*
Gastric Acid Inhibitor	28 (65.1)	10 (23.2)*
CR Utilization		
Wait Times		
Cardiac Surgery to Program Initiation,		
Mean months (min/max)	26.6±49.0 (2.2-213.2)	4.1±3.7 (1.3-23.3)*
Median (IQR) months	6.1 (13.6)	2.9 (2.0)
Cardiac Surgery to Referral,		
Mean months (min/max)	24.9±48.9 (0.7-213)	2.1±3.6 (0.13-22.1)†
Median (IQR) months	5.2 (13.2)	1.03 (1.4)
Referral to Program Initiation,		
Mean days (min/max)	52.5±33.6 (7-154)	61.9±35.5 (14-181)
Median (IQR) days	47 (39)	55 (39)
Attendance to all weekly classes, n	19.4±18.9	15.7±11.8
Attendance to all monthly classes, n	14.2±25.4	15.9±26
Attendance within first 6 months, n classes (%)	11.2±6.1 (46.8±25.5)	11.8±7.2 (49.1±29.9)
Program Completion, n (%)	31 (72.1)	27 (62.8)
Withdrawal owing to Medical/Non Medical		
Reasons, n(%)	6 (50)/6(50)	3(18.8)/13(81.3)
$\dot{V}O_{2peak}$, mL·kg ⁻¹ ·min ⁻¹	15.3±3.9	18.5±5.6*
$\dot{V}O_{2peak}$, % Age and Gender-Predicted Norms	51.0±14.5	60.3±16.2*
Peak Respiratory Exchange Ratio	1.18±0.10	1.21±0.11

VAT achieved, n (%)	34 (79.1)	39 (90.7)
VAT mL·kg ⁻¹ ·min ⁻¹	12.0 ± 3.2	13.6±4.3
VAT mL·kg ⁻¹ ·min ⁻¹ , % $\dot{V}O_{2peak}$	76.7	74.3
Resting HR, beats·min ⁻¹	97.4 ± 12.9	71.5± 11.6†
Peak HR, beats·min ⁻¹	120 ±18.5	128.0 ±22
Resting DBP, mmHg	78.1 ±12.1	75.4± 9.6
Peak DBP, mmHg	80.0 ± 11.5	82.8 ± 10.9
Resting SBP, mmHg	125.1 ± 16.3	127.4 ± 18.4
Peak SBP, mmHg	160.1 ±28.1	178.6±28.5*

Values are mean±SD unless otherwise indicated.

*p=<0.05 and †p=<0.001 between HT and CABG

cabg=Coronary artery bypass graft, *cad*=coronary artery disease, $\dot{V}O_{2peak}$ = peak

oxygen uptake, *vat*=ventilatory anaerobic threshold, *hr*=heart rate, *dbp*=diastolic

blood pressure, *sbp*=systolic blood pressure

Table 2. Characteristics and Outcomes of Cardiac Rehabilitation Completers

Variable	Heart Transplant			Coronary Artery Bypass Graft			Between Group
	n=23			n=25			Change
	Pre- Program	6 Months	p value	Pre- Program	6 Months	p value	p Value
Sociodemographic							
Age, years	49.6±11.4	-----		49.4±10.7	-----	-----	-----
Sex, male, n(%)	13 (56.5)	-----		15 (60)	-----	-----	-----
Partnered, n(%)	9/20 (45)	-----		16/24 (66.7)	-----	-----	-----
Not Employed, n(%)	20/21 (95.2)	17/21 (81.0)	0.2	17/24 (70.8)	16/24 (66.7)	0.6	-----
Clinical							
Body Mass Index, kg·m ²	26.4±7.2	26.9±7.3	0.2	26.6±4.4	27.1±5.0	0.1	0.9
Body Fat (%)	26.1 ± 10	25.8±10.0	0.6	27.3±10.4	27.3±10.4	1.0	0.8
Waist Circumference, cm	92.5±15.3	92.3±17.5	0.9	91.9±11.4	92.9±12.9	0.3	0.4
Waist >88 cm >102 cm*,	10 (43.5)	10 (43.5)	1.0	7 (28.0)	8 (32.0)	1.00	-----

n(%)

Hip Circumference, cm	98.1±10.6	98.9±10.9	0.5	101.2±8.2	101.1±9.3	0.9	1.0
Waist-to-Hip Ratio	0.94±0.1	0.92±0.12	0.2	0.91±0.07	0.92±0.07	0.3	0.1
Resting HR, beats ·min ⁻¹	97.8 ± 10.0	94.4 ± 10.1	0.2	72.9±12.2	74.3±14.3	0.6	0.2
Peak HR, beats ·min ⁻¹	121.2±12.7	129.3±16.2	0.03	134.6±18.1	145.8±22.2	0.009	0.6
RSBP (mmHg)	127.1 ± 14.1	126.9 ± 16.9	0.96	126.3±19.3	122.9±18.8	0.3	0.5
RDBP (mmHg)	82.1 ± 12.1	80.2 ± 9.0	0.5	75.6±10.9	75.5±8.9	0.98	0.6
Peak SBP (mmHg)	165.9±33.3	169.4± 31.1	0.4	182.3±28.7	189.9±25.0	0.1	0.5
Peak DBP (mmHg)	83.8±11.9	80.5±6	0.1	82.9±10.8	81.5±11.3	0.6	0.5
Peak Oxygen Uptake, mL·kg ⁻¹ ·min ⁻¹	15.9±3.9	18.3±5.6	0.02	20.2±5.6	25.7±8.4	<0.001	0.04
VAT mL·kg ⁻¹ ·min ⁻¹	12.3±3.3	14.1±4.8	0.08	14.1±3.9	19.1±7.3	<0.001	0.05
Peak RER	1.20±0.1	1.22±0.1	0.3	1.22±0.11	1.17±0.11	0.2	0.1

Values are mean+/- SD unless specified otherwise;

hr = heart rate, *rspb* = resting systolic blood pressure, *rdbp* = resting diastolic blood pressure, *vat*=ventilatory anaerobic threshold, *rer*=respiratory exchange ratio.

**Abdominal obesity was considered for waist circumference >88 and >102 cm for women and men, respectively.*