Does Pre-Operative Frailty Predict Cardiac Rehabilitation Completion in Cardiac Surgery Patients?

By

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Abstract

The typical cardiac surgery patient is increasing in age and level of frailty. Frailty can be defined as an increased vulnerability to stressors due to decreased physiological reserve. Previous investigations have demonstrated the benefit of cardiac rehabilitation (CR) programming on surgical outcomes. However, the link between pre-operative frailty and post-operative CR completion is unclear. The purpose of this study was to determine if pre-operative frailty status impacts CR completion post-operatively. A total of 114 cardiac surgery patients with an average age of 71 years were included in the analysis. CR completers were significantly less frail than CR non-completers at baseline based on the Clinical Frailty Scale (CFS; p=0.01), Modified Fried Criteria (MFC; p=0.0005), Short Physical Performance Battery (SPPB; p=0.007) and the Functional Frailty Index (FFI; p=<0.0001). The change in frailty status from baseline to 1-year post-operatively was not statistically different between CR completers and non-completers; CFS (p=0.90), MFC (p=0.70), SPPB (p=0.06) and FFI (p=0.07). However, the MFC frailty domains of cognitive impairment (p=0.0005) and low physical activity (p=0.04), in addition to the FFI physical domain of frailty (p=0.009), did significantly improve among CR completers when compared to non-completers. CR attendance measured by swipe card access did not correlate with frailty modifications. Collectively, these data suggest that participants deemed to be frail at the pre-operative time point attend and complete CR less frequently than non-frail participants. Furthermore, CR completion does not appear to modify frailty status overall; although, some frailty domains appear to be more sensitive to change than others.

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Chapter 1: Introduction

By the year 2051 it is speculated that 25% of the Canadian population will be ≥65 years of age.[1] With an aging population, the prevalence of chronic disease is on the rise. Although people are living longer than ever before, they are often living the last decade of their lives in sickness and disability related to chronic diseases, such as cardiovascular disease (CVD).[2] The Canadian health care system is feeling this burden as 2009 statistics reflect that health care spending per capita was 4.5 times greater among those aged 65 years or older when compared to those aged 20 to 64.[3] Furthermore, there is a subset of the older adult population that is frail and requires enhanced care when compared to their non-frail counterparts. This concept of frailty has been revealed as a medically distinct syndrome when compared to disability and comorbidity, which in the past have been terms used interchangeably.[4]

There has been confusion in the literature regarding a widely accepted definition of frailty. However, frailty can generally be defined as the slowing and/or dysregulation of multiple physiological systems, which render the individual vulnerable to stressors due to decreased physiological reserve.[4] Although frailty can exist in a wide variety of age groups, frailty generally increases in prevalence with age and appears to be more common among certain sub-sections of the general population, including: women,[5] older adults,[6] the less educated,[7] and those of African American ethnicity.[8] A recent systematic review by Collard and colleagues[9] identified that roughly 10% of community dwelling older adults (65 years and older) are frail. However, frailty prevalence rates can increase dramatically up to 50% among those undergoing cardiac surgery for CVD.[10] The increased frailty prevalence rates among the cardiac surgery cohort when compared to community-dwelling older adults is likely due to a whole host of factors, including advancing age and comorbidities. Elevated frailty prevalence among the cardiac surgery cohort is problematic given the link between frailty and poor health outcomes, including delirium[10] and mortality.[11]

Those who have attended a cardiac rehabilitation (CR) program following their cardiac surgery have demonstrated improved lipid profiles in addition to a reduced risk of all-cause and cardiac mortality when compared to those who do not attend a CR program.[12,13] The CR program can be defined as a multidisciplinary approach specifically aimed at improving quality of life and exercise tolerance while reducing mortality rate and modifiable risk factors through a diet and exercise intervention.[14] Exercise has been shown to improve cardiovascular health;[15] however, it remains unclear if exercise can improve frailty. Sourial and colleagues[16] demonstrated that the highest contribution of individual frailty differences among the 7 frailty domains (i.e., nutrition, energy, mobility, physical activity, strength, cognition and mood) are deficits in physical strength, mobility and energy. Therefore, exercise may be instrumental to frailty modification. In fact, a recent systematic review concluded that exercise appeared to benefit the frail older adult cohort.[17] Currently, there is a paucity of literature examining the link between pre-operative frailty and CR completion and non-completion in cardiac surgery patients. Furthermore, the impact of CR completion or CR dose among CR attenders on frailty status 1-year post-cardiac surgery is not clear. CR completion is defined as those individuals who attended a baseline stress test, attended at least some CR classes throughout the program duration and had a formal re-assessment at program conclusion.[18] CR non-completion is defined as those individuals who did not attend either the baseline stress test, the formal re-assessment at CR program conclusion or attended ≤1 CR class throughout the program duration.[19] Finally, a CR attender is defined as all individuals who attended ≥1 CR class. To clarify, all CR completers and non-completers attending ≥1 CR class are considered CR attenders.

There are 4 specific objectives for this project: 1) to determine if pre-operative frailty status impacts CR completion rates post-operatively in cardiac surgery patients. I hypothesized that pre-operative frailty will negatively impact CR completion rates; 2) to determine if CR completion impacts the change in frailty (Δfrailty) status from baseline to 1-year post-cardiac surgery. I hypothesized that CR completers will improve their frailty status to a greater extent than CR non-completers; 3) to determine if any domains of frailty within the MFC (i.e., shrinking, weakness, exhaustion, slowness, low physical activity, depression and cognitive impairment), SPPB (i.e., 5-metre gait speed, balance and repeated chair stand) and FFI (i.e., physical, functional, nutrition and exhaustion, quality of life and mood and cognition) are modified by CR completion in cardiac surgery patients. I hypothesized that the domains of frailty most strongly associated with increased physical activity (i.e., weakness, 5-meter gait speed, and low self-reported physical activity levels) will improve the most with CR completion in cardiac surgery patients; and 4) to determine if CR swipes, measured by swipe card records, impacts frailty status among post-cardiac surgery CR attenders. I hypothesize that CR attenders who had a higher swipe count will improve their frailty status to a greater degree when compared to those who had a lower swipe count over the CR program duration.

Chapter 2: Literature Review

This literature review will begin by discussing frailty and some of the potential underlying causes and pathophysiology of this syndrome. The focus will then shift to the most common measures of frailty and the association between frailty and survival. The prevalence of frailty among community-dwelling older adults and those with CVD will then be described in addition to how frailty can impact the outcomes among those with CVD. Finally, we will conclude by describing the benefits of exercise among those with CVD and the frail before discussing best practice CR programming.

2.1 Frailty

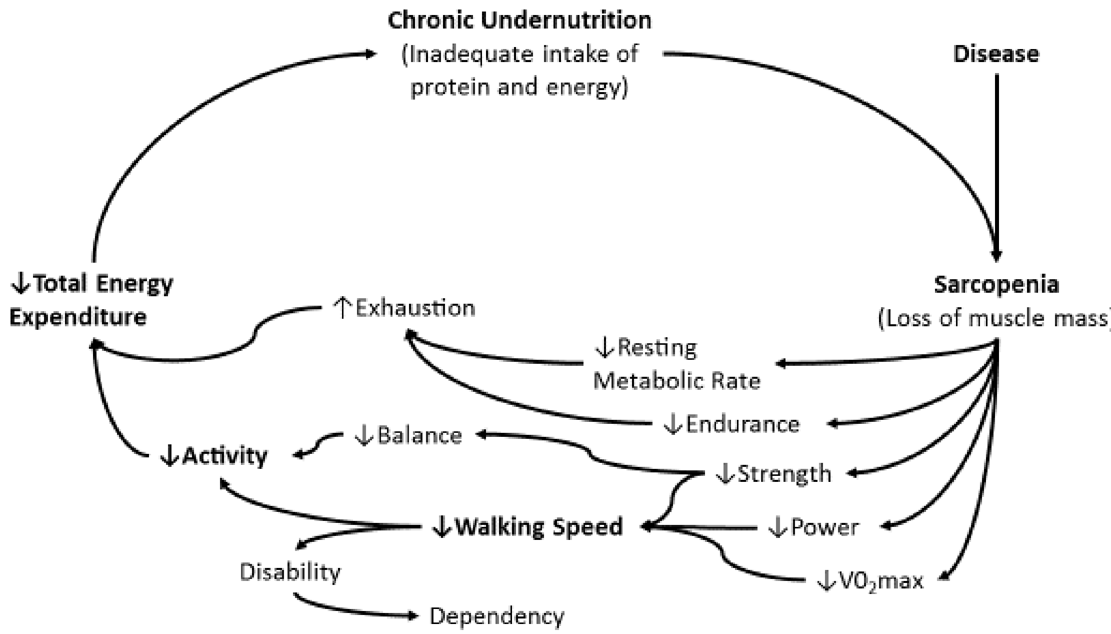
The academic interest surrounding the concept of frailty has been increasing exponentially since the term "frail elderly" was introduced as a Medline Medical Subject Heading (MeSH) term back in 1991.[20,21] Despite the influx in frailty related research, there is still considerable controversy regarding a widely acceptable definition of the term.[22] For the purposes of this study, frailty will be defined as the slowing and/or dysregulation of multiple physiological systems, which render the individual vulnerable to stressors due to decreased physiological reserve.[4]

Frailty, like aging, is not experienced uniformly between individuals. In fact, early onset of frailty can lead to premature aging, which can significantly advance an individual's biological age past that of their chronological age.[23] With deficit accumulation highly correlated with risk of death, frailty measured in this fashion becomes an accurate estimator of biologic age, which tends to accelerate in the years prior to death.[24] This leaves deficit accumulation and resulting frailty as one of the main contributors to heterogeneous aging.

Pathophysiology

Frailty is a complex syndrome characterized by multi-system dysregulation and decline.[4] Among the systems impacted by frailty are the immune, hormonal and endocrine systems,[25] which could negatively impact levels of important androgens and estrogens[26] leading to a whole host of physiological changes.[27] Due to the multifaceted nature of frailty, there is little consensus regarding the physiological pathways responsible for frailty.[25] Furthermore, not all frail individuals reach disease status. However, when stressors are placed on the frail body, subclinical impairments are brought to light where undernutrition, sarcopenia and decreased energy expenditure can accelerate decline.[28,29] Figure 1 illustrates the frailty cycle, which includes the interaction of multiple variables that have been shown to impact frailty development and progression.

Figure 1: Frailty Cycle.



Note: This figure has been modified from Fried and colleagues[28]

Inflammation may be an important underlying foundation of frailty[30,31] since connections have been made between high levels of proinflammatory cytokines [interleukin (IL)-6, IL-1, tumor necrosis factor-α and C-reactive protein (CRP)] and morbidity and mortality risk among older adults.[32] Furthermore, a recent systematic review and meta-analysis linked elevated CRP and IL-6 among those who were either pre-frail or frail.[33] Proinflammatory cytokines, such as the ones listed above, have a catabolic effect on muscle mass over time and can lead to the characteristic loss of muscle mass among the frail.[34] The Cardiovascular Health Study looked at 4735 community-dwelling older adults (57% female and 43% male) aged 65 years or older who were categorized as either frail, intermediate or non-frail via the Fried phenotype model[28] which constituted 6%, 45% and 48% of the sample size respectively.[35] The inflammatory markers of CRP, factor VIII and fibrinogen were all significantly associated with the presence of frailty, which was an effect that persisted after controlling for potential confounding variables such as sex, age and race. This finding suggests a link between inflammation system alterations and the presence of frailty.[35] Furthermore, increased inflammatory biomarkers are also seen among those with CVD.[36,37] This biological link between frailty and CVD is supported with high coexistence, meaning that frailty is often present in individuals with CVD. In fact, frailty is associated with a 2- to 3-fold increase in CVD prevalence, with frailty being an important predictor of mortality among the CVD cohort.[38]

Measuring frailty

There are currently numerous tools that measure frailty. A systematic review by De Vries and colleagues[39] identified 20 frailty assessment tools validated in the literature. With this many tools, researchers are becoming confused as to which tool produces the optimal frailty measurement. Going forward, I will focus on four popular tools to measure frailty, which are the clinical frailty scale (CFS; Appendix A)[40], the modified Fried criteria (MFC; Appendix B),[28] the Short Physical Performance Battery (SPPB; Appendix C)[41] and the frailty index (FI; Appendix D).[42]

The CFS, created by Rockwood and colleagues,[40] is a 9-category scale that is subjectively based on clinical judgement. Scoring ≥4 on the CFS is considered to be frail (Table 1). Despite the simplicity of the CFS, high correlations can be observed with more objective measures of frailty, such as the FI (r=0.80),[40] which makes the CFS attractive to hospital settings based on its time efficiency and ease of implementation. However, the problem with assessing frailty in this manner is that many important factors such as nutritional status, depression and cognition are not considered. Furthermore, frailty may not be visually obvious, leading to inconsistent clinical judgement influenced by erroneous factors such as the environment, time of day, recent sleeping patterns and mood.[43]

Overall, the Fried phenotype model[28] is cited in the literature with the highest frequency.[37] Originally, the Fried phenotype model, employing data from the Cardiovascular Health Study,[44,45] was developed to assess 5 separate variables including: shrinking, weakness, exhaustion, low physical activity, and slowness. The frailty cut point in this model required ≥3 of the aforementioned 5 criteria to be present in the given individual for a frailty diagnosis (Table 1). However, the 5 criteria included in the Fried phenotype model focused on physical variables only and as the literature advanced to better understand frailty, important questions were raised regarding the impact of frailty on cognition and other biological processes. The addition of cognitive impairment and depression to the original scale gave birth to the MFC which is arguably a more comprehensive measurement of frailty, employing the same frailty cut point as the original scale.[20,28]

The SPPB[46] is a physical assessment of frailty that measures 3 variables including: 5-metre gait speed, a balance test (side-by-side, semi-tandem, and tandem stance) and the repeated chair stand test. Each variable is scored out of a possible 4 points for a perfect score of 12.[46] The frailty cut-point for the SPPB has been set such that those attaining a score of ≤9 are deemed frail (Table 1).[47] The SPPB has gained popularity as a measure of frailty based on its objectivity and clinical practicality.[48] However, the SPPB is limited by the ceiling effect occurring in the healthier cohort and over-emphasis on lower body function.

Originally introduced by the Canadian Study of Health and Aging, accumulation of deficits is a separate measure of frailty that expresses frailty along a continuum.[42] What separates the FI from other frailty measures is the use of an unspecified set of criteria that can produce a meaningful measure of frailty in everyone, regardless of functional status or age.[49] A FI can be created by including a whole host of components or deficits in health. The FI typically includes 30 to 75 deficits such as symptoms, conditions, disabilities and diseases with more deficits resulting in an increased FI score.[50,51,40,52] However, FIs have more recently been validated to include as little as 11 variables in the cardiac surgery cohort among several other surgical cohorts.[53,54,55,56,57] All FI variables included (e.g., categorical, ordinal, and interval) are scored along a continuum between 0 (deficit absence) and 1 (deficit presence) based on previously established cut-points.[52] The FI score is then calculated by dividing deficits present by total deficits analyzed[52] with a score of $\geq$0.25 generally accepted as a typical frailty cut-point (Table 1).[58] Furthermore, a FI score typically increases by 0.03 for every chronological year an individual ages, which reflects the FI's age association.[42,58] Our research team has created a 25-variable functional frailty index (FFI) that will be described in greater detail in the methods section of this report.

Table 1: Frailty Measurement Tools & Cut Points.

Tool	Variables Considered	Frailty Cut Point
CFS	Subjective 9-point scale (Appendix A)	≥4 points out of 9
MFC	Slowness, weakness, weight loss, exhaustion, depression, low physical activity, cognitive impairment (Appendix B)	≥3 of the 7 variables present
SPPB	5 m gait speed, balance tests, repeated chair stand test (Appendix C)	≤9 points out of 12
FFI	25 separate variables (Appendix D)	deficits/variables ≥0.25

CFS, Clinical Frailty Scale; ***MFC***, Modified Fried Criteria; ***SPPB***, Short Physical Performance Battery; **FFI**, Functional Frailty Index.

Prevalence

Frailty prevalence depends on the population being analyzed and on the frailty measurement tool employed.[5] To date, there is not a frailty measurement tool that is widely accepted in the literature. However, the tool used with the highest frequency is the Fried phenotype model.[37] A recent systematic review, that employed the Fried phenotype model, revealed that frailty prevalence was 9.9% among community-dwelling older adults aged ≥65 years, which increased to 13.6% when psychosocial factors were considered.[9] Furthermore, in the Cardiovascular Health Study which included 5317 community-dwelling men and women ≥65 years of age, 6.9% were frail according to the Fried phenotype model.[28] Frailty prevalence appears to be slightly higher among women, as the Women's Health and Aging Studies reported a frailty prevalence rate of 11.3% among community dwelling women ≥65 years when employing the Fried phenotype model.[59]

2.2 Frailty and CVD

As outlined previously, numerous sub-sections of the adult population appear to have an elevated prevalence of frailty. However, the cohort displaying particularly elevated frailty prevalence rates are those with CVD undergoing cardiac surgery, which have been observed to be as high as 50% pre-operatively.[10] Although the evidence is unclear regarding causality between CVD and frailty, the evidence linking these two concepts among older adults is strong.[60,37]

It has been shown that frailty risk increases with lifestyle cardiovascular risk factors such as smoking,[61] disordered eating habits,[62] and physical inactivity.[63] Furthermore, a link has been identified between individuals with elevated Framingham cardiovascular risk scores and an increased likelihood of becoming frail in the future.[64] The prevalence of frailty within the CVD cohort can range dramatically from 10-60% depending on the frailty definition employed and a magnitude of other factors, such as education level, ethnicity, and age.[38] A systematic review conducted by Afilalo and colleagues[38] explored the link between CVD and frailty. The review involved 9 studies including 54,250 patients in total aged ≥60 years with a 6.2 year mean follow-up. The study concluded that among community dwelling older adults, CVD was associated with an odds ratio (OR) of 2.7 to 4.1 for prevalent frailty and an OR of 1.5 for incident frailty.[38] Prevalence can be defined as the widespread presence of the disease in question at a single point in time while incidence can be defined as the frequency of new cases developed for a given time period.[65] Furthermore, a secondary analysis of the Zutphen Elderly Men's Study found that 62% of men who were frail also had CVD.[66] These findings were supported by the Cardiovascular Health Study which concluded that CVD was linked to a 3-fold increase in frailty prevalence.[67] Although the link between CVD and frailty is strong, it is unclear whether CVD leads to frailty or frailty leads to CVD. However, this relationship may be bidirectional in nature with the diagnosis of one leading to an increased risk of developing the other.[38] It is the coexistence of CVD and frailty, however, that is problematic, due to the association between frailty and negative health outcomes following surgical intervention of CVD.[11]

The impact of frailty on cardiac surgery outcomes

Frailty has numerous negative impacts when it comes to cardiac surgery recovery. According to a recent systematic review by Sepehri and colleagues,[11] frail patients had an increased likelihood of experiencing mortality, morbidity, functional decline and major adverse cardiac and cerebrovascular events following cardiac surgery when compared to their non-frail counterpart. Furthermore, Green and colleagues[68] conducted a prospective cohort study design of 159 older adults (≥60 years of age) deemed high-risk undergoing transcatheter aortic valve replacement (TAVR) surgery. The study, employing the MFC to assess frailty, concluded that frailty was associated with increased 1-year mortality following TAVR. Furthermore, frailty has been linked to a 3- to 8-fold increased risk of delirium following cardiac surgery which appears to follow a gradient, with the most frail (FI score ≥0.3) at increased risk when compared to the less frail (FI score ≥0.25 or ≥0.2).[10]

According to a systematic review and meta-analysis of studies that examined the link between frailty and quality of life (QOL) in community-dwelling older adults, frailty, assessed using the Fried Phenotype model, had an inverse association with QOL as determined via the 36-Item Short Form Survey.[69] In other words, as an individual becomes increasingly frail, their QOL diminishes. This is an important finding because if interventions can be found to prevent the progression of frailty or reduce frailty levels among the CVD cohort, QOL may also be positively impacted.

2.3 Physical Activity

Regular physical activity is shown to prevent a host of diseases and disorders including: osteoporosis, stroke, hypertension, multiple cancers, type 2 diabetes, CVD and premature mortality.[70,71,72] Physical activity can be defined as any bodily movement via skeletal muscle activity that elevates energy expenditure beyond that of resting values which encompass all leisure and non-leisure activities.[73] The Canadian Physical Activity Guidelines (CPAG) have been created as an important initiative to promote and increase the level of physical activity in the Canadian population. The CPAG for adults aged 18-64 recommend accumulating 150 minutes of aerobic activity at a moderate to vigorous intensity in bouts of at least 10 consecutive minutes or more and to incorporate at least two days of muscle and bone strengthening activities per week.[74] These guidelines are the same for individuals ≥65 years of age with the added emphasis on balance activities among those with poor mobility to preserve functioning and reduce the risk of falls.[74] However, physical activity tends to decline with increasing age.[75] Colley and colleagues[76] determined that 17% of Canadians aged 20 to 39 years achieve the current CPAG, while only 13% aged 60 to 79 years achieve this mark.

Benefits of physical activity among those with CVD

Regular physical activity has been shown to have a beneficial impact on both the primary and secondary prevention of numerous chronic diseases, including CVD.[71] Those engaging in regular physical activity also have improved survival rates. A study conducted by Myers and colleagues[77] concluded that there was approximately a 12% improvement in survival for every 1-MET increase in exercise capacity regardless of the presence of CVD. Furthermore, a dose-response relationship between physical activity and physiological benefit has been established such that increased levels of physical activity are associated with increased benefit.[71] Those exercising at higher intensities may also experience increased health benefits when compared to those exercising at lower intensities.[78] Alternatively, a sedentary lifestyle is linked to a whole host of negative health outcomes including: dyslipidemia, hypertension, type II diabetes, increased vascular inflammation, and mortality.[79,36] A sedentary lifestyle leads to a diminished exercise capacity, which is a strong prognostic factor in patients with CVD, as well as a strong predictor of mortality risk among otherwise healthy individuals.[77]

Benefits of physical activity among the frail

In addition to the benefits of physical activity and exercise identified in the previous section, exercise also has the potential to improve frailty status among older adults[17] through improved muscle strength,[80] balance,[81] and gait speed.[80] This literature is supported by Fiatarone and colleagues[82] who identified that frail nursing home patients with a mean age of 87 years can benefit by following a 10-week progressive resistance training program focused on hip and knee extensors. This 10-week program, which featured 3 resistance training sessions of 45 minute duration each week, produced a near 2-fold increase in lean body mass along with increases in strength and walking speed when compared to non-exercising controls.[82] Furthermore, several randomized controlled trials have supported the potential for exercise therapy to positively modify frailty among older adults[83,84,85] even when the intervention is telephone based.[86] A group of experts from major international frailty-related societies took part in a Frailty Consensus Conference (FCC) in Orlando, Florida in 2012.[87] The FCC sought to tackle main issues surrounding the concept of frailty, including potential treatments, and concluded that exercise, protein-calorie supplementation, vitamin D and polypharmacy reduction all showed at least some efficacy in the treatment of frailty. Exercise was deemed to provide the most consistent frailty benefits.[87] Therefore, it seems plausible that exercise therapy programs could alter the prevalence of persistent frailty following cardiac surgery.

2.4 CR Programming and Outcomes

There is substantive evidence to support the contention that CR programs are beneficial in CVD secondary prevention by reducing mortality and hospital readmission rates significantly when compared to those who do not attend.[19,88,89] However, the opportunity to attend a CR program was not always available. Before CR programs were in place, hospitals would keep cardiac patients who suffered an acute coronary event for lengthy durations and restrict patients to 6-8 weeks of bedrest.[90] Medical staff feared that any physical activity during this time period would exacerbate the condition and potentially stimulate a subsequent myocardial infarction (MI). This practice of 6-8 weeks of bed rest only increased patient deconditioning and ultimately had a negative impact on recovery.[91] Worsening the situation, after hospital discharge, patients were often left to exercise on their own without further supports, which often lead to increased levels of physical disability, especially in the older adult population.[91] To address this growing problem, CR programs came about in the 1960s[92,93] and by the 1980s CR became a standardized outpatient therapy focused mainly on exercise in the form of ambulation as a re-adaptation strategy back to normal life.[94] Today, CR programs include a multidisciplinary approach aiming to improve quality of life and exercise tolerance while reducing mortality rates and modifiable risk factors through diet and exercise interventions.[14] These programs remain an important secondary prevention strategy against all cardiovascular related diseases, disorders and procedures including Coronary Artery Disease (CAD), acute MI, coronary revascularization, chronic angina symptoms, heart failure patients, cardiac transplantation, cardiac valve replacement and those with Peripheral Artery Disease (PAD).[91,19] To ensure quality, CR programs are recommended to adhere to 30 secondary prevention quality indicators created by the Canadian Cardiovascular Society (CCS) through implementation of the Canadian Heart Health Strategy developed via a national consensus process (Appendix E).[18]

Among patients attending a CR program, lower hospital re-admission rates, in addition to reduced all-cause mortality, are experienced when compared to standard of care.[88,19] More specifically, CR is linked with a 20-30% reduction in mortality among those with CAD.[95,96] A 10% reduction in cardiovascular mortality can be experienced by CR participants for every 1 mL $O_2 \cdot kg^{-1} \cdot min^{-1}$ increase in peak VO_2.[97] Furthermore, when compared to controls, numerous modifiable risk factors have been shown to be significantly reduced throughout the CR program including total cholesterol (-0.37 mmol/L), triglycerides (-0.23 mmol/L), systolic blood pressure (-3.2 mm Hg) and self-reported smoking.[13] However, the association between pre-operative frailty status and CR completion is largely unknown. Additionally, the link between CR completion and the prevalence of persistent frailty following cardiac surgery is unclear.

Chapter 3: Statement of the Problem and Methods

With an aging population, the prevalence of chronic diseases, such as CVD, is on the rise.[1] Morbidity and mortality from cardiac-related illnesses have decreased over the past 2 decades resulting in routinely operating on older and increasingly frail patients.[98] Therefore, secondary prevention programs such as CR will have to adapt to accommodate this older and increasingly frail cohort. Although the benefits of physical activity, particularly among those with CVD, are well established,[12,13] there is a paucity of literature examining the link between pre-operative frailty and CR completion and non-completion post-operatively. Furthermore, the impact of CR completion or CR swipe count (i.e., CR dose) on frailty status 1-year post-cardiac surgery is unclear.

I have 4 specific objectives for this project: 1) the primary objective of this study is to determine the impact of pre-operative frailty on CR completion rates in the older adult cardiac surgery patient. I hypothesize that pre-operative frailty will negatively impact CR completion rates. Secondary objectives include: 2) to determine if CR completion impacts frailty status from baseline to 1-year post-operatively. I hypothesize that CR completers will improve their frailty status to a greater extent than CR non-completers; 3) to determine if any of the aforementioned domains of frailty within the MFC, SPPB or FFI are modified by CR completion. I hypothesize that the domains of frailty most strongly associated with increased physical activity (i.e., weakness, 5-meter gait speed, and low self-reported physical activity levels) will improve the most with CR completion; and 4) to determine if CR swipe count impacts frailty status among CR attenders. I hypothesize that CR attenders who have a higher swipe count over CR program duration will improve their frailty status to a greater degree when compared to those who have a lower swipe count.

3.1 Ethics and Study Population

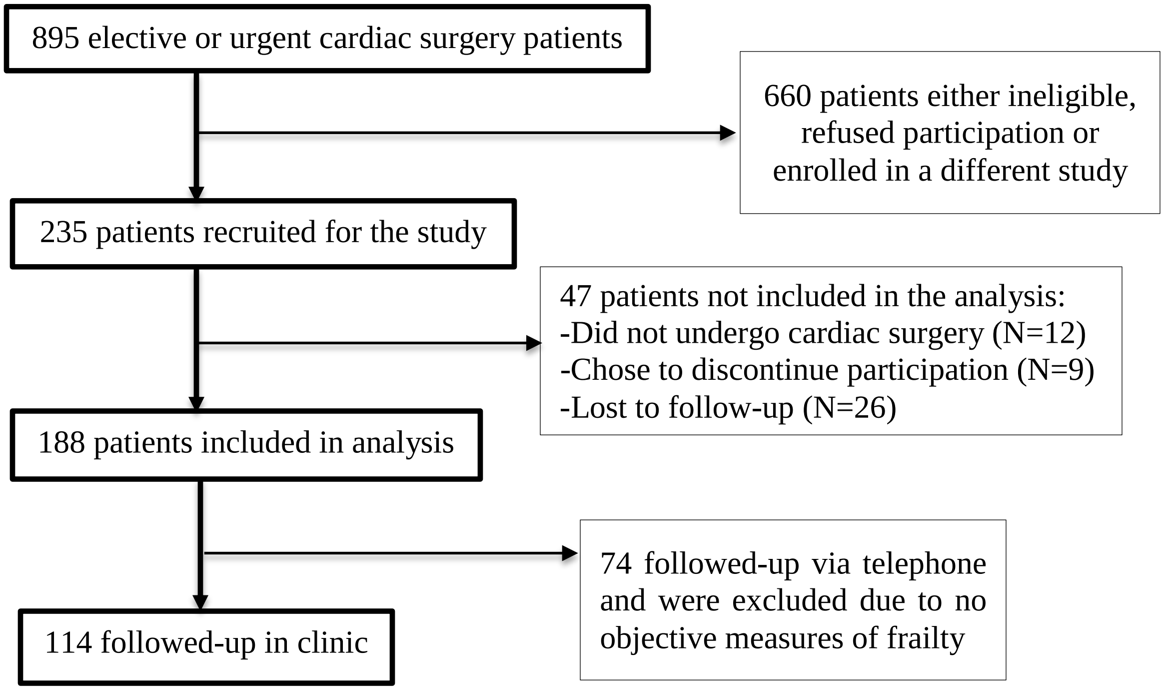
This study is a targeted follow-up analysis, which has ethical approval from both the University of Manitoba Health Research Ethics Board (HREB) and the CR research review committee located at the St. Boniface General Hospital. Ethical approval enabled our research team to extract data from both the Reh-Fit Centre and the Wellness Institute. The data needed for our study included the CR start and end dates, along with pre-CR stress test completion, post-CR stress test completion and the number of CR sessions attended via swipe card access records. Attendance records for CR programming were used to objectively confirm participant CR completion and non-completion data.

Patients were included in this targeted follow-up analysis if they met the following eligibility criteria: 1) ≥18 years of age, 2) undergoing either elective or urgent coronary artery bypass graft (CABG) and/or valve procedures, and 3) admitted to the St. Boniface Hospital Intensive Care Cardiac Surgery unit for post-operative care. Patients were excluded if they had dementia, hearing disabilities, or an inability to understand English.

The primary objective of the original frailty study conducted by Lytwyn and colleagues[99] was to determine if pre-operative frailty measures improved the 1-year functional survival prediction of the EuroSCORE II. Functional survival was defined as being alive at the 1-year post-operative time point in addition to self-reporting quality of life to be >60 on the EuroQol-Visual Analogue Scale (EQ-VAS). It was concluded that adding any of the three frailty measures (MFC, SPPB and CFS), employed in the original frailty study, to the EuroSCORE II, improved its ability to predict poor functional survival. Additionally, it was found that pre-operative frailty was associated with a 2- to 3.5-fold increased risk of poor functional survival at the 1-year post-cardiac surgery time point when compared to their non-frail counterparts.

A total of 235 participants were recruited for the original frailty study between July 2012 and June 2013.[99] Of the initial 235 participants, 188 completed their follow up assessment 1-year post-operatively (114 came into clinic and 74 completed a phone call interview). It is important to note that objective measures of frailty were not collected for the 74 individuals who completed phone call interviews for their 1-year post-operative follow-up assessment. Therefore, those 74 participants were excluded from this analysis. As a result, our data included the 114 participants for whom we have obtained both pre-operative (i.e., baseline) and 1-year post-operative data. In order to objectively capture CR completion status of the 114 individuals who followed-up in clinic 1-year post-operatively, we went back to both the Reh-Fit Centre and Wellness Institute located in Winnipeg, MB to collect CR swipe card access as well as pre- and post-CR stress test completion. The data that we collected included the number of CR classes attended by each individual, via swipe card access, as well as pre- and post-CR stress test completion as a dichotomous yes/no variable. The reason for collecting pre- and post-CR stress test completion data is so that we can objectively determine which individuals met the current quality indicator definition of CR completion as previously identified. See Figure 2 for participant flow through the original study.

Figure 2: Participant flow.



3.2 Frailty Assessment

Frailty status was measured pre-operatively, 3-months post-operatively and 1-year post-operatively in the initial study. However, due to incomplete data and variable CR start times among participants following cardiac surgery, the follow-up assessment completed at the 3-month post-operative time point was eliminated from this study. Therefore, only the baseline and 1-year post-operative time points were analyzed for the purposes of this study. Four definitions of frailty, which contribute to our overall understanding of frailty, have been included in this study. The reasoning for the inclusion of four separate frailty definitions is due to the fact that a widely accepted frailty definition remains controversial. Furthermore, we would like to analyze which frailty definition appears to be most sensitive to change in frailty over time. The four frailty definitions employed in this study include: 1) CFS[40] (Appendix A), 2) MFC[28] (Appendix B), 3) SPPB[47] (Appendix C), and 4) the FFI (Appendix D).

Clinical Frailty Scale. Under the 9-point CFS (Appendix A) definition, patients are deemed "frail" if their given scores, which are based upon a clinical judgement regarding their level of activity, comorbidities, and disabilities, are ≥4.[40]

Modified Fried Criteria. The MFC (Appendix B) employes a frailty cut point of ≥3 out of the following 7 criteria: shrinking (i.e., self-reported weight loss),[28] weakness (i.e., hand grip strength),[28] exhaustion (i.e., the modified 2-item Centre for Epidemiologic Studies Depression Scale),[100] slowness (i.e., 5-meter gait speed),[101] low physical activity (i.e., the Paffenbarger Physical Activity Index),[102] depression (i.e., the 5-item Geriatric Depression Scale)[103,104] and cognitive impairment (i.e., the Montreal Cognitive Assessment).[105]

Short physical performance battery. Under the SPPB (Appendix C) definition, patients are classified as frail if their composite scores are ≤9 after the following 3 functional assessments, each scored from 0-4: a 5-metre gait speed measurement,[101] a side-by-side, semi-tandem, and tandem stand balance tests,[106] and the repeated chair stand test.[106]

Functional Frailty Index. The FFI (Appendix D) has been created by our research group specifically for the context of this study and will also be employed as a definition of frailty. The FFI will place an emphasis on deficits that may potentially be modifiable with exercise to optimize the ability of the tool to capture exercise induced changes in frailty. This FFI includes 25 variables, with each being scored along a continuum of 0 (i.e., no deficit present) to 1 (i.e., full expression of the deficit). The FFI score will be calculated by dividing deficits present by total deficits analyzed with a score of ≥0.25 accepted as a frailty cut-point.[58]

3.3 Statistical Analyses

Statistical analyses were performed using Statistica (version 13). Baseline characteristics between CR completers and non-completers in addition to CR attenders and non-attenders were compared using the Mann-Whitney test for continuous variables and the Chi-Square test for categorical variables. Pre-operative frailty measured as a continuous variable was compared to the dichotomous grouping variable of CR completion or non-completion using the non-parametric Mann Whitney test. Furthermore, Δfrailty defined as the change in frailty score over time (1-year post-operative frailty measure – baseline frailty measure) and the change in each individual frailty domain have been compared to the dichotomous grouping variable of CR completion and non-completion with the non-parametric Mann-Whitney test. To correlate the number of CR swipes with frailty status at baseline and 1-year post-operatively, the Spearman Rank Correlation Coefficient was calculated. A p-value of ≤0.05 was determined to be statistically significant.

Chapter 4: Results

4.1 Baseline Characteristics

Baseline demographics and other relevant personal characteristics, including pre-surgery risk, comorbidities, frailty status and surgical parameters were collected retrospectively for the purposes of this study via the original frailty study database (Table 2 & 3). Basic patient demographics and surgical parameters, including age, sex, BMI, education, smoking status, surgery type and intensive care unit (ICU) length of stay did not differ between CR completers and CR non-completers at baseline. However, CR non-completers were significantly more likely to live alone and have a longer length of hospital stay when compared to CR completers. The pre-surgery risk as assessed by the European System for Cardiac Operative Risk Evaluation II (EuroSCORE II) was not statistically different between CR non-completers and CR completers. Furthermore, the majority of co-morbidities assessed including previous MI, Chronic Heart Failure (CHF), Chronic Renal Failure (CRF) and depression did not differ between groups. However, CR non-completers were significantly more likely to have comorbid diabetes and Chronic Obstructive Pulmonary Disorder (COPD) when compared to CR completers. CR non-completers were also significantly more likely to be frail at baseline when compared to CR completers. This can be observed with all 4 measures of frailty analyzed. Note, the aforementioned baseline differences between CR completers and non-completers were similar when CR attenders and non-attenders were compared (Appendix F). More specifically, CR non-attenders were significantly more likely to have a lower education, live alone and be frail at baseline when compared to CR attenders.

There were also statistically significant baseline differences among the frailty domains of the MFC, SPPB and FFI when CR completers were compared to non-completers (Table 4). The MFC frailty domains of slowness, weakness, weight loss in the past year, depression and cognitive impairment were not statistically different between groups. However, the MFC frailty domains of exhaustion and low physical activity were statistically different among CR completers and non-completers suggesting that CR completers had lower levels of self-reported exhaustion and increased levels of physical activity at baseline when compared to CR non-completers. Furthermore, the SPPB frailty domains of 5-metre gait speed and repeated chair stand were not statistically different between CR completers and non-completers at baseline. However, the SPPB frailty domain of balance was statistically different among CR completers and non-completers suggesting that CR completers had improved balance at baseline when compared to CR non-completers. Lastly, the FFI frailty domains of functional and mood and cognition were not statistically different between CR completers and non-completers at baseline. However, the physical, nutrition and exhaustion and quality of life FFI frailty domains were statistically different among CR completers and non-completers suggesting that CR completers had improved physical parameters, improved self-reported nutrition and exhaustion and improved self-reported quality of life at baseline when compared to CR non-completers.

Table 2: Baseline Characteristics comparing CR Completers to Non-Completers.

	CR Completers (n=48)	CR Non-Completers (n=66)	p-value
Demographics			
Age	70.5 (66-72)	71.5 (66.3-78)	0.08
Sex (Female)	18 (38%)	24 (36%)	0.29
BMI (kg/m^2)	29.0 (25.0-31.6)	28.3 (25.4-32.2)	0.90
Lives Alone	6 (13%)	20 (30%)	*0.02*
Education (College or more)	25 (52%)	23 (35%)	0.07
Smoker (never smoked)	19 (40%)	28 (42%)	0.71
Pre-Surgery Risk			
EuroSCORE II	1.26 (1-2.1)	1.77 (1.2-3.0)	0.07
Comorbidities			
Previous MI	11 (23%)	23 (35%)	0.17
CHF	23 (48%)	33 (50%)	0.70
Diabetes	6 (13%)	23 (35%)	*0.006*
CRF	1 (2%)	3 (5%)	0.48
COPD	2 (4%)	11 (17%)	*0.04*
Depression	5 (10%)	8 (12%)	0.78
Frailty			
CFS	2.5 (2-3)	3 (2-4)	*0.01*
MFC	2 (1-3)	3 (2-4)	*0.0005*
SPPB	10 (9-11)	9 (7.3-10)	*0.007*
FFI	0.09 (0.1-0.2)	0.21 (0.1-0.3)	*<0.0001*

Continuous variables expressed as median (interquartile range) and categorical variables expressed as N (%). The Mann-Whitney test compared continuous variables, Chi-Square Test compared categorical variables. ***BMI***, Body Mass Index; ***EuroSCORE II***, European System for Cardiac Operative Risk Evaluation; ***MI***, Myocardial Infarction; ***CHF***, Chronic Heart Failure; ***CRF***, Chronic Renal Failure; ***COPD***, Chronic Obstructive Pulmonary Disorder; ***CFS***, Clinical Frailty Scale; ***MFC***, Modified Fried Criteria; ***SPPB***, Short Physical Performance Battery; ***FFI***, Functional Frailty Index. A lower score for the CFS, MFC and FFI signifies an individual who is less frail. However, the opposite is true for the SPPB, where a higher score signifies an individual who is less frail.

Table 3: Surgical Parameter Comparison between CR Completers and Non-Completers.

	CR Completers (n=48)	CR Non-Completers (n=66)	p-value
Surgical Characteristics			
Surgery Type			0.19
Isolated CABG	23 (48%)	29 (44%)	
Isolated Valve	11 (23%)	18 (27%)	
CABG + Valve	8 (17%)	17 (26%)	
Other	6 (12%)	2 (3%)	
ICU Length of Stay (days)	1 (1-2.25)	1 (1-3)	0.39
Length of Hospital Stay (days)	6 (5-8.5)	10 (6-14)	*0.002*

Continuous variables expressed as median (interquartile range) and categorical variables expressed as N (%). The Mann-Whitney test compared continuous variables, Chi-Square Test compared categorical variables. ***CABG***, coronary artery bypass graft; ***ICU***, intensive care unit.

Table 4: Baseline Frailty Domains comparing CR Completers to Non-Completers.

	CR Completers (n=48)	CR Non-Completers (n=66)	p-value
MFC			
Slowness (5-metre gait speed; s)	4.6 (3.8-5.6)	5 (4.2-6.3)	0.07
Weakness (grip strength; kg)	36.5 (25.5-41.3)	30 (20-40)	0.10
Weight loss in the past year (kg)	1.3 (0-4.5)	4.5 (2-9.3)	0.11
Exhaustion (CESD)	0 (0-2)	2 (0-3)	*0.01*
Depression (HADS)	2 (1-4)	3 (1-6)	0.05
Cognitive impairment (MOCA)	25 (23-27)	24 (21-27)	0.34
Low physical activity (Paffenbarger; kcal/wk)	437.5 (155-886)	96 (28.8-338.8)	*0.0009*
SPPB			
5-metre gait speed (points)	4 (4-4)	4 (4-4)	0.25
Balance (points)	4 (4-4)	4 (2.3-4)	*0.02*
Repeated chair stand (points)	2 (1-3)	2 (1-3)	0.42
FFI			
Physical	0.2 (0.1-0.3)	0.35 (0.2-0.45)	*<0.0001*
Functional	0 (0-0)	0 (0-0.05)	0.25
Nutrition and exhaustion	0.1 (0-0.2)	0.2 (0.1-0.4)	*<0.0001*
Quality of life	0.2 (0.2-0.3)	0.35 (0.2-0.78)	*0.01*
Mood and cognition	0.33 (0-0.33)	0.33 (0-0.33)	0.31

Continuous variables expressed as median (interquartile range). The Mann-Whitney test compared continuous variables. The FFI domains include the following variables: **Physical**: balance, gait speed, chair stand, timed up-and-go, physical activity; **Functional**: help eating, dressing, cleaning, bathing, toileting, shopping, cooking, driving, medicating, banking; **Nutrition and Exhaustion**: 2-item CESD, past 3 month food decline, weight loss in the past 3 and 12 months; **Quality of life**: rating of own health, falls efficacy scale; **Mood and cognition**: depression, anxiety, MOCA. ***MFC***, Modified Fried Criteria; ***CESD***, Center for Epidemiologic Studies Depression Scale; ***HADS***, Hospital Anxiety and Depression Scale; ***MOCA***, Montreal Cognitive Assessment; ***SPPB***, Short Physical Performance Battery; ***FFI***, Functional Frailty Index.

CR Time Frames and Attendance

The time frame between hospital discharge and the first swipe access recorded in the CR program was a median 51 days (Table 5). The current quality indicator for CR wait time from hospital discharge to CR enrollment is 30 days.[18] Therefore, CR programming in Winnipeg is not meeting the current quality indicator recommended wait time. CR programming participation days, calculated by taking the difference in days between the first recorded CR program swipe card access to the last recorded CR program swipe card access was a median 108 days.

There is no current quality indicator recommending an appropriate attendance rate or dose of CR programming. However, there was a quality indicator regarding CR dose that was one of the last cuts from the final list based on results of the CR quality indicator rating survey.[18] This quality indicator (i.e., CR-33) stated that on-site CR programming should strive for a dose of 1 to 3 visits per week over a period of 3 to 12 months (Appendix E). With a median CR program participation range of 108 days, which is over 3 months, Winnipeg CR programming is meeting this draft quality indicator. Finally, the average number of days elapsed between the last CR swipe card access and the 1-year post-operative frailty assessment was a median 261 days. This is a significant period of time that may serve as a detriment to our findings in this study.

Table 5: Days Elapsed between Hospital Discharge to CR Start, Program Participation and CR End to 1-year Follow-Up Assessment.

	CR Attenders (N=60)
Days elapsed between hospital discharge and first CR swipe	51 (38-66)
Days elapsed participating in the CR program	108 (83-115)
Days elapsed between last CR swipe and 1-year follow-up assessment	261 (226-321)

Continuous variables expressed as median (interquartile range). CR attenders can be defined as all individuals who attended ≥1 CR class.

CR Attendance data was retrospectively collected for the purposes of this study using a patient specific swipe card system located at both the Reh-Fit Centre and Wellness Institute. CR attenders had a median swipe count of 27 throughout the CR program. Furthermore, CR completers and non-completers had median swipe counts of 31.5 and 20 respectively. Overall, 79% of CR attenders went on to complete the CR program (Table 6).

Table 6: Comparing Swipes among CR Completers, Non-Completers and Attenders.

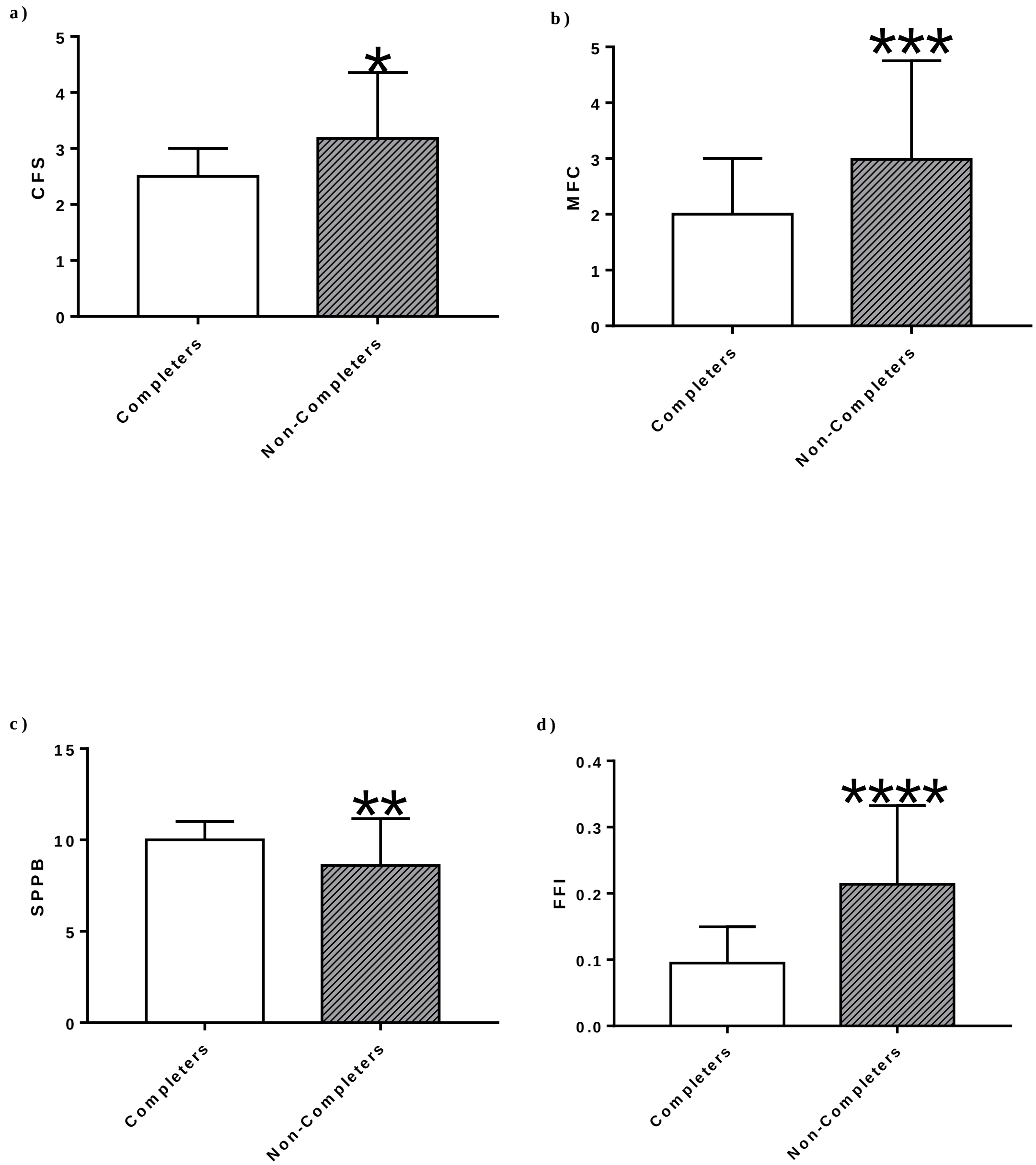
	CR Attenders (N=61)
Number of people who completed CR	48 (79%)
Swipes among CR completers	31.5 (18-41.5)
Number of people who attended but did not complete CR	13 (21%)
Swipes among CR non-completers	20 (9-28)
Swipes among all CR attenders	27 (13-40)

Continuous variables expressed as median (interquartile range). Categorical variables expressed in frequencies (percentage of group). CR completion is defined as those individuals who attended a baseline stress test, attended at least some CR classes throughout the program duration and had a formal re-assessment at program conclusion. CR non-completion is defined as those individuals who did not attend either the baseline stress test, the formal re-assessment at CR program conclusion or attended ≤1 CR class throughout the program duration. A CR attender is defined as all individuals who attended ≥1 CR class.

4.2 Primary Outcome

Non-parametric Mann-Whitney tests identified significant differences in frailty status at baseline between CR completers and CR non-completers (Figure 3). The four measures of frailty analyzed included the CFS, MFC, SPPB and FFI, which yielded p-values of 0.01, 0.0005, 0.007 and <0.0001 respectively. This suggests that pre-operative frailty results in significantly lower rates of CR completion post-operatively.

Figure 3: Pre-Operative Frailty Scores Among CR Completers and Non-Completers. Values are median ± interquartile range. Completers n=48; non-completers n=66. Statistical comparisons were calculated using a non-parametric Mann-Whitney test. *=non-completers different from completers ($p<0.05$), **=non-completers different from completers ($p<0.01$), ***=non-completers different from completers ($p<0.001$), ****=non-completers different from completers ($p<0.0001$). A lower score for the CFS, MFC and FFI signifies an individual who is less frail. However, the opposite is true for the SPPB, where a higher score signifies an individual who is less frail.

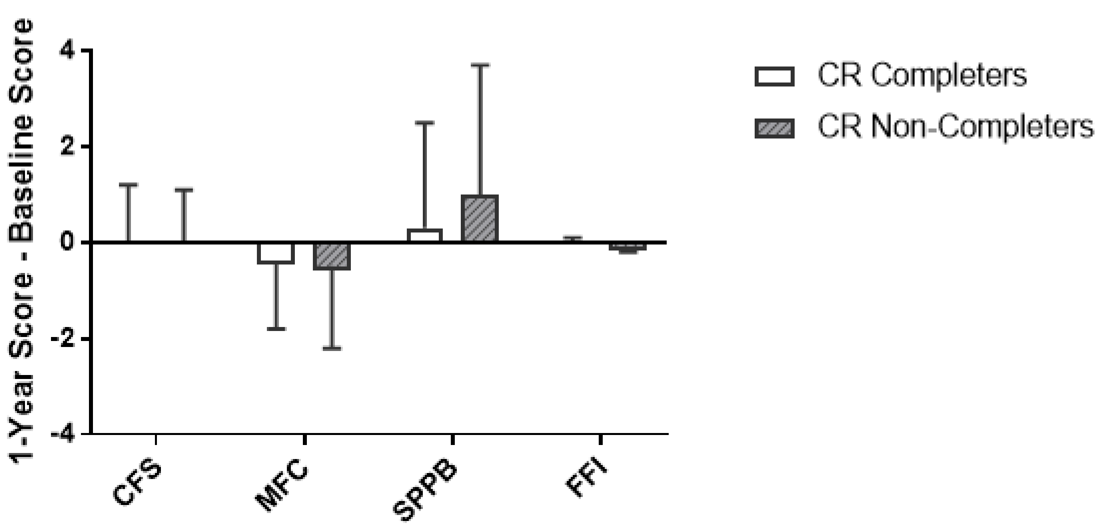


4.3 Secondary Outcomes

Changes in Frailty

This targeted follow-up analysis examined 4 frailty measures, which include the CFS, MFC, SPPB and FFI. As described previously, the FFI was developed for the specific objectives of this research to provide a measure of frailty that may be sensitive to small changes in frailty over time yet still representative of an individual's frailty status. The 4 measures of frailty analyzed (CFS, p=0.90; MFC, p=0.70; SPPB, p=0.06; FFI, p=0.07) did not detect a significantly different Δfrailty among CR completers and non-completers. This suggests that CR completion was unable to significantly modify frailty status when compared to CR non-completers (Figure 4).

Figure 4: ΔFrailty Scores from Baseline to 1-Year Post-Operatively.
Values are mean ± standard deviation. Completers n=48; non-completers n=66. Statistical comparisons were calculated using a non-parametric Mann-Whitney test.



Changes in Frailty Domains

To examine if any specific domains of the MFC, SPPB and FFI improved over time, the Mann-Whitney test was employed to compare the difference in the given variable (1-year – baseline) to the binomial grouping variable of CR completion status (completers or non-completers; Table 7). The difference in change between the MFC frailty domains of slowness, weakness, self-reported weight loss over the past year, exhaustion and depression were not statistically different among CR completers and non-completers. However, 2 frailty domains did reach significance, namely the change in cognitive impairment (i.e., MOCA) and the change in physical activity (i.e., Paffenbarger), which yielded p-values of 0.005 and 0.04 respectively. This finding suggests that CR completers made significant improvements in their cognition and PA change scores (1-year – baseline) when compared to non-completers. In contrast, the difference in change between all 3 of the SPPB frailty domains of 5-metre gait speed, balance score and repeated chair stand were not statistically different among CR completers and non-completers. Moreover, the FFI frailty domains of functional, nutrition and exhaustion, quality of life and mood and cognition were not statistically different among CR completers and non-completers. However, the physical domain of the FFI, which included the following 5 variables: balance score, 5-metre gait speed, chair stand test, timed up-and-go test and level of physical activity, did reach significance ($p=0.009$). This suggests that CR completers made significant improvements in their physical domain change scores when compared to non-completers.

Table 7: Change in Frailty Domains between Baseline and 1-Year Post-Operative.

	CR Completers (n=48)		CR Non-Completers (n=66)		
	Baseline	1-Year	Baseline	1-Year	p-value
MFC					
Slowness (5-metre gait speed; s)	4.6 (3.8 – 5.6)	4.5 (4 – 5.4)	5 (4.2 – 6.3)	5.1 (4.7 – 5.7)	0.46
Weakness (grip strength; kg)	36.5 (25.5 – 41.3)	32 (22.5 – 41)	30 (20 – 40)	27 (18 – 37.5)	0.72
Weight loss in the past year (kg)	1.3 (0 – 4.5)	0 (0 – 0)	4.5 (2 – 9.3)	0 (0 – 0)	0.50
Exhaustion (CESD)	0 (0 – 2)	0 (0 – 1)	2 (0 – 3)	2 (0 – 3)	0.47
Depression (HADS)	2 (1 – 4)	1 (1 – 2)	3 (1 – 6)	3 (1 – 5)	0.32
Cognitive impairment (MOCA)	25 (23 – 27)	25 (22 – 28)	24 (21 – 27)	23 (18.3 – 25.8)	*0.005*
Low physical activity (Paffenbarger; kcal/wk)	437.5 (155 – 886)	1591 (672 – 3150)	96 (28.8 – 338.8)	658 (215.8 – 2105.8)	*0.04*
SPPB					
5-metre gait speed (points)	4 (4-4)	4 (4-4)	4 (4-4)	4 (4-4)	0.69
Balance (points)	4 (4-4)	4 (4-4)	4 (2.3-4)	4 (3-4)	0.06
Repeated chair stand (points)	2 (1-3)	3 (1.8-4)	2 (1-3)	3 (1.3-4)	0.87
FFI					
Physical	0.2 (0.1-0.3)	0.05 (0-0.17)	0.35 (0.2-0.45)	0.1 (0.05-0.31)	*0.009*
Functional	0 (0-0)	0 (0-0)	0 (0-0.05)	0 (0-0)	0.28
Nutrition and exhaustion	0.1 (0-0.2)	0 (0-0.2)	0.2 (0.1-0.4)	0.2 (0.03-0.2)	0.18
Quality of life	0.2 (0.2-0.3)	0.2 (0.1-0.3)	0.35 (0.2-0.78)	0.2 (0.2-0.3)	0.18
Mood and cognition	0.33 (0-0.33)	0.33 (0-0.33)	0.33 (0-0.33)	0.33 (0.33-0.33)	0.62

Continuous variables expressed as median (interquartile range). P-values indicate the difference in change between baseline and 1-year for CR completers and non-completers. The FFI domains include the following variables: **Physical**: balance, gait speed, chair stand, timed up-and-go, physical activity; **Functional**: help eating, dressing, cleaning, bathing, toileting, shopping, cooking, driving, medicating, banking; **Nutrition and Exhaustion**: 2-item CESD, past 3 month food decline, weight loss in the past 3 and 12 months; **Quality of life**: rating of own health, falls efficacy scale; **Mood and cognition**: depression, anxiety, MOCA. ***CESD***, Center for Epidemiologic Studies Depression Scale; ***HADS***, Hospital Anxiety and Depression Scale; ***MOCA***, Montreal Cognitive Assessment.

CR Swipes and Frailty

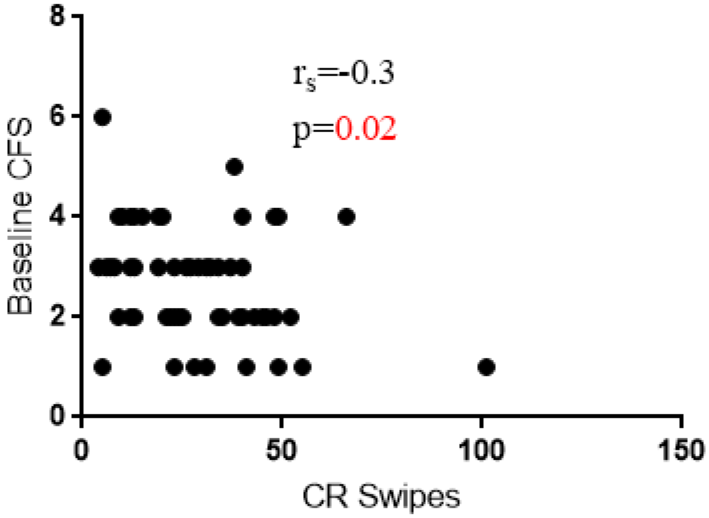
The Spearman Rank Correlation Coefficient was used to examine the relationship between CR swipes and frailty. The literature supports a dose-response effect between CR attendance and enhanced health outcomes, such as mortality, in the long-term.[95,107,108] Although the impact of CR attendance on frailty measures has not been explored, to our knowledge, physical activity interventions have shown some efficacy in frailty modification,[17,80,82] making it plausible that CR programming may also impact an individual's frailty status in the long-term. For the purposes of this study we analyzed the correlation between CR swipes with baseline frailty, CR swipes with 1-year post-operative frailty and CR swipes with Δfrailty (e.g., 1-year – baseline). We defined the Spearman Rank Correlation Coefficient strength based on the following criteria: 0.00 to 0.25 as little to no correlation, 0.25 to 0.50 as a fair correlation, 0.50 to 0.75 as a moderate to good correlation and >0.75 as a good to excellent correlation.[109] Our study found that CR swipes had a fair negative correlation (r_s=-0.29) with baseline frailty as assessed by the CFS, which also reached significance (p=0.02; Table 7). This suggests that those individuals with a lower CFS score (e.g., more robust) were more likely to attend CR programming with a higher frequency post-operatively among CR attenders. This observed relationship adds to our primary objective finding (i.e., pre-operative frailty is significantly linked to CR non-completion), such that those who were less frail pre-operatively not only were significantly more likely to complete CR programming post-operatively but also accumulated more CR swipes throughout program duration. For a better visual representation of the negative correlation between CR swipes and baseline CFS score among CR attenders, refer to Figure 5. Note, all other correlations calculated between CR swipes and frailty measures among CR attenders had correlation strengths denoting little to no correlation with non-significant p-values ($p=<0.05$; Table 7).

Table 7: Correlations between CR Swipes and Frailty Among CR Attenders.

	CFS			MFC			SPPB			FFI		
	Baseline	**1-Year**	**Delta**	**Baseline**	**1-Year**	**Delta**	**Baseline**	**1-Year**	**Delta**	**Baseline**	**1-Year**	**Delta**
r_s	-0.29	-0.24	0.062	-0.15	-0.082	0.072	0.025	0.16	0.15	-0.23	-0.21	0.0049
p-value	*0.02*	0.06	0.64	0.25	0.53	0.58	0.85	0.23	0.26	0.07	0.11	0.97

Spearman correlations are shown. ***CFS***, Clinical Frailty Scale; ***MFC***, Modified Fried Criteria; ***SPPB***, Short Physical Performance Battery; **FFI**, Functional Frailty Index.

Figure 5: Baseline CFS compared to CR Swipes Among CR Attenders.



Chapter 5: Discussion

5.1 Pre-Operative Frailty and CR Completion

Our primary objective was to determine if pre-cardiac surgery frailty status impacts CR completion rates post-operatively. Individuals who are frail pre-operatively, when compared to their more robust, non-frail counterparts, carry a heavy burden of increased post-operative mortality, morbidity, functional decline and major adverse cardiac and cerebrovascular events post-cardiac surgery.[11] Furthermore, this trend appears to follow a gradient with those who are more frail pre-operatively experiencing an increased risk of post-cardiac surgery complications.[10] Mitigating post-surgery complications are CR programs that have been shown to improve lipid profile, hospital readmission and all-cause and cardiac mortality.[13,19,88]

Despite the aforementioned benefits of CR programming, my data indicate that those who are frail pre-operatively are significantly less likely to complete a CR program post-operatively, when compared to their less frail counterpart. A similar finding can be observed between CR attenders and non-attenders, as demonstrated by all 4 measures of frailty analyzed (Appendix F).

Measuring frailty pre-cardiac surgery can help unmask subclinical frailty and gain key insights into projected patient risk of unfavorable outcomes. However, the volume of frailty measurement tools in the literature and the lack of a gold standard measure creates a problem as to which frailty measurement tool strikes the best balance between sensitivity, specificity and feasibility. Given the dynamic and multifactorial nature of frailty, it is intuitive that an appropriate frailty assessment tool should measure multiple frailty components and be rooted in robust evidence.[110] However, the fundamental issue with current measures of multicomponent frailty assessment tools is that they are often cumbersome and time consuming to implement in a clinical setting. This problem has led researchers to strive for a quick and simple measure of frailty that has not only the sensitivity and specificity but also the feasibility to be implemented clinically. The push for ease of clinical implementation led Rockwood and colleagues[40] to develop the CFS which is essentially the "eye ball" test. The patient is simply observed and scored based on appearance. Although this measure of frailty is quick and simple to implement in a clinical setting, it is subjective in nature and has reliability issues with inconsistent scoring between observers making it inappropriate.[111] Furthermore, single component measures of frailty such as grip strength, gait speed and the timed up-and-go test have the feasibility and ease of implementation to peak clinical interest.[112] However, limited specificity remains an issue for these frailty assessment tools, suggesting that they are not optimal for frailty assessment in a clinical setting and may be out-performed by multi-component frailty assessment tools.[112,113,114]

The Fried criteria is a multi-component frailty assessment tool that is employed in the literature with the highest frequency, however, it is the frailty index that appears to more strongly link with mortality.[115] The problem with the frailty index, is that it can get confusing with regards to the optimal amount of variables to include, given the range of non-standardized indices ubiquitous in the literature.[42] When we compare the frailty prevalence rates of Canadians assessed by the Fried criteria and the frailty index, we can observe differing prevalence rates based on age group. Kehler and colleagues[116] have observed 5.38%, 5.65%, 6.93% and 7.77% prevalence rates using the Fried criteria in the

18-34, 35-49, 50-64, and ≥65 age categories respectively. However, the frailty prevalence rates calculated by the frailty index were 1.83%, 4.30%, 11.59%, and 20.15% among the 18-34, 35-49, 50-64, and ≥65 age categories respectively. These data support low agreeance between these two frailty assessment tools and suggest that frailty may present differently among younger adults (i.e., 18-34 years) when compared to older adults (i.e., ≥65 years). This is where care is needed regarding the application of a frailty assessment tool into a clinical setting. Furthermore, we must not lose sight of the population in which the frailty assessment tool was validated.[110] Given that many current frailty assessment tools have been developed through the employment of previously collected longitudinal study data, we must shift our focus to primary research with the sole intent of developing a valid and reliable multi-component tool that can be used in a research and clinical setting.[117,110]

It was also observed that CR non-completers were significantly more likely to have a longer length of hospital stay, to live alone and be more comorbid, at baseline, when compared to CR completers (Table 2 & 3). Given the current strain on the health care system, there has been an increasing pressure to shorten hospital length of stay to free up hospital beds and maximize resources.[118] This strain, coupled with an aging population, is leading to the hospital discharge of patients who are sicker and more dependent on family caregivers than ever before.[119,120,121,122] This increased demand placed on family caregivers places an added emphasis on effective hospital discharge planning. Discharge planning involves the tailored care of patients through education, assessment and discharge plan development which involves the health care team effectively communicating and working with patients and their families.[123,120] The goal of discharge planning is to bridge the gap patients experience between in-hospital care and in-home care, which aims to both reduce hospital length of stay and improve outcomes.[118,120] However, effective discharge becomes more complex among frail older adults who often need more social support post-cardiac surgery.

It is well documented in the literature that frailty leads to increased length of hospital stay among the cardiac surgery cohort.[117,124,125] However, adding to the complexity of hospital discharge is cardiac surgery patients who live alone. Our data identified that the more-frail CR non-completers were significantly more likely to live alone when compared to the less-frail CR completers at baseline. This finding suggests a link between frailty and living alone which is consistent with the literature.[126,127] However, the problem with discharging frail elderly back to their home setting when they live alone is that they are at a high risk of re-hospitalization.[128] In fact, living alone may be the most accurate predictor of 30-day hospital readmission rates, with those living alone experiencing a 3-fold increased risk of readmission following a CABG procedure.[128] Furthermore, Parker and colleagues[129] conducted a systematic review to explore hospital discharge planning among older adults and found that the educational component, when included in discharge planning, can reduce hospital readmission rates. Therefore, individualized patient education may be the key to effective discharge of frail older adults post-cardiac surgery.[130] Going forward, perioperative education regarding the self-management of risk factors in the home setting will be essential among the cardiac surgery cohort, especially for those individuals who are frail and living alone.[131,132]

COPD is a considerable cause of morbidity and mortality which is suspected to increase in prevalence over time on a global scale.[133] COPD is problematic given its link with reduced muscle strength, muscle mass and functional decline.[134,135] In the past, little was known about the link between COPD and frailty. However, a recent population-based cohort study by Lahousse and colleagues[136] established a link between COPD and frailty among older adults. They found that participants with COPD were at a near 2.5-fold increased risk of frailty, which appeared to follow a gradient, with severe COPD participants at a 10-fold increased risk of frailty when compared to controls. Furthermore, COPD and frailty have similar risk factors such as increasing age and smoking.[137] However, when COPD and frailty coexist within an individual, they significantly increase risk of disability and mortality.[138,137] Although, the current literature has mixed results on the outcomes of COPD patients undergoing cardiac surgical procedures,[139,140] it appears that there is not enough robust evidence to suggest that COPD places the cardiac surgery patient at increased risk of short-term mortality or hospital readmission rates when compared to cardiac surgery patients without COPD.[141] However, COPD may place the cardiac surgery patient at an increased risk of long-term mortality.[140]

Diabetes prevalence is increasing exponentially on a global scale.[142,143] Although diabetes is being observed in a younger age demographic than ever before,[144,145] over half of all American cases are among those aged >60 years.[146] Diabetes and CVD are linked, with diabetics over 60 years of age considered to be at high risk of CVD development.[147,148] Furthermore, individuals with the coexistence of diabetes and CVD undergoing cardiac surgery can be at an increased risk of negative post-operative outcomes, particularly among those with poor intraoperative blood glucose control.[149]

As an individual reaches 50 years of age, lean muscle mass tends to decrease at a rate of 1-2% each year.[150,151] However, among those with Diabetes, this rate of decline can be accelerated.[152] In fact, among older adults, diabetes has been linked with lower muscle quality, strength and power which may be the result of increased fat infiltration.[153] This finding helps support the observed linkage between diabetes and frailty,[151] with diabetics incurring a 2-fold increased risk of frailty over 3.5 year follow-up.[154] Furthermore, sarcopenia and obesity can, in fact, co-exist in an individual which leads to increased functional decline when compared to either condition alone.[155] Villareal and colleagues[156] observed that the implementation of a 26-week diet and exercise intervention among obese older adults improved the physical functioning and frailty status of the intervention group when compared to controls. These data help support that active lifestyle promotion can help mitigate functional decline associated with sarcopenia and frailty in which resistance training in conjunction with improved physical activity levels may be optimal.[157]

Since it is those who are frail pre-cardiac surgery who typically experience the worst outcomes post-operatively, it is intuitive that they may also have the most to gain from completing CR programming post-surgically.[10] There is an increasing need to develop strategies to help mitigate the unique barriers that frail older adults experience with CR attendance and completion. Future research should focus on the development of an approach that will help support frail individuals to make the choice to attend and complete CR post-cardiac surgery.

5.2 CR and ΔFrailty

CR Completion and Frailty Status

Our second objective was to determine if CR completion impacts Δfrailty over time from baseline to 1-year post-operatively. Frailty has been repeatedly demonstrated in the literature to be detrimental in cardiac surgery outcomes.[10,11,68,158] In fact, frailty can be associated with a near 5-fold (OR: 4.89 95% CI 1.64-14.60) increased risk of negative health outcomes post-cardiac surgery.[11] Furthermore, traditional cardiac surgery risk evaluation tools (e.g., EuroSCORE II) have improved discrimination and predicted risk when combined with frailty measures for outcomes such as post-operative delirium, major morbidity and mortality.[10,158] Although an individual's perioperative frailty status is important to monitor in order to better assess associated risk of adverse outcomes following surgery, few studies have effectively modified frailty status.[17,87] Moreover, interventions to modify frailty have yet to be optimized.[159,160] Those that have shown improvements in frailty status typically employ physical activity as the main driver.[17,80,82,161] CR programming focuses on physical activity through a multidisciplinary intervention in order to improve outcomes among patients with CVD.[14] However, the efficacy of exercise based CR programming on frailty status modification is unclear despite its importance to the cardiac surgery cohort.

Our data demonstrate that Δfrailty among CR completers and non-completers were not significantly different. This lack of change in frailty status was observed with all 4 measures of frailty analyzed: CFS (p=0.90), MFC (p=0.70), SPPB (p=0.06), FFI (p=0.07). Furthermore, Δfrailty for SPPB and FFI appeared to slightly favor CR non-completers over CR completers. This is plausible given that CR non-completers were shown to be significantly more comorbid and frail at baseline when compared to CR completers; therefore more room for frailty improvements were experienced among the CR non-completers.[162] Even so, Δfrailty were not statistically different among CR completers and non-completers which could suggest: 1) CR programming is ineffective at modifying the frailty status of individuals that persists 1-year post-cardiac surgery; or 2) current tools used to measure frailty are not sensitive enough to assess changes in frailty status over time. Both possibilities will be discussed in the following sections.

Li and colleagues[163] randomized 310 community-dwelling older adults scoring ≥1 on the Fried criteria (i.e., classified as either pre-frail or frail) to either an intervention group (n=152) or a control group (n=158). It was reported that a 6-month multi-factorial care plan which included exercise instruction, nutritional support and physical rehabilitation was ineffective at significantly improving the frailty status of the intervention group when compared to controls. Furthermore, Peterson and colleagues [86] randomized 81 male veterans (mean age 78.4 years) scoring ≥1 on the Fried criteria (i.e., classified as either pre-frail of frail) to either a 6-month telephone counseling intervention (n= 39) or a control group (n=42). It was reported that the intervention group did make some improvements in frailty when compared to the control group. However, these improvements did not reach statistical significance ($p = 0.08$). Collectively, these findings suggest that multi-factorial interventions lasting up to 6 months may not be effective at significantly improving frailty status as measured by the Fried criteria. Furthermore, CR programming may not be sufficient at significantly improving frailty status over this program duration. A systematic review conducted by Theou and colleagues[162] included

47 studies exploring the impact of exercise interventions on frailty management. They reported that physical activity interventions of increasing duration (≥5 months) appeared to improve the management of frailty to a greater extent than shorter interventions. Given that CR programming at both the Reh-Fit Center and Wellness Institute are of 4 months duration, perhaps CR programming is not long enough to produce a detectable change in frailty with current assessment tools.

In our study, an average of 261 days had elapsed between the participants last CR session attended and the 1-year post-operative frailty assessment time point. Although collecting 3 month post-cardiac surgery frailty data was part of the original frailty study protocol, it was not fully completed and did not capture enough data to be included as an additional time point in our targeted follow-up analysis. The majority of literature supports that any increases in physical activity levels experienced by individuals engaging in CR programming are not sustained in the long-term.[164,165,166] Likewise, short-term benefits of post-cardiac surgery diet and exercise interventions surrounding numerous variables including quality of life, physical activity adherence and diet control appear to fade over time.[167] Given that these important variables tend to fade over time, it is plausible that potential frailty benefits experienced by CR completers could have diminished by the 1-year post-operative time point. Had we re-assessed frailty status immediately following CR completion, perhaps a more favorable frailty modification would have been observed like some physical activity interventions have shown.[82,159] However, the long-term impact that CR programming has on frailty status remains unclear and our data add to the literature by identifying that Δfrailty are not statistically different between CR completers and non-completers 1-year post-cardiac surgery.

Current frailty measurement tools may lack the sensitivity required to detect small changes in frailty over time. In a recent study, Cameron and colleagues[84] randomized 216 frail community-dwelling older adults (mean age 83.3 years) to either a 1-year interdisciplinary frailty intervention or to standard care. Frailty, assessed by the Fried criteria was not statistically different between the intervention and control group at baseline or 3-month time points. However, a significant between-group difference was observed at the 1-year time point (p=0.02) in that study. This finding further supports that longer interventions (e.g., 1-year) may have improved impact on frailty status when compared to shorter interventions (e.g., <5 months).[162] Perhaps the intervention at the 3-month time point was not long enough to produce a detectable change in frailty as measured by the Fried criteria. However, this could also suggest that the Fried criteria may not be sufficiently sensitive to smaller changes in frailty accumulated over shorter time periods. Additionally, the SPPB was used by Cameron and colleagues[84] as a measure of mobility which showed no significant change within the intervention group when baseline was compared to 3-month or 1-year follow-up. Although the authors fail to speculate why the SPPB may not have changed, Theou and colleagues[162] report that frail individuals may experience a ceiling effect on some interventional outcome measures such as mobility and balance, which seems to be particularly true among younger frail individuals. This finding supports that the SPPB as a measure of frailty may not be sensitive enough to interventional changes over time. Collectively, this data indicates that both the Fried criteria and the SPPB measures of frailty may lack sensitivity to small changes in frailty over time, specifically with interventions lasting 3 months or less. Although the Fried criteria did detect a significant change at the 1-year time point, it cannot be directly compared to our data due to differing intervention durations. The ambiguity surrounding the clinical definition of frailty adds to the confusion throughout the literature and likely plays a role in the unclear responsiveness of frailty to various interventions.[168] Therefore, there is a need to create a standardized definition of frailty that is widely accepted. Furthermore, there is a need to improve our current understanding of which frailty domains are able to detect change over time and which seem to be change resistant. Once modifiable domains of frailty are better established, current frailty assessment tools can be evaluated regarding their sensitivity to frailty modification.

ΔFrailty Domains

Our third objective was to determine which domains of frailty, if any, within the MFC (i.e., shrinking, weakness, exhaustion, slowness, low physical activity, depression and cognitive impairment), SPPB (i.e., 5-metre gait speed, balance and repeated chair stand) and FFI (i.e., physical, functional, nutrition and exhaustion, quality of life and mood and cognition) are modifiable through CR completion. In our analysis, the MFC domain of low physical activity had a significant change score (e.g., 1-year post-operative – baseline) when CR completers were compared to CR non-completers. Our finding suggests that the change in physical activity significantly improved ($p=0.04$) among CR completers when compared to CR non-completers, which is important because this shows that improved self-reported levels of physical activity are sustainable in our cohort up to an average of 261 days following the last CR session attended. The current physical activity guidelines recommend accumulating 150 minutes of aerobic activity at a moderate to vigorous intensity in bouts of 10 minutes or more and to incorporate at least two days of muscle and bone strengthening activities per week.[74] Furthermore, the American College of Sports Medicine suggest that if older adults with severe chronic disease or comorbidities cannot meet the recommended guidelines of physical activity due to limitation they should strive to be as physically active as their abilities and conditions allow.[169] Since the amount and intensity of physical activity tend to decline with age, physical activity becomes more important among older adults especially those with chronic diseases such as CVD in order to maintain functional status and quality of life.[71,170,171,172] Increasing physical activity levels among cardiac surgery patients is one of the main focuses of CR programming.[173]

There is some literature that reports increases in daily physical activity levels following a CR program,[174] however, the majority of literature support that levels of physical activity upon CR completion mirror that observed at baseline.[165,166] Furthermore, Kehler and colleagues report that objectively measured physical activity peaks 1 month into CR programming which returns to baseline levels (i.e., at first CR intake appointment) at 4, 6 and 12 months post-baseline assessments.[164] This finding suggests that CR programming may not lead to sustainable increases in physical activity.[175] Although our study shows a significant improvement in levels of physical activity when CR completers were compared to CR non-completers, perhaps biasing this finding is an over-estimate of self-reported physical activity. Participants using the International Physical Activity Questionnaire-Short Form to self-report their weekly physical activity levels tend to overestimate by an average of 84% when compared to more objectively assessed physical activity measures (e.g., accelerometers).[176] This problem of physical activity overestimation is not exclusive to any 1 questionnaire as Helmerhorst and colleagues[177] report that few physical activity questionnaires demonstrate acceptable validity and reliability which can be further complicated by cognitive degeneration among the older adult cohort.[178] This finding suggests that all self-report physical activity questionnaires should be used with caution and treated as supplemental to more objective measures of physical activity where possible.[177]

The way that physical activity data is collected appears to matter with those self-administering the physical activity assessment tool reporting a 2-fold increase in physical activity when compared to values obtained through interview-administration.[179] This difference is likely attributable to the misunderstanding of physical activity assessment questions under the self-administered condition, which could have been clarified by an interviewer administering the physical activity assessment tool. Note, the original frailty study obtained self-reported physical activity levels under an interview-administered condition, which may have mitigated some potential bias in physical activity overestimation.

With the MFC of low physical activity improving 1-year post-operatively compared to baseline, it would be intuitive to think that other domains of the MFC that are closely linked with levels of physical activity would also improve. However, the MFC domains of slowness ($p=0.46$), weakness ($p=0.72$), unintentional weight loss ($p=0.50$) and exhaustion ($p=0.47$) did not reach significant change scores when CR completers were compared to non-completers. This finding does not intuitively align but appears to be consistent with the current literature. Cesari and colleagues[85] conducted a 12 month, multicenter randomized controlled trail where 424 sedentary community dwelling older adults (mean age=76.8 years) were randomized to either a physical activity intervention (including aerobic, strength, flexibility and balance training) or a successful aging health education program (control group). The Fried score was used to conduct frailty assessments at baseline, which were then re-assessed at the 6 month and 12 month follow-up time points. It was reported that the Fried frailty domain of low physical activity was the only domain of frailty that showed a significant between-group difference at 6 and 12 month follow-up while the frailty domains of slowness, weakness, unintentional weight loss and exhaustion did not significantly improve when compared to the control group. However, when specifically targeted, physical activity interventions of varying durations have been shown to improve variables such as slowness and weakness among older adults.[80,180] Furthermore, CR programming has shown some efficacy in improving slowness and weakness in the short-term.[181] Therefore, perhaps it is not the absence of change among the Fried score frailty domains but that the cut-points employed as derived from the Cardiovascular Health Study are not appropriate for all individuals throughout the frailty spectrum.[28,35]

The MFC domain of cognitive impairment also had a significant change score (e.g., 1-year post-operative – baseline). Our findings suggest that the change in cognitive impairment, measured by a MOCA score, was significantly different (p=0.005) when CR completers were compared to CR non-completers. It appeared that CR completers showed little to no change when baseline cognition was compared to 1-year post cardiac surgery, while CR non-completers showed some decline. This finding is consistent with the literature which suggests that physical activity has the capacity to improve certain aspects of cognitive function and minimize overall decline.[182,183,184] The impact of physical activity on cognition is important considering that cognitive decline is common among those with CVD.[185] Furthermore, frail older adults have been shown to experience accelerated cognitive decline and to be at a higher risk of experiencing delirium post-cardiac surgery when compared to their non-frail counterparts.[10,186] Showing a lack of cognitive decline over time among CR completers is important because it suggests the slowing of cognitive decline among older adults with CVD.

CR programming is much more than physical activity alone and typically involves a variety of therapies and behavior modification strategies in an attempt to improve CVD risk factors, smoking habits, physical activity status and diet.[89] CR programming has been demonstrated to have a beneficial effect on cognition among older adults with CVD.[187,188] Furthermore, a strong link has been observed between cognition and improved quality of life among the CVD cohort participating in CR.[189] The significant difference in cognition (i.e., measured with a MOCA score) change score observed in our study between CR completers and non-completers may be influenced by the improvements in self-reported physical activity levels as identified previously in addition to CR programming as a whole.

Given the link between cognition and depression,[190] the MFC domain of depression may also have been expected to be different when CR completers were compared to non-completers. However, our findings show that the change score of the MFC frailty domain of depression was not significantly different (p=0.32). This finding is not consistent with the literature, which suggests that CR programming improves depressive symptoms over program duration[191] and appears to be sustained at 1-year follow-up.[192] Although our findings are surprising, cognition and depression may fluctuate independent of each other.[193] This suggests that even though the MFC frailty domain of cognitive impairment may have changed significantly between CR completers and non-completers, it could have done so without a significant change in depression.

Our data showed that none of the 3 SPPB domains of frailty showed significant change scores when CR completers were compared to non-completers. This observation may have been due to a ceiling effect within two of the SPPB frailty domains which were observed in the 5-metre gait speed and balance tests. The ceiling effect created a large group of individuals scoring perfect at both baseline and 1-year post-operative time points, which diminished the ability of the SPPB to detect any potential benefit of CR programming. This may help explain why CR non-completers had a slightly better SPPB change score than CR completers. It may also help explain why the total SPPB change score did not reach significance as observed in objective 2.

Alternatively, our data showed that only 1 of the 5 FFI domains of frailty showed a significant change score when CR completers were compared to non-completers. Namely, the physical domain of frailty significantly improved among CR completers when compared to non-completers. The increased sensitivity to change within the physical domain of frailty is supported in the literature, which suggests that gait velocity and timed-up-and-go test can be sensitive to change over a 2-week multidisciplinary intervention among frail elderly adults.[194] This shows that either the physical domain of frailty was the only FFI domain that is sensitive enough to change over time or that the physical domain was the only modifiable domain. Numerous studies have shown improvements in cognition, mood, anxiety and quality of life among CR participants over program duration.[187,188,195,191]

Based on these data, few of the analyzed domains of frailty showed significant change over time. The MFC domains of cognitive impairment and low physical activity in addition to the FFI physical domain of frailty all had significant change scores, which favored CR completers when compared to non-completers. These data address our second objective and suggest that traditional CR may be ineffective for modifying frailty.

5.3 CR Swipe Card Access

Our fourth objective was to determine if CR swipes, measured by swipe card records, impacts frailty status among CR completers and non-completers. Similar to the relationship between increased physical activity leading to improved benefit, a dose-response relationship also appears to exist between CR sessions attended and enhanced health outcomes.[95,108] It appears that the more CR sessions attended by the participant, the more favorable their outcomes become. Suaya and colleagues[95] found that individuals attending ≥25 CR sessions were almost at a 20% reduced risk of death over a 5 year period when compared to CR users attending ≤24 CR sessions among those hospitalized for coronary conditions or cardiac revascularization procedures. Furthermore, Hammill and colleagues[108] found that attending 24, 12 or 1 CR session(s) had a 14%, 22% and 47% higher risk of death and a 12%, 23% and 31% higher risk of myocardial infarction respectively when compared to those who attended ≥36 CR sessions over a 4-year follow-up period. This literature suggests that increased adherence to CR programming leads to improved benefit, which appears to be sustained in the long-term. Although the efficacy of CR programming on frailty modification has never been studied to our knowledge, it seems plausible given previous literature suggesting at least some impact of physical activity on frailty status.[17,80,82] Therefore, it is intuitive that CR programming may be able to modify frailty status particularly among CR attenders with increased adherence to CR programming. However, our data suggest that CR swipes did not correlate strongly with any of the 4 measures of frailty analyzed. This result appeared to be true for the baseline time point, 1-year post-operative time point and the Δfrailty score. However, the correlation between baseline CFS and CR swipes did reach significance (p=0.02), suggesting that cardiac surgery patients with a favorable baseline CFS score were more likely to demonstrate improved CR program adherence when compared to those who had a less favorable CFS. This observation supports our primary objective finding that it is the healthier less-frail cardiac surgery cohort that is more likely to complete CR programming post-operatively. However, the observed correlation can be classified only as a “fair” correlation and should be interpreted with caution. These data further support our second objective which suggest that CR may be ineffective at modifying frailty status. Moving forward, our results will need to be confirmed and alterations to the current CR program will need to be made in order to better impact frailty status. Additionally, frailty assessment tools reflecting increased sensitivity to change will need to be developed.

Our primary objective was to determine if pre-operative frailty status impacts CR completion rates post-operatively in cardiac surgery patients. Our hypothesis was confirmed that cardiac surgery patients who were frail at baseline were significantly less likely to complete CR programming post-operatively. However, while exploring our data, we also discovered that cardiac surgery patients who were frail at baseline that did attend CR programming post-operatively may also be more likely to not complete CR when compared to their non-frail counterparts (Appendix G). This finding was not one of our original objectives. However, given the link between social support and frailty,[196,197] perhaps the frail older adult needs more support than their non-frail counterparts in order to effectively attend and complete CR programming following cardiac surgery.

5.4 Limitations

It is important to acknowledge that this study is not free from limitation. First, this study is retrospective in nature which limited our ability to choose which variables were collected at the baseline and 1-year post-operative time points. Furthermore, the accuracy of our results are based largely on the databases and data collection abilities of the individuals involved in the original frailty study.

Secondly, this study likely had a sample bias. The sample bias resides in the fact that only people who had both a baseline frailty assessment and an in-clinic 1-year post-operative frailty assessment in the original frailty study were included in this analysis. All individuals who completed a 1-year post-operative telephone call follow-up (n=74) in the original frailty study were excluded from this study because these individuals lacked objective measures of frailty at the 1-year post-cardiac surgery time point. It is intuitive that those individuals who followed-up in clinic at the 1-year post-operative time point were likely a healthier cardiac surgery cohort with increased access to transportation when compared to those who followed-up by telephone or did not follow-up at all. Additionally, 83% of our cohort were elective cardiac surgery patients, with the remaining 17% being either urgent or emergent cardiac procedures. This is important because elective cardiac surgery patients typically experience less detrimental outcomes compared to urgent cardiac procedures.[99] Supporting the thought that our cohort was healthier than a nationally representative sample was the fact that 54% of our sample attended a CR program post-cardiac surgery when the Canadian national average is significantly below this mark at 34%.[173] Furthermore, the 2015/16 Winnipeg Region Annual Report calculated that there were 809 cardiac surgical cases in the Winnipeg region, of which 35% started CR programing.[198] Given that CR completers in our cohort were significantly less likely to live alone, have comorbidities such as Diabetes and be frail, when compared to CR non-completers, perhaps our cohort was more likely to have the social supports and functional ability to confidently attend a CR program when compared to a nationally representative sample. Therefore, the results of this study are limited regarding the generalizability to the entire cardiac surgery population. Furthermore, by assessing the frailty change scores and frailty domain change scores, our study attempted to mitigate any baseline differences among CR completers and non-completers. However, we cannot rule out a potential group effect of bias. Even so, there was a clear distinction that frail patients complete CR at a lower rate than their non-frail counterpart.

Third, there was a considerable period of time that elapsed between the final CR session attended and our 1-year post-operative frailty assessment. On average, this period of time was 261 days long among all CR attenders. This period of time is significant considering that there is some literature supporting that physical activity among other variables may dissipate over time following CR program conclusion.[175,199] Furthermore, self-reported physical activity levels were used in the original frailty study, which may have led to an overestimation of physical activity levels among participants.[176]

Finally, our study did experience instances of missing data which may have created an analytical bias. We tried to mitigate this potential bias where possible by employing intention to treat analysis which allowed us to carry baseline data forward to the 1-year post-cardiac surgery time point which both minimized missing data and made it harder to observe a statistically significant difference.

5.6 Future Research Directions

Our novel data show that non-frail individuals at the pre-cardiac surgery time point are significantly more likely to attend and complete CR programming post-cardiac surgery. In other words, the frailer you are pre-cardiac surgery the less likely you are to both attend and complete CR programming post-operatively. This is an important finding that requires further investigation through larger multisite observational trials to confirm the link between pre-operative frailty and post-operative CR non-attendance and non-completion. Researchers could then focus on learning more about the frail cardiac surgery patient and why they do not attend or complete CR to the same extent as their non-frail counterpart. Perhaps a patient-oriented approach could be implemented that closely follows the health research roadmap developed by the Canadian Institutes of Health Research.[200]

An improved understanding of the unique perspective of older adults surrounding cardiac surgery will need to be advanced with patient-identified priorities at the forefront. This will aid CR programs to better identify which supports are important to mitigate the most common barriers experienced by the frail older adult.[200] Increasing supports may take the form of a more encompassing family intervention where additional aid can be tailored to the unique needs of the frail older adult in an effort to improve CR program attendance and adherence. Increasing CR attendance and adherence among frail older adults will be important going forward given the strong dose-response effect of CR programming on mortality.[19,108] Improved CR adherence may be achieved among frail older adults through innovative strategies using motivational rewards which could also have a positive impact on self-efficacy.[201,202] More specifically, Pack and colleagues[202] report that each $100 spent on rewards result in an additional 6.6 (95% CI 1-14) CR sessions attended throughout program duration.[202] Furthermore, employing the strategy of motivational rewards in an effort to increase adherence to healthy behavior change are considered to be acceptable when administered correctly.[203] Perhaps CR programming could approach organizations such as the Heart and Stroke Foundation, given their interest in improving cardiovascular health, so they could potentially provide compensation that CR programming could use to purchase rewards for CR participation. This would create a CR reward system that could be feasible and sustainable. Additionally, an intervention to more vigorously recruit frail cardiac surgery patients post-operatively could also be developed. This recruitment strategy will need to consider the physical and cognitive limitations in addition to the increased barriers experienced by the frail older adult.[159] Once an improved recruitment strategy has been developed and deemed feasible, it could then be implemented and tested through rigorous multi-site randomized controlled trials which would help increase the generalizability of findings.

Our data also show that CR is ineffective at modifying frailty status 1-year post-operatively. Innovative strategies to maximize the impact of CR programming on frailty status need to be implemented in order to further improve quality of life and functional status following cardiac surgery. Lengthening the duration of CR programming (e.g., ≥5 months) may also be a strategy to improve the impact of CR programming on frailty modification. A longer CR program would better align with the current literature which suggests that longer interventions may demonstrate improved effectiveness surrounding frailty modification.[84,162] However, the frail older adult may require increased support to effectively attend and adhere to CR programming post-operatively when compared to their less-frail counterpart. Additionally, there needs to be more research surrounding the potential for frailty modification during the pre-operative waiting period among the elective cardiac surgery cohort.[204] The implementation of a pre-cardiac surgery intervention could be crucial in better surgery preparation, reduced hospital length of stay and frailty reduction that could result in more favorable post-operative outcomes.[204,205,206,207]

Perhaps frailty did not significantly change in our data when the 1-year post-operative time point was compared to baseline because current frailty assessment tools lack sensitivity to change in frailty over time. Future research should focus on the development of a frailty measurement tool that is more sensitive to small changes in frailty accumulated over a 3-12 month intervention period. Given that exercise capacity has a strong link with mortality[208,209,210] and has been shown to be responsive to interventions such as CR,[211,212] perhaps exercise capacity could be further explored for its efficacy as part of a multi-component frailty assessment tool. This could be done by creating a frailty measurement tool that includes only those frailty domains shown to be more sensitive to change over time with the implementation of a diet and exercise focused intervention. In terms of my data, these frailty domains would include the MFC domains of low physical activity levels and cognitive impairment in addition to the FFI physical domain of frailty. Likewise, domains of frailty that appear to be resistant to change may be excluded.

5.7 Conclusions

This study demonstrated that elective cardiac surgery patients who were frail pre-operatively were significantly less likely to complete CR post-operatively compared to their more robust counterpart. This primary finding supports our hypothesis that pre-operative frailty negatively impacts CR completion rates. However, our study did not find that CR completion was associated with a significant frailty modification. This second finding did not support our hypothesis which stated that CR completers would improve their frailty status to a greater extent than CR non-completers. Even so, the MFC frailty domains of cognitive impairment and low physical activity in addition to the FFI physical domain of frailty were significantly improved among CR completers when compared to CR non-completers. This third objective finding was in partial support of our hypothesis that domains of frailty most strongly associated with increased physical activity would improve the most with CR completion. Finally, this study demonstrated that swipes recorded over CR program duration did not appear to correlate with improved frailty status. This fourth objective finding did not support our hypothesis that CR attenders who had a higher swipe count would improve their frailty status to a greater degree when compared to those who had a lower swipe count. In summary, the novel data presented in this thesis suggests that pre-operative frailty negatively impacts post-operative rates of CR completion and that CR completion appears to be unable to significantly modify frailty status at the 1-year post-operative time point. Further study is needed to confirm our findings and to develop an approach that will empower frail individuals to make the choice to attend and complete CR. Moreover, interventional researchers need to develop an efficacious intervention with the capacity to modify frailty in the pre or post-operative period. Finally, our component analysis of frailty assessment tools indicates that there is an urgent need to reconsider how existing frailty tools assess changes in frailty over time. In fact, frailty measurement tools with improved sensitivity to intervention need to be developed.

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Appendix

Appendix A- Clinical Frailty Scale (CFS)

Patients scoring ≥4 on the following scale were deemed frail.

Clinical Frailty Scale*

1 **Very Fit –** People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 **Well –** People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.

3 **Managing Well –** People whose **medical problems are well controlled,** but are **not regularly active** beyond routine walking.

4 **Vulnerable –** While **not dependent** on others for daily help, often **symptoms limit activities.** A common complaint is being "slowed up", and/or being tired during the day.

5 **Mildly Frail –** These people often have **more evident slowing,** and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 **Moderately Frail –** People need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 **Severely Frail – Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 **Very Severely Frail –** Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9. **Terminally Ill** - Approaching the end of life. This category applies to people with **a life expectancy <6 months**, who are **not otherwise evidently frail.**

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

* 1. Canadian Study on Health & Aging, Revised 2008.
2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.

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Appendix B- Modified Fried Criteria (MFC)

Patients meeting the criteria for ≥3 of the following 7 criteria were deemed frail.

1) Slowness – After two trials of a 5 m walk, average time>6 s

2) Weakness – After three grip strength measurements with each hand, maximum value 30 kg if male or 20 kg if female

3) Weight loss – Self-reported weight loss >4.5 kg (10 lbs) or >5% body weight in past 12 months

4) Exhaustion – Two-item Center for Epidemiologic Studies Depression (CES-D) scale 1 out of 2

5) Depression – Five-item Geriatric Depression Scale (5-GDS) 2 out of 5

6) Low physical activity – Paffenbarger Physical Activity Index <383 kcal per week if male or <270 kcal per week if female

7) Cognitive impairment – Montreal Cognitive Assessment (MoCA) score <26 out of 30

Appendix C-Short Physical Performance Battery (SPPB)

Patients scoring ≤9 on the following test are deemed frail.

1) *5 metre gait speed measurement*

-After 2 trials, average time	≤6.5 s: 4 points
	6.6-8.3 s: 3 points
	8.4-11.6 s: 2 points
	≥11.7 s: 1 point
	Unable: 0 points

2) *Balance tests*

-side-by-side stand time	≥10 s: 1 point
	<10 s: 0 points
-Semi-tandem stand	≥10 s: 1 point

	<10 s: 0 points
-Tandem stand	≥10 s: 2 points
	3-9.99 s: 1 point
	<3 s: 0 points

3) *Repeated chair stand test*

-Time to stand up from chair 5 times	≤11.19 s: 4 points
	11.20-13.69 s: 3 points
	13.70-16.69 s: 2 points
	16.70-59.99 s: 1 point
	≥60 s or unable: 0 points

Appendix D-Functional Frailty Index (FFI)

	Domain	Tool Used to Measure	Variable	Cut-Off Point	References/Justification
1	Physical	Short Physical Performance Battery (SPPB)	Balance (Side-by-side, semi-tandem, tandem)	Unable to complete=1 Side-by-Side = 0.67 Semi-Tandem = 0.33 Tandem = 0	Guralnik et al. (1994) Participants unable to hold side by side stance for 10 seconds (HR: 3.54 95% CI 3.04 – 4.13) and those unable to hold semi-tandem stance for 10 seconds (HR: 1.78 95% CI 1.51-2.09) more likely to die compared to those able to complete the tandem balance task.
2	Physical	SPPB	Chair Stand	Unable = 1 ≥16.7 seconds = 0.75 13.7 – 16.6 seconds = 0.5 11.2 – 13.6 seconds = 0.25 ≤11.1seconds = 0	Cut-offs as defined by Guralnik et al. (1994) Cooper et al. (2010) Compared to participants in the highest quartile, those in the lowest quartile (HR: 1.96 95% CI 1.56-2.46), second quartile (HR: 1.40 95% CI 1.18-1.66) and third quartile (HR: 1.24 95% CI 1.08-1.42) at a higher risk of mortality.
3	Physical	Fried Criteria	5-metre Gait Speed	Males Height > 173 cm: GS ≤ 6.56 s = 1,	Cut-offs as defined by Fried et al. (2001)

				GS > 6.56 s = 0 Height ≤ 173 cm: GS ≤ 7.66 s = 1, GS > 7.66 s = 0 Females Height > 159 cm: GS ≤ 6.56 s = 1, GS > 6.56 s = 0 Height ≤ 159 cm: GS ≤ 7.66 s = 1, GS > 7.66 s = 0	Studenski et al. (2011) Gait speed associated with survival (HR per 0.1 m/sec: 0.88 95% CI 0.87-0.90).
4	Physical	Timed Up-and-Go	Mobility	Freely mobile ≤10 s = 0 Mostly independent 11-20 s = 0.25 Variable mobility 21-29 s = 0.75 Impaired mobility ≥30 s = 1	Mathias et al. (1986) Podsiadlo & Richardson (1991)
5	Physical	Paffenbarger Physical Activity Questionnaire	Self-Report Physical Activity	Males < 383 kcal/week = 1 ≥ 383 kcal/week = 0 Females < 270 kcal/week = 1 ≥ 270 kcal/week = 0	As recommended by Afilalo et al. (2014), questionnaires providing measures of activity in kcal/week recommended in frailty assessment using these cut-offs. Ainsworth et al. (1993) confirmed validity of the Paffenbarger Physical Activity Questionnaire in community-dwelling adults.
6	Functional	OARS Functional Assessment Questionnaire	Help Eating	Dependent = 1, Assisted = 0.5, Independent = 0	Searle et al. (2008)
7	Functional	OARS Functional	Help Dressing	Dependent = 1, Assisted = 0.5,	Searle et al. (2008)

		Assessment Questionnaire		Independent = 0	
8	Functional	OARS Functional Assessment Questionnaire	Help Cleaning	Dependent = 1, Assisted = 0.5, Independent = 0	Searle et al. (2008)
9	Functional	OARS Functional Assessment Questionnaire	Help Bathing	Dependent = 1, Assisted = 0.5, Independent = 0	Searle et al. (2008)
10	Functional	OARS Functional Assessment Questionnaire	Help Toileting	Dependent = 1, Assisted = 0.5, Independent = 0	Searle et al. (2008)
11	Functional	OARS Functional Assessment Questionnaire	Help Shopping	Dependent = 1, Assisted = 0.5, Independent = 0	Searle et al. (2008)
12	Functional	OARS Functional Assessment Questionnaire	Help Cooking	Dependent = 1, Assisted = 0.5, Independent = 0	Searle et al. (2008)
13	Functional	OARS Functional Assessment Questionnaire	Help Driving	Dependent = 1, Assisted = 0.5, Independent = 0	Searle et al. (2008)
14	Functional	OARS Functional Assessment Questionnaire	Help Taking Medication	Dependent = 1, Assisted = 0.5, Independent = 0	Searle et al. (2008)

15	Functional	OARS Functional Assessment Questionnaire	Help Banking	Dependent = 1, Assisted = 0.5, Independent = 0	Searle et al. (2008)
16	Exhaustion	Center for Epidemiologic Studies Depression Scale	Feel everything is an effort	Most of the time = 1, Some of the time = 0.5, Rarely = 0	Searle et al. (2008)
17	Exhaustion	Center for Epidemiologic Studies Depression Scale	Have trouble getting going	Most of the time = 1, Some of the time = 0.5, Rarely = 0	Searle et al. (2008)
18	Nutrition	Self-Report	Unintentional Weight Loss in Past 3 months	Yes = 1, No = 0	Jung et al. (2014)
19	Nutrition	Self-Report	Unintentional Weight Loss more than 10 lbs in the past year	Yes = 1, No = 0	Searle et al. (2008)
20	Nutrition	Self-Report	Decline in food intake in past 3 months	Severe decrease = 1, Moderate decrease = 0.5, None = 0	Jung et al. (2014)
21	Quality of life	Self-report	Rating of own health	Very poor = 1 Poor = 0.8 Average = 0.6 Good = 0.4 Very good = 0.2	Searle et al. (2008) -Intuitively coded

22	Depression	Hospital Anxiety and Depression Score (HADS) -Just using depression score	HADS	Depression 11-21 = 1 8-10 = 0.5 0-7 = 0	Bjelland et al. (2002)
23	Anxiety	Hospital Anxiety and Depression Score (HADS) -Just using anxiety score	HADS	Anxiety 11-21 = 1 8-10 = 0.5 0-7 = 0	Bjelland et al. (2002)
24	Cognition	Montreal Cognitive Assessment (MoCA)	Montreal Cognitive Assessment	≥ 26 = 1 ≤ 25 = 0	Nasreddine et al. (2006) As per MoCA scoring protocol, a cut-off score of 26 has a sensitivity of 90% and a specificity of 87% in identifying mild cognitive impairment. This is a clinical state that often progresses to dementia.
25	Falling	Falls Efficacy Scale (FES)	Falling concern	≥19 = 1 <19 = 0	Tinetti et al. (1990)

Appendix E - Quality Indicators (QI)

Legend:

*=Top 5 QI's

**=QIs removed from the final list of indicators based on results of the CR QI rating survey.

Referral, access and wait times

Indicator Number	**Type**	**Recommended**	**Components (QI's)**	**Definition**
CR-1 *	Process	85% referral	In-patients referred to a CR program.	Percentage of eligible in-patients referred to a CR program.
CR-2a	Process	30 days after hospital discharge	CR wait time from hospital discharge.	Percentage of eligible in-patients who were referred to CR and who enroll in CR within 30 days after hospital discharge.
CR-2b *	Process	All patients referred to CR should undergo entry assessment in a timely fashion so their CR program can be initiated.	CR wait time from referral to enrollment.	Number of days between receipt of referral at the CR program to patient enrollment for eligible patients.
CR-3	Process	All eligible CR in-patients should enroll in a CR program following hospital discharge.	CR enrollment.	Percentage of CR-eligible patients enrolled in a program post hospital discharge.

Secondary Prevention, assessment, risk stratification and control

CR-4	Process	All patients entering CR programs must have a medical assessment and undergo determination of their cardiometabolic fitness prior to the initiation of therapy	Risk assessment for adverse cardiovascular events.	Percentage of CR patients who received a comprehensive assessment of the risk for adverse cardiovascular events.
CR-7	Outcome	AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients with Coronary and other Atherosclerotic Vascular Disease: 2011 Update: • Aspirin 75–162 mg daily is recommended in all patients with coronary artery disease unless contraindicated.	Secondary prevention medications: Acetylsalicylic acid (ASA).	Percentage of patients who were taking ASA at time of CR program discharge.
CR-8	Outcome	CCS 2011 Antiplatelet Guidelines.	Secondary prevention medications: Antiplatelet agents other than ASA	Percentage of patients on antiplatelet agents other than ASA (i.e. Clopidogrel, Prasugrel, Ticagrelor) at time of CR program discharge.
CR-9	Outcome	All patients with clinically-significant coronary artery disease or heart failure who have an indication for betablockade, without clear contraindications or a history of beta-blocker intolerance,	Secondary prevention medications: Beta blockers.	Percentage of patients on a Betablocker at CR discharge.

		should be considered for chronic beta-blocker therapy		
CR-10	Outcome	In addition to therapeutic lifestyle changes, statin therapy should be prescribed in the absence of contraindications or documented adverse effects	Secondary prevention medications: Statins.	Percentage of CR patients on statins at program discharge.
CR-11 **	Outcome		Secondary prevention medications: Other hypolipidemic drugs **	Percentage of patients on other hypolipedemic drugs at discharge.
CR-12	Outcome	• ACE inhibitors a. ACE inhibitors should be started and continued indefinitely in all patients with left ventricular ejection fraction ≤40% and in those with hypertension, diabetes, or chronic kidney disease, unless contraindicated. (Class I; Level of Evidence: A) b. It is reasonable to use ACE inhibitors in all other patients.126 (Class IIa; Level of Evidence: B) • ARBs a. The use of ARBs is recommended in patients who have heart failure or who have had a myocardial infarction with left ventricular ejection fraction ≤40% and who are ACE-inhibitor	Secondary prevention medications: Angiotensinconverting enzyme (ACE) / Angiotensin Receptor Blockers (ARB)	Percentage of patients at CR discharge on ACE/ARBs.

		intolerant. (Class I; Level of Evidence: A) b. It is reasonable to use ARBs in other patients who are ACE-inhibitor intolerant. (Class IIa; Level of Evidence: B)		
CR-13	Process	Canadian Hypertension Education Program Recommendations 2012 a. Health care professionals who have been specifically trained to measure BP accurately should assess BP in all adult patients' at all appropriate visits to determine cardiovascular risk and monitor antihypertensive treatment (Grade D). b. Use of standardized measurement techniques is recommended when assessing BP (Grade D). AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients with Coronary and other Atherosclerotic Vascular Disease: 2011 Update a. All patients should be counseled regarding the need for lifestyle modification to achieve blood pressure control: weight control; increased physical activity; alcohol moderation; sodium reduction; and emphasis on increased consumption	Assessment of blood pressure control.	Percentage of patients in CR program who received individualized assessment of blood pressure (BP) control.

		of fresh fruits, vegetables, and low-fat dairy products. (Class I; Level of Evidence: B) b. Patients with blood pressure ≥140/90 mm Hg should be treated, as tolerated, with blood pressure medication, treating initially with beta-blockers and/or ACE inhibitors, with addition of other drugs as needed to achieve goal blood pressure. (Class I; Level of Evidence: A) **Programs should aim to achieve blood pressure control in at least 90% of patients (benchmark).**		
CR-14	Process	CCS Dyslipidemia Guidelines 2012 • All patients with evidence of atherosclerosis should undergo lipid profile screening. Targets as defined by current Canadian secondary prevention guidelines (Treatment target is for LDL-C <2.0 mmol/L or >50% reduction).	Assessment of lipid control	Percentage of patients in CR who received individualized assessment of lipid control.
CR-15	Process	AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients with Coronary and other Atherosclerotic Vascular Disease: 2011 Update -If waist circumference (measured horizontally at the iliac crest) is <35	Assessment of adiposity.	Percentage of patients in CR program who received individualized assessment of adiposity

		inches in women and <40 inches in men, therapeutic lifestyle interventions should be intensified and focused on weight management. (class I; Level of Evidence: B) -The initial goal of weight loss therapy should be to reduce body weight by approximately 5% to 10% from baseline. With success, further weight loss can be attempted if indicated. (class I; Level of Evidence: C)		
CR-16	Process	AACVPR Statement: "Recommendations for Managing Patients with Diabetes Mellitus in Cardiopulmonary Rehabilitation" 2012 • A key recommendation for patients with diabetes mellitus is optimal blood glucose control. An important role of the CR team is to assess risk factors for recurrent coronary events and guide patients in risk modification.	Individual assessment of blood glucose control (HbA1C).	Percentage of patients in CR who received individualized assessment of blood glucose control.

Behavioral change, program adherence, psychosocial, education and return to work

CR-5 *	Process	• Includes an informational component which: 1. Discusses specific health goals; 2. Is personalized; 3. Explains the risks of not changing, the benefits of changing, 4. Often emphasizes proximal risks and benefits over distal ones; 5. Seeks to heighten self-efficacy concerning possible effective self-regulation of specific behaviours; and, 6. May seek to elicit positive emotions, to increase optimism • Is led by professional staff, and not by lay persons. • Can be delivered as stand-alone sessions (which is preferred) or incorporated into other activities. • Education can be delivered in individual or group settings.	Patient self-management education.	Percentage of patients in the CR program who received individual or group patient self-management
CR-6 **	Process		Assessment of adherence to secondary prevention medications. **	Percentage of CR patients for whom adherence to cardiovascular secondary prevention medications was assessed.
CR-17 *	Outcome	Assessment of exercise capacity should be made at program entry and exit in order to evaluate change	Increase in exercise capacity.	Percentage of CR patients who achieved a half metabolic equivalent (MET) increase in

		in exercise capacity. -Should achieve at least a 0.5 MET increase over program duration		their exercise capacity form pre- to post-program
CR-18	Outcome	Canadian Association of Cardiac Rehabilitation guidelines, 3rd Edition • Adherence and persistence with prescribed exercise, health behaviour interventions and pharmacological therapies (i.e., improvements in cardiometabolic fitness) is associated with significantly improved outcomes. - All patients in CR should be encouraged to attend all sessions during CR, as the number of CR sessions attended correlates with improved prognosis	Adherence to CR program.	Percentage of prescribed CR exercise sessions completed by patient.
CR-19 **	Process		Assessment of physical activity. **	Percentage of CR patients who received individualized assessment of physical activity.
CR-20	Outcome	AHA/ACCF Secondary Prevention and Risk Reduction Therapy for Patients with Coronary and other Atherosclerotic Vascular Disease: 2011 Update • For all patients, the clinician should encourage 30 to 60 minutes of moderate-intensity aerobic activity, such as brisk walking, at	Meeting physical activity guideline target.	Percentage of CR patients meeting the target amount of 150 minutes of physical activity per week at program completion.

		least 5 days and preferably 7 days per week, supplemented by an increase in daily lifestyle activities (e.g., walking breaks at work, gardening, household work) to improve cardiorespiratory fitness (Class I, Level of evidence B) - Achieving 150 minutes per week of moderate to vigorous-intensity aerobic physical activity is associated with lower long-term mortality and morbidity.		
CR-22	Process	All patients entering a CR program should be screened for depression using a reliable, valid and change-sensitive psychometric instrument or enquiry, to permit timely clinical management of depression	Assessment of depression.	Percentage of CR patients with assessment for depression or depressive symptoms
CR-23	Outcome	All CR patients who screen positively for depression at any point in CR should be referred to an appropriately qualified health professional for assessment or treatment.	Referral of patients screening positive for possible depression.	Percentage of CR patients with suspected clinical depression who were referred for mental health management
CR-24 **	Process		Assessment of quality of life. **	Percentage of CR patients who received a quality of life assessment.
CR-25 **	Process		Assessment of return to work. **	Percentage of CR patients with an assessment of medical fitness to return to usual workplace during or following CR

CR-26	Process	"It is the view of CCS that all patients should have their smoking status systematically identified and documented and be offered specific assistance initiating a cessation attempt."	Smoking cessation support.	Percentage of CR patients who are current or recent smokers and who were referred for smoking cessation.
CR-27	Outcome	European Guidelines on Cardiovascular Disease Prevention in Clinical Practice (v2012) • All smoking is a strong and independent risk factor for CVD and has to be avoided.	Smoking cessation.	Percentage of CR patients who were current or recent smokers at enrollment in the program who were not smoking at program completion.
CR-28 **	Process		Assessment of anxiety. **	Percentage of patients who received an assessment for anxiety or anxiety symptoms.
CR-29 **	Outcome		Referral of patients screening positive for possible anxiety. **	Percentage of CR patients with suspected clinical anxiety who were referred for mental health treatment
CR-30	Process	Stress or psychosocial management is defined as a core component in both the AACVPR guidelines (Circulation. 2000; 102: 1069-1073) and is a recommended element of the CACR guidelines	Stress management	Percentage of CR patients who were referred to a stress management intervention.
CR-37	Outcome	CACR guidelines, 3rd Edition • Adherence and persistence with prescribed exercise, health behaviour interventions and pharmacological therapies (i.e.,	CR program completion.	Percentage of patients enrolled in CR who completed the program.

		improvements in cardiometabolic fitness) is associated with significantly improved outcomes		

CR Program model and structure

CR-31	Structure	The physician Medical Director is ultimately responsible for the medical well-being of the patients within the CR Program and provides oversight of safety, efficacy and connection with the referring medical community	Medical director supervision.	Percentage of CR programs that have a physician medical director providing program oversight.
CR-32 *	Structure	• All CR programs require a process in place that addresses site-specific facility equipment in conjunction with safety requirements and considerations • All CR programs require policies and procedures for the management of medical emergency situations.	Emergency response strategy.	The percentage of CR programs with a documented emergency response strategy and appropriately qualified staff.
CR-33 **	Structure		CR dose. **	CR program design for the core onsite supervised CR program includes 1 to 3 visits per week over a period of 3 to 12 months

Discharge Transition, Linkage and Communication

CR-21	Outcome	-CACR Guidelines, 3rd Edition • Programs should incorporate designated components of the trans-behavioural framework designed to train CR participants in self-management skills. -EACPR Position Paper, 2010 "Secondary Prevention through CR: Physical Activity Counselling and Exercise Training" • Educate on the need for lifelong continuation of physical conditioning and the risk of relapses.	Promotion of post-CR physical activity.	Percentage of CR patients who were provided an intervention to promote long-term physical activity post-CR.
CR-34	Outcome	• On programme completion there should be a formal assessment. This should be communicated by discharge letter to the referrer and the patient as well as those directly involved in the continuation of healthcare provision. • There should be communication and collaboration between primary and secondary care services to achieve the long-term management plan.	Communication with the primary health care practitioner (PHCP).	Percentage of CR patients with a documented communication between the CR program and PHCP.
CR-35	Process	• On program completion there	Recommended	Percentage of CR discharge

		should be a formal assessment of lifestyle risk factors (physical activity, diet and smoking as relevant), psychosocial health status, medical risk factors (blood pressure, lipids and glucose) and use of cardioprotective therapies together with long-term management goals. This should be communicated by discharge letter to the referrer and the patient as well as those directly involved in the continuation of healthcare provision.	elements in discharge summary.	summaries that include the recommended elements.
CR-36	Outcome	• On programme completion there should be a formal assessment of lifestyle risk factors (physical activity, diet and smoking as relevant), psychosocial health status, medical risk factors (blood pressure, lipids and glucose) and use of cardioprotective therapies together with long-term management goals. This should be communicated by discharge letter to the referrer and the patient.	Summative communication with patient.	Percentage of patients with a documented summative communication from the CR program

Appendix F

Table 8: Baseline Characteristics comparing CR Attenders to Non-Attenders.

	CR Attenders (n=61)	CR Non-Attenders (n=53)	p-value
Demographics			
Age	71 (67-73)	71 (63-78)	0.55
Sex (Female)	16 (26%)	21 (40%)	0.22
BMI (kg/m2)	28.9 (25.2-31.5)	28.4 (25.4-32.4)	0.90
Lives Alone	9 (15%)	17 (32%)	*0.02*
Education (College or more)	31 (51%)	17 (32%)	*0.04*
Smoker (never smoked)	22 (36%)	25 (47%)	0.20
Pre-Surgery Risk			
EuroSCORE II	1.36 (1-2.2)	1.77 (1.2-3)	0.13
Comorbidities			
Previous MI	17 (28%)	17 (32%)	0.62
CHF	28 (46%)	28 (53%)	0.34
Diabetes	12 (20%)	17 (32%)	0.13
CRF	1 (2%)	3 (6%)	0.24
COPD	4 (7%)	9 (17%)	0.07
Depression	6 (10%)	7 (13%)	0.57
Frailty			
CFS	3 (2-3)	3 (3-4)	*0.003*
MFC	2 (1-3)	3 (2-4)	*0.007*
SPPB	10 (9-11)	9 (7-10)	*0.001*
FFI	0.11 (0.1-0.2)	0.21 (0.1-0.3)	*0.0002*

Continuous variables expressed as median (interquartile range) and categorical variables expressed as N (%). The Mann-Whitney test compared continuous variables, Chi-Square Test compared categorical variables. ***CR***, Cardiac Rehabilitation; ***BMI***, Body Mass Index; ***EuroSCORE II***, European System for Cardiac Operative Risk Evaluation; ***MI***, Myocardial Infarction; ***CHF***, Chronic Heart Failure; ***CRF***, Chronic Renal Failure; ***COPD***, Chronic Obstructive Pulmonary Disorder; ***CFS***, Clinical Frailty Scale; ***MFC***, Modified Fried Criteria; ***SPPB***, Short Physical Performance Battery; **FFI**, Functional Frailty Ind

Appendix G

Table 9: CR Completion Rates among Frail and Non-Frail CR Attenders.

Frailty Tool	Baseline Frailty Status	CR Completers	CR Non-Completers	p-value
CFS	Frail CR attenders (n=13)	11 (85%)	2 (15%)	0.72
	Non-frail CR attenders (n=48)	37 (77%)	11 (23%)	
MFC	Frail CR attenders (n=21)	14 (67%)	7 (33%)	0.10
	Non-frail CR attenders (n=40)	34 (85%)	6 (15%)	
SPPB	Frail CR attenders (n=21)	15 (71%)	6 (29%)	0.32
	Non-frail CR attenders (n=40)	33 (83%)	7 (17%)	
FFI	Frail CR attenders (n=10)	5 (50%)	5 (50%)	*0.03*
	Non-frail CR attenders (n=51)	43 (84%)	8 (16%)	

Categorical variables expressed as N (%). The Chi-Square Test compared categorical variables where frail CR attenders were ≥15 (i.e., MFC and SPPB), whereas the Fisher Exact Test compared categorical variables where frail CR attenders were ≤15 (i.e., CFS and FFI). ***CFS***, Clinical Frailty Scale; ***MFC***, Modified Fried Criteria; ***SPPB***, Short Physical Performance Battery; ***FFI***, Functional Frailty Index.

Appendix H

Table 10: Baseline Frailty Compared between CR Completers and Non-Completers

	CR Completers	CR Non-Completers	p-value
Frailty Measure			
CFS	2.5 (2-3)	3 (2-4)	*0.01*
MFC	2 (1-3)	3 (2-4)	*0.0005*
SPPB	10 (9-11)	9 (7.3-10)	*0.007*
FFI	0.1 (0.08-0.2)	0.2 (0.1-0.3)	*<0.0001*

Continuous variables are expressed as median (interquartile range). The Mann-Whitney test compared all continuous variables. ***CR***, Cardiac Rehabilitation; ***CFS***, Clinical Frailty Scale; ***MFC***, Modified Fried Criteria; ***SPPB***, Short Physical Performance Battery; **FFI**, Functional Frailty Index.