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Cancer and cardiovascular disease: The impact of cardiac rehabilitation and cardiorespiratory fitness on survival

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Abstract

Background: Cancer survivors are at increased risk for cardiovascular disease (CVD)-related morbidity and mortality. Exercise-based cardiac rehabilitation (CR) programs improve CVD risk factors, including cardiorespiratory fitness (CRF). The purpose of this study was to investigate: (1) the association between CR completion and survival, and (2) whether CRF improvements translate to increased survival among patients with comorbid cancer and CVD.

Methods: Patients with CVD and pre-existing cancer (any type) were referred to a 12-week exercise-based CR program between 01/1996 and 03/2016. Peak metabolic equivalents (METs) were assessed by graded exercise test pre-CR and at 12-weeks. Kaplan-Meier survival and multivariate cox regressions were performed to evaluate impact of CR completion and clinically-meaningful CRF improvements [ΔMETs≥1] on survival, adjusting for relevant covariates.

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Authors' contributions
TW co-conceptualized the study, performed the data analyses, co-wrote the manuscript, and revised the manuscript. CM assisted with analyses, co-wrote the manuscript, and revised the manuscript. DC co-conceptualized the study, assisted with the data analyses, and critically revised the manuscript. CO provided consultation regarding the statistical approach and critically revised the manuscript. RA co-conceptualized the study and critically revised the manuscript. SA facilitated the data merge and critically revised the manuscript. TC supervised the student collaborators (TW and CM) and critically revised the manuscript. DL conceptualized the research question, co-conceptualized the study and statistical approach, and critically revised the manuscript.

Declaration of Competing Interest
None.

Disclosures
None.

Prior presentation
Parts of this work were presented as a poster by TW at the 2020 Canadian Cardiovascular Society Virtual Congress.

Results: Among 442 patients with CVD and cancer referred to CR (67 ± 10 years; 22% women), 361 (82%) completed CR. 102 deaths were recorded during the 12-year observation period. Compared to patients who did not complete CR, patients with comorbid cancer who completed CR demonstrated a survival advantage (63% vs 80.1%, $p < .001$). CRF improved among completers during the 12-week program (mean change = 0.87 ± 0.93 METs, $p < .001$); 41% experienced a clinically-meaningful ΔMETs≥1. A survival advantage was not observed in completers who experienced a ΔMETs≥1 improvement ($p = .254$).

Conclusion: Completing a 12-week exercise-based CR program improved CRF and increased survival in patients with CVD and comorbid cancer. The results highlight the survival benefits of completing a CR program among CVD patients who experience added barriers imposed by cancer treatment and survival.

Keywords

Cardiac rehabilitation; Survival; Cardiovascular disease; cancer; Cardio-oncology; Exercise capacity; Cardiorespiratory fitness

1. Introduction

Cancer and cardiovascular disease (CVD) represent the top two causes of mortality worldwide, and together account for half of all deaths in North America [1]. Increased prevention and screening efforts along with advances in cancer treatment in recent decades have resulted in a rapidly growing population of cancer survivors, with the number of persons survived from any type of cancer projected to exceed 20 million by 2026 [2]. With increased survival rates, associations between cancer and risk of CVD are becoming increasingly prevalent. Five-year cancer survivors have up to a four-fold increased risk of CVD-related mortality, and 1.7–18.5-fold greater risk of developing CVD risk factors, relative to age-matched controls without cancer [3]. A population-based study of 3.2 million American cancer survivors found that three quarters had CVD and that approximately 1-in-10 died from a CVD-related diagnosis [4].

Various behavioral (e.g., smoking, sedentary behavior) and treatment-related (e.g., cardiotoxic effects of chemotherapy and radiation) factors have been elucidated to explain the increased risk and higher incidence of CVD among patients with cancer. These not only promote the development of CVD and related adverse cardiac events, but also contribute to the sequalae of decrements in physiological and functional capacity that lend to a reduction in cardiorespiratory fitness (CRF) – a universal and critical vital sign to health and cancer survivorship [5,6].

Exercise-based cardiac rehabilitation (CR) is a multi-component secondary prevention program that is recognized as a Class I level (strong evidence) indication in patients with CVD. CR has substantial evidence supporting its effectiveness at reducing or preventing morbidity or mortality associated with CVD, and improving overall quality of life and CRF upon completion [7,8].

Among those with comorbid cancer and CVD, changes in CRF and other CVD risk factors in response to CR, as well as the long-term implications on mortality, has received limited attention. A small number of studies have reported that CR leads to improvements in CRF and vascular function, and decreased risk of CVD events and mortality [9] among patients with cancer, yet it is currently not known whether CR completion improves survival outcomes relative to those who enroll, but do not complete the program. Further, no studies have investigated whether improvements in CRF achieved by cancer survivors who complete CR predict increased survival in the long-term.

The purpose of the present study was to: (1) compare baseline patient characteristics, cardiovascular risk factors, and survival between patients with comorbid CVD and cancer who completed and who did not complete 12-weeks of exercise-based CR; and (2) investigate the relationship between improvements in CRF, defined by peak METs, and survival over a median follow-up time of 144 months. We hypothesized that patients with comorbid CVD and cancer who completed the 12-week CR program would demonstrate a survival advantage relative to non-completers, and that clinically meaningful improvements in CRF achieved during CR would be associated with longer survival time among cancer survivors who completed CR.

2. Methods

2.1. Data sources

The study population included individuals with CVD referred to outpatient CR with TotalCardiology™ Rehabilitation (formerly Cardiac Wellness Institute of Calgary), in Calgary, Alberta, between January 1996 through March 2016 [10]. The database used for this secondary analysis was created through linking patient data from various sources using provincial health numbers (PHN). Data were linked on March 7, 2017. Participant baseline demographics, reason for referral, and PHN were recorded prospectively by TotalCardiology Rehabilitation. Information on patient co-morbidities, coronary anatomy, vital statistics, and therapeutic interventions (i.e., coronary artery bypass grafting or percutaneous coronary intervention) were obtained through a merge with the Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH) database [11] and administrative databases from Alberta Health Services. The APPROACH dataset includes all patients who underwent cardiac catheterization and/or revascularization in Alberta since 1995 [11,12]. Clinical covariates are captured only at the time of the initial catheterization. Thus, only those who were referred for CR within 1 year of their first catheterization were included to ensure that the covariate data reasonably reflected the state of the patient as he or she appeared at CR [10]. Data were also linked with the National Ambulatory Care Reporting System (NACRS), Vital Statistics, and the Discharge Abstract Database (DAD). A waiver of consent was granted for use of this dataset for secondary analyses by the Conjoint Health Ethics Review Board of the University of Calgary.

2.2. Study population

Patients were considered to be diagnosed with comorbid CVD and cancer if a cancer diagnosis (historical or current) was indicated in their hospital chart at the time of cardiac catheterization. Patients were included in this study if they: 1) were 18+ years; 2) had a documented diagnosis of coronary artery disease and comorbid cancer (any type); 3) were within one year of their first catheterization at the time of joining CR; and 4) were enroled in the CR program, defined as attending the initial CR orientation appointment and completing a symptom-limited maximal graded exercise test (GXT).

Patients included in the sub analyses addressing whether improvements in CRF translate to increased survival additionally needed to have completed a GXT at completion of the 12-week CR program.

2.3. Cardiac rehabilitation program

Details regarding the TotalCardiology CR program have been described previously [8,13]. Briefly, the 12-week multidisciplinary program offered included 1-h supervised exercise sessions performed twice weekly and encouraged independent exercise sessions on 2–3 additional days per week. All referred patients completed a baseline assessment including a physical examination, anthropometric measurements (body mass index [BMI] and waist circumference), and phlebotomy to assess fasting lipid profile. Patients performed a GXT at baseline (i.e., during their CR orientation appointment, scheduled immediately after referral) and immediately following CR completion (i. e., at 12 weeks) to assess CRF through the determination of peak metabolic equivalents (METs), and to determine individual exercise prescriptions (intensity level). The GXT followed the Bruce or Modified Bruce Protocol using a treadmill and peak METs were calculated through established equations using peak speed and grade achieved during GXT [14].

Each exercise session began with a 5-min warm-up, followed by 20–60 min of steady-state aerobic training at 45–85% of heart rate reserve (derived from GXT test results), followed by a 5-min cool down. Stretching or resistance training with elastic tubing was offered to participants following each exercise training session. To supplement the exercise program, patients were offered education classes in nutrition, stress management, and smoking cessation, with referral to dietitians and psychologists within the program as needed.

Patients were considered CR completers if they completed both the initial (baseline) and 12-week GXT. CR non-completers were defined as patients who did not complete the 12-week GXT (i.e., dropped out at any point between exercise sessions 1 and 24).

2.4. Outcome definition

Primary outcomes of interest for this study were: 1) long-term survival assessed by mortality; and 2) baseline and 12-week peak MET levels. Survival time was calculated as months elapsed from the first CR exercise session date to the patient’s death, date of data linkage or 144 months, whichever occurred first. Information on deaths were recorded and linked to data from Vital Statistics and the DAD; patients with a recorded date of death were coded as deceased, whereas patients with no date of death at data linkage (March 7th, 2017) were coded as alive at follow-up. Improvement in peak METS was calculated based on the difference between baseline to 12-week assessment, with change (Δ) $\geq$1 METs considered as a clinically significant change for the primary analyses [6].

2.5. Study covariates

Baseline demographic characteristics (i.e., age, sex), clinical variables (measured during the CR orientation appointment, i.e., waist circumference [cm], blood pressure, cholesterol, high-density lipoprotein [HDL], low-density lipoprotein [LDL], total cholesterol and triglycerides; mmol/L) smoking status and information about the CR program (i.e., completion of clinic-based or home-based CR) were obtained from TotalCardiology Rehabilitation. The APPROACH database linkage was used to derive information regarding clinical covariates including: 1) body mass index (BMI; weight [kg]/height [m^2]); and 2) comorbidity status (e.g., type 2 diabetes, hypertension, congestive heart failure [CHF], chronic obstructive pulmonary illness [COPD], liver disease, gastrointestinal disease, renal disease and peripheral vascular disease [PVD], myocardial infarction [MI], and percutaneous coronary intervention [PCI] or coronary artery bypass grafting (CABG), and results of coronary catheterization, including coronary anatomy, as summarized by the Duke jeopardy score [15]).

2.6. Analysis plan

Differences in patient demographics, lifestyle behaviors and clinical characteristics between CR completers and non-completers at baseline were examined by independent *t*-tests and chi square tests. Kaplan Meier analysis was performed to compare survival between CR completers versus non-completers over the 144-month observation period. Cases were censored at data merge (March 7, 2017), or 144 months of follow up. A multivariate cox proportional hazards model was estimated in CR completers to evaluate the association between improvements in CRF, (defined as a ΔMETs≥1) and survival. The dichotomous variable indicating improvement in METs (yes/no) was added in Step 1; age, sex, and BMI were added in Step 2, and systolic and diastolic blood pressure, current or former smoking status, comorbid diabetes, and comorbid COPD, were added as covariates in Step 3. Covariates were chosen based on known determinants of survival in patients with CVD and cancer (e. g., age, sex, BMI, blood pressure, smoking status) [31] in addition to a priori analyses indicating no statistically significant differences between CR completers and non-completers (e.g., lipids, triglycerides).

Post-hoc exploratory analyses were performed to explore whether this patient population may experience a lower clinically-relevant ΔMETs threshold (i.e., ΔMETs ≥ 0.5) (i.e., 0.5 MET change [16]) or a higher ΔMETs (i.e., ΔMETs ≥ 1.5) to achieve a survival advantage. Separate exploratory cox regressions were performed with ΔMETS ≥ 0.5 and ≥1.5 as dichotomous independent variables adjusting for the same covariates described above.

3. Results

Four hundred forty-two patients (67 ± 10 years old; 22% women) with comorbid CVD and malignant cancer were included in the analysis. Eighty-two percent (n = 361) completed CR. The mean survival time of the overall sample was 119.76 months (95% CI 115.45–124.07), and 102 deaths were recorded during the observation period. Characteristics of the sample, including differences between patients who completed and did not complete CR, are presented in Table 1.

3.1. Patient characteristics and survival among CR completers and non-completers

Compared to patients with cancer who completed CR, those who did not complete the program were more likely to be women, have a BMI indicative of obesity, have lower baseline CRF levels, and present with a comorbid diagnosis of Type II Diabetes and/or COPD (all $p < .05$; Table 1).

During a follow-up period of 144 months, mean survival time among CR completers and non-completers was 124 months (95%CI = 120–129 months) and 99.65 months (95% CI 97.46–111.84), respectively. Kaplan Meier survival analysis indicated that patients who completed CR survived longer than patients who did not complete the program (80% versus 63% survival at final follow-up, $p < .001$, Fig. 1).

3.2. Improvements in CRF and other cardiovascular risk factors associated with survival among CR completers

Changes in CRF and other CVD risk factors among patients with cancer who completed the 12-week CR program ($n = 361$) are presented in Table 2. On average, peak METs improved from baseline to 12 weeks among completers (6.7 ± 12.01 to 7.59 ± 2.09), with mean change in CRF of 0.87 ± 0.93 METs ($p < .001$). Forty-two percent ($n = 150$) of completers achieved a ΔMETs ≥ 1 at 12-weeks (Table 2). Of note, CR completers who had a ΔMETs ≥ 1 during CR had *lower* baseline MET levels, relative to those who did not reach the ΔMETs ≥ 1 threshold (6.41 ± 1.97 vs. 6.93 ± 2.02 METs, respectively; $p = .016$, data not shown). CR completers experienced significant improvements in HDL, LDL, total cholesterol, and triglyceride levels, and waist circumference over the duration of the CR program. No significant improvements in BMI were observed.

Table 3 presents the fully adjusted HRs for the association of pertinent clinical risk with survival over the 144-month observation period. Among cancer patients who completed CR, comorbid COPD was associated with reduced survival over the 144-month follow-up time (HR = 2.15, 95%CI = 1.21–3.80). Covariates that were non-significant predictors of survival in completers with CVD and cancer included age, sex, BMI, comorbid diabetes, systolic and diastolic blood pressure (all $p > .05$). Achieving a gain in peak METs ≥ 1 at 12-weeks was not associated with survival ($p = .359$, Table 3). Further addition of lipids (i.e., triglycerides, HDL, and LDL) to the fully adjusted model resulted in lower HR (greater survival benefit); however, hazard risk estimates were not statistically significant (Supplemental Table 1).

3.3. Exploratory analyses

Table 4 presents results of the post-hoc cox proportional hazards models examining thresholds of ΔMETs≥0.5 and ≥ 1.5 in CRF at 12-weeks as potentially clinically-relevant predictors of survival in this sample. Whereas experiencing ΔMETs ≥0.5 was not statistically associated with a survival benefit among CR completers with comorbid CVD and cancer, ΔMETs ≥1.5 was associated with a lower hazard risk of mortality after full covariate adjustment (HR = 0.41, 95% CI = 0.17–0.99).

4. Discussion

Co-morbidity in CR is increasingly recognized as a key clinical factor related to CR outcomes. In the present study of nearly 450 patients with comorbid CVD and cancer, we identified important survival differences between CR participants with cancer according to CR program completion status. Specifically, we found that over a 144-month observation period, patients with comorbid CVD and cancer who completed CR demonstrated significantly greater survival compared to non-completers, with the majority of completers (80% versus 63% non-completers) alive at the end of the 144-month follow up period.

Our study showed that patients with comorbid cancer and CVD who did not complete the 12-week CR program had decreased survival over the follow-up period. Compared to CR completers, the group of non-completers had a greater proportion of women, a higher average BMI, lower CRF, and increased multimorbidity (i.e., diabetes and/or COPD in addition to cancer/CVD) at baseline, which is consistent with previous observations [17–19]. Patients with a history of cancer or similar comorbidities are more vulnerable to fatigue, deconditioning, weight gain, sleep disturbance, depression, and joint pain/stiffness [3,9] — factors that are specific to the side effects of cancer treatment and may otherwise preclude participation and/or adherence to structured exercise programs such as CR. However, it is important to note that less than 20% of our sample of patients with comorbid cancer and CVD failed to complete the 12-week CR program. This finding adds to the knowledge base regarding the potential practical application of multicomponent CR to improve fitness and other risk factors (e.g., smoking, high blood pressure, dyslipidemia, body weight) [9,20,21] in patients with comorbid cancer and CVD. This finding also highlights the need to include targeted strategies (e.g., physical therapist-assisted/individualized exercise program, online models) in standard CR to address cancer-treatment related morbidities and optimize CR uptake and adherence in this specialized population.

A large body of evidence has shown that improvements in CRF by at least 1 MET confer survival benefit in patients with CVD over median follow-ups ranging from 1 to 17 years [8,22–26], supporting its role as an important clinical vital sign for cardiovascular and overall health [6]. In the present study, we found that 12-week improvements in CRF by at least 1 MET was not associated with long-term overall survival. Our exploratory findings suggest that patients with cancer and comorbid CVD who achieve at least a 1.5 MET improvement in CRF had a significant and substantially lower risk of death (adjusted HR = 0.41) as compared to patients who achieve <1.5 MET improvement (adjusted HR = 0.91), in whom lower risk was not statistically significant. Although findings of this post-hoc analysis should be interpreted with caution, it remains plausible that patients with cancer and CVD must aim for a higher threshold of improvement in fitness (i.e., at least 1.5 METs) to experience the survival benefits of CR.

On average, patients in this sample improved by 0.87 ± 0.93 METs (13.1% increase) following CR completion. While the magnitude of the average improvements is less than average post-CR MET improvements of 1.55 (95% CI 1.21–1.89) pooled from a recent meta-analysis [27], it is difficult to make a distinct comparison as CRF improvements reported in our analysis are specific to patients with a comorbid diagnosis of cancer and

CVD. In patients with cancer, CRF levels are estimated to decline between 5 and 26% throughout the course of various anti-cancer regimens alone [28] and are likely to be exacerbated in those with comorbid CVD. As such, average improvements of nearly 1 MET in this sample of patients with comorbid cancer and CVD who completed CR is certainly notable.

Given that gains in CRF ≥ 1 MET were not associated with improved survival, the greater survival benefit observed in CR completers versus non-completers may be partly explained by improvements in CVD risk factors. For example, improved adherence to medications and psychological counselling to reduce depression are alternative pathways through which survivorship may be improved among patients with CVD and cancer. Future studies are needed in this population to explore these and other factors that may be responsible for increased survival.

A few limitations of this study should be noted. The present dataset only included information about the presence or absence of malignancy. Additional information about the diagnosis (e.g., type, stage, treatment received, or time since diagnosis) may be important in predicting CR non-completion, CRF improvement, and/or long-term survival, but these details were not known. Further, different types of cancers may have heterogenic effects on the cardiovascular system and thus differentially impact survival [31]. We were also unable to determine if there was a survivor bias influencing the results. That is, patients who completed CR may be further removed from cancer diagnosis/treatment and in better health to participate in CR, compared to patients with a more recent diagnosis. Cause of death was also unknown; it is impossible to know whether patients died from CVD-related, cancer-related, or other causes. Further, important information unavailable for analysis included reasons for non-completion of CR, CR attendance (defined as the number of exercise sessions attended), and types of activities or volume or duration of exercises completed independent of the clinic-based exercise program were not recorded. Given the dose-response relationship between exercise volume and CRF gains and survival benefits, information about CR session attendance and adherence to exercise specifically would provide insight into the differential exposure to the cardioprotective benefits of exercise within CR completers. Further, other aspects of CR beyond supervised exercise may confer survival advantage among CR completers, such as improved medication monitoring/adherence and dietary changes. These various components of the CR program may have a differential impact on survival which cannot be assessed with the current study design. Finally, the current study was completed within a Canadian CR program which may have implications for generalizability to American CR context.

The results of this study provide new information regarding survival benefits and prognostic determinants of CR program completion among CVD patients with comorbid cancer. Completion of a 12-week CR program was associated with increased survival. This has important implications for integrated cardio-oncology care. Efforts are needed to identify patients at risk of CR dropout, and support patients in completing their CR program as prescribed. Accommodations that have proven useful for patients with multimorbidity (e.g., home programs, etc.) should be provided to patients in CR with comorbid cancer. Further, preserving CRF during and following cancer treatment may be particularly important for mitigating future mortality risk in patients who go on to develop CVD. This finding lends support to recent calls for greater access to specialized multidisciplinary cardio-oncology programs to improve survivorship from both cancer and CVD [3,29,30].

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2021.09.004.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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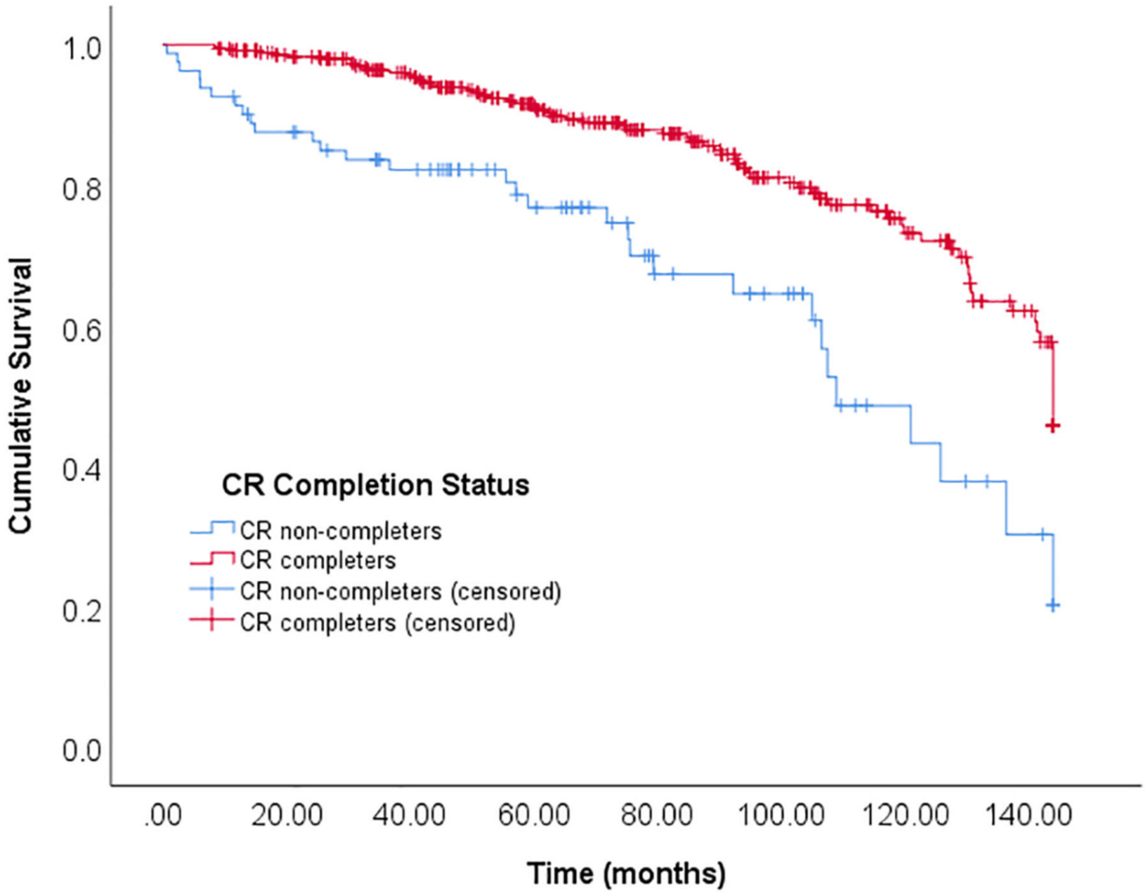

Fig. 1.

Survival among the total sample of patients with CVD and cancer (*N* = 442; 361 CR completers, 81 CR non-completers). CR = cardiac rehabilitation; CVD = cardiovascular disease.

Table 1

Patient characteristics and CVD risk factors among cancer survivors who completed and did not complete CR (*N* = 442).

Variable (baseline values)	Total sample (N = 442)	CR completer (*N* = 361)	CR non-completers (*N* = 81)	*t*-Test/Chi-square test *p*-Value
Male sex	344 (77.80)	288 (80.00)	56 (69.00)	**0.037**
Age (Years; group means/SD)	67.36 (9.53)	67.73 (9.12)	65.73 (11.13)	0.088
Age (categories) *N* (%)				0.082
30–39.9 years	3 (0.7)	1 (0.3)	2 (2.5)	
40–49.9 years	17 (3.8)	12 (3.3)	5 (6.2)	
50–59.9 years	80 (18.1)	65 (18.0)	15 (18.5)	
60–69.9 years	153 (34.6)	123 (34.1)	30 (37.0)	
70–79.9 years	157 (35.5)	136 (37.7)	21 (25.0)	
≥80 years	32 (7.2)	24 (6.6)	8 (9.9)	
Smoking status				
Former smoker	192 (43.4)	158 (43.8)	34 (42.0)	0.769
Current smoker	67 (15.2)	51 (14.1)	16 (19.7)	0.202
Never smoked	183 (41.4)	152 (42.1)	31 (38.3)	
Waist circumference (cm)	102.04 (13.75)	101.74 (13.75)	103.47 (13.76)	0.415
Mean body mass index (kg/m^2)	28.09 (4.90)	27.99 (4.67)	28.57 (5.80)	0.345
BMI by category; *N* (%)				**0.036**
< 18.5	2 (0.50)	0	2 (2.5)	
18.5–24.99	108 (24.4)	93 (25.8)	15 (18.5)	
25.0–29.99	188 (42.5)	154 (42.7)	34 (42)	
30.0–34.99	91 (20.6)	73 (20.2)	18 (22.2)	
35.0–39.99	25 (5.7)	20 (5.5)	5 (6.2)	
≥40.00	9 (2.0)	6 (1.7)	3 (3.7)	
Attended home CR program	85 (19.2)	65 (18)	20 (25)	0.168
HDL(mmol/L)	1.21 (1.15)	1.20 (0.37)	1.22 (0.45)	0.714
LDL (mm/L)	1.98 (0.86)	1.98 (0.88)	1.99 (0.78)	0.892
Total cholesterol (mmol/L)	3.84 (1.02)	3.81 (1.01)	3.99 (0.94)	0.277
Triglycerides (mmol/L)	1.49 (0.90)	1.45 (0.89)	1.70 (0.92)	0.053
Resting SBP (mmHg; *N* = 414)	119.74 (19.51)	120.43 (19.64)	116.26 (18.58)	0.105
Resting DBP (mmHg; *N* = 416)	71.59 (10.06)	71.63 (10.14)	71.35 (9.74)	0.830
Comorbidities				
Type II Diabetes	100 (22.6)	71 (20)	25 (31)	**0.027**
Hypertension	284 (64.3)	230 (64)	54 (67)	0.616
CHF	45 (10.2)	32 (9)	13 (16)	0.053
COPD	98 (22.2)	73 (20)	25 (31)	**0.037**
Liver/GI disease	63 (14.3)	52 (14)	11 (14)	0.848
Renal disease	17 (3.8)	12 (3)	5 (6)	0.228
PVD	21 (4.8)	17 (5)	4 (5)	0.930

Variable (baseline values)	Total sample (N = 442)	CR completer (*N* = 361)	CR non-completers (*N* = 81)	*t*-Test/Chi-square test *p*-Value
Cardiac history				
Prior CABG	47 (10.6)	35 (10)	12 (15)	0.177
Prior PCI	47 (10.6)	34 (9)	13 (16)	0.080
Prior MI	85 (19.2)	66 (18)	19 (23)	0.286
[a]Duke Jeopardy Score (time of catheterization)				0.426
0		51	13	
2		109	28	
4		46	10	
6		70	10	
[a]Duke Jeopardy Score (time of catheterization)				
8		22	7	
10		21	1	
12		32	8	

Note. BMI = body mass index, CABG = coronary artery bypass graft, CHF = coronary heart failure, COPD = chronic obstructive pulmonary disease, CR = cardiac rehabilitation, CVD = cardiovascular disease, HDL = high density lipoprotein, GI = gastrointestinal, LDL = low density lipoprotein, MI = myocardial infarction, PCI = percutaneous coronary intervention, PVD = peripheral vascular disease, STEMI = ST elevation myocardial infarction.

Missing: Waist circumference, $n = 148$; BMI, $n = 19$; LDL, $n = 84$; HDL, $n = 78$; Total Cholesterol, $n = 79$; Triglycerides, n = 79; Resting SBP, $n = 28$; Resting DBP, $n = 26$.

Bold print indicates statistical significance; $p<0.05$.

[a]The Duke Jeopardy score estimates myocardium risk according to location of coronary artery stenoses. Greater Jeopardy Scores are associated with lower left ventricular ejection fraction post-MI and decreased five-year survival in patients with CAD [15].

Table 2

Improvements in risk factors from baseline to 12-weeks among patients with cancer who completed CR (n = 361).*

CVD risk factor	N	Baseline	12-Weeks	Cohen's *d*
METs peak	361	6.71 (2.01)	7.59 (2.09)	0.94***
HDL (mmol/L)	233	1.18 (0.35)	1.23 (0.35)	0.23**
LDL (mmol/L)	227	1.97 (0.88)	1.69 (0.68)	0.33***
Total Cholesterol (mmol/L)	232	3.79 (1.00)	3.52 (0.87)	0.29***
Triglycerides (mmol/L)	231	1.47 (0.88)	1.35 (0.93)	0.18**
BMI (kg/m^2)	208	27.86 (5.12)	27.82 (5.00)	0.04
Waist circumference (cm)	202	101.50 (12.97)	100.51 (13.07)	0.25***

Note. BMI = body mass index; CR = cardiac rehabilitation; CVD = cardiovascular disease; HDL = high density lipoprotein; LDL = low density lipoprotein; METs = metabolic equivalents.

* $p < .05$.

** $p < .001$.

*** $p < .001$.

Table 3

Cox proportional hazard model for change in cardiorespiratory fitness ≥1 MET (pre-CR to 12-weeks) as a predictor of survival among patients with cancer and CVD (n = 330)[†].

Model	HR (95% CI)
1	0.80 (0.48–1.36)
2	0.84 (0.49–1.44)
3	0.77 (0.44–1.35)

Note.

[†]Sample size of CR-completers of 330 includes participants with complete covariate and outcome data. CR = cardiac rehabilitation; MET = peak metabolic equivalent; CVD = cardiovascular disease. Model 1 represents the unadjusted model. Model 2 was minimally adjusted (age, sex, and body mass index) and Model 3 fully adjusted (comorbid type II diabetes; comorbid chronic obstructive pulmonary disease; pre-CR diastolic and systolic BP; current or former smoking).

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Table 4

Exploratory cox proportional hazards models of the association between 12-week ΔMET ≥ 0.5 and ≥1.5 and survival among CR completers with cancer, adjusting for relevant covariates ($N = 330$)[†].

ΔMET ≥ 0.5	**HR (95% CI)**
Model 1	0.83 (0.50–1.40)
Model 2	0.90 (0.53–1.52)
Model 3	0.91 (0.54–1.54)
ΔMET ≥ 1.5	HR (95% CI)
Model 1	0.57 (0.24–1.31)
Model 2	0.55 (0.24–1.28)
Model 3	0.41[*] (0.17–0.99)

Note.

[†]Sample size of CR-completers was reduced to 330 owing to 15 participants who were missing BMI data and 16 participants who were missing systolic and/or diastolic blood pressure data. CR = cardiac rehabilitation; MET = peak metabolic equivalent; CVD = cardiovascular disease. Model 1 represents the unadjusted model. Model 2 was minimally adjusted (age, sex, and body mass index) and Model 3 fully adjusted (comorbid type II diabetes; co-morbid chronic obstructive pulmonary disease; baseline diastolic and systolic BP; current or former smoking status).

[*]$p < .05$.