Identifying exercise prescription components that predict improvements in functional capacity among participants enrolled in cardiac rehabilitation

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Identifying exercise prescription components that predict improvements in functional capacity among participants enrolled in cardiac rehabilitation

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ABSTRACT
Exercise during cardiac rehabilitation (CR) leads to an improvement in functional capacity, which in turn decreases the mortality risk. The purpose of this study was to determine the role of exercise prescription variables on functional capacity change among CAD patients who complete 36 sessions of CR. Methods: Exercise testing and prescription data for 151 patients were extracted from the American Association of Cardiovascular and Pulmonary Rehabilitation registry and the New Heart Center for Wellness, Fitness, and Cardiac Rehabilitation database. Patients completed a modified
Atterbom submaximal exercise test for determination of functional capacity, measured in metabolic equivalents (METs), pre- and post-CR. All patients completed 36 sessions of CR. The data were entered into an Excel Spreadsheet for analysis. A regression equation to determine the influence of exercise prescription components (intensity-percentage based of intake peak METs, duration-minutes of treadmill walking, and frequency-days per week) on change in peak METs when age and sex are held constant was established.

**Results:** The average functional capacity at intake and discharge was 4.4 ± 1.9 and 6.7 ± 1.7 METs, respectively. The average increase in functional capacity among patients was 2.2 ± 1.7 METs. Over the 36 sessions of CR, patients averaged 10.92 ± 3.58 minutes of treadmill exercise at an intensity of 92 ± 25.7% of pre-CR peak METs. The regression equation established was: \[ \Delta\text{METs} = -1.288 - (0.024*\text{age}) + (0.331 (*1 \text{ if men, *0 if women})) + (0.417*\text{frequency}) + (0.109*\text{average treadmill duration}) + (0.029*\text{average intensity}) \] (R=.536, SEE=1.44). Treadmill walking intensity and duration were significant predictors of change in functional capacity (p<0.01). Frequency was not a significant predictor but was clinically meaningful with an increase of 0.4 METs for each day of CR a patient completes weekly. **Conclusions:** Every 35% increase in intensity averaged over 36 CR-sessions leads to an improvement of functional capacity by 1 MET. Every 10 minutes of treadmill walking equate to an increase in functional capacity by 1 MET. Therefore, clinical exercise physiologists and others on the CR team should strive to progress patients throughout CR and increase treadmill walking duration and intensity continuously and encourage exercising on most days of the week.
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SYMBOLS / ABBREVIATIONS

<: less than

≤: less than or equal to

>: greater than

≥: greater than or equal to

±: plus or minus

AACVPR: American Association of Cardiovascular and Pulmonary Rehabilitation

ACSM: American College of Sports Medicine

AHA: American Heart Association

ANOVA: analysis of variance

BP: blood pressure

CABG: coronary artery bypass graft

CAD: coronary artery disease

CHD: coronary heart disease

CHF: chronic congestive heart failure

CR: cardiac rehabilitation

CT: continuous training

CVD: cardiovascular disease

FC: functional capacity

HIIT: high intensity interval training

HR: heart rate

HR_{max}: maximal heart rate

HR_{rest}: resting heart rate
HRR: heart rate reserve

kg: kilogram

MET: metabolic equivalent

METmins: metabolic equivalent minutes

MI: myocardial infarction

ml/kg/min: milliliter per kilogram per minute

mph: miles per hour

NHCR: New Heart Center for Wellness, Fitness and Cardiac Rehabilitation

PTCA: percutaneous transluminal coronary angioplasty

RPE: rating of perceived exertion

SD: standard deviation

VIF: variance inflation factor

VO₂max: maximal oxygen consumption

VO₂peak: peak oxygen consumption
CHAPTER 1: INTRODUCTION

With over 17 million deaths per year, cardiovascular disease is the leading cause of mortality worldwide (Mozaffarian et al., 2015). For heart disease survivors, rehabilitation is recommended to reduce the mortality risk for recurring events. According to the American Heart Association (AHA), cardiac rehabilitation (CR) is a medically supervised program with the ultimate goal of restoring and maintaining patients’ optimal physical, psychological, social, and vocational status (American Heart Association, 2016). Phase two CR is a standard exercise-based outpatient program in the United States focusing heavily on aerobic exercise. Patients commonly receive a prescription of 36 exercise sessions which are completed over a 12 to 18 week time frame (Lavie & Milani, 2011). Each session consists of aerobic exercise lasting between 20 and 60 minutes performed at 40-80% of peak oxygen uptake (VO₂peak) (AACVPR, 2013). Medicare and Medicaid cover CR for patients suffering from the following cardiac disorders: myocardial infarction (MI), acute coronary syndrome, coronary artery bypass graft (CABG), stable angina pectoris, valve replacement or repair, or heart and heart-lung transplant (Lavie & Milani, 2011). Patients are also eligible for CR if they suffer from one of the following heart diseases: chronic heart failure, or peripheral artery disease (Kachur et al., 2017; Lavie & Milani, 2011). The primary goal for patients is an improvement in functional capacity which is achieved through enhanced hemodynamics and functioning of the peripheral vasculature (Hambrecht et al., 2000). Additional positive outcomes include enhanced psychological wellbeing, improvements in risk factor management, and a heightened quality of life (QoL) (Belardinelli, Capestro,
What is functional capacity and is it clinically relevant?

As previously stated, the primary exercise outcome of CR is to improve functional capacity, which is defined as the ability to perform activities of daily living such as walking or climbing stairs (Arena, Myers, & Guazzi, 2008). Functional capacity is measured as maximal/peak oxygen consumption (VO$_{2\text{max}}$ or VO$_{2\text{peak}}$), and is an assessment of central hemodynamics (cardiac output) and peripheral skeletal muscle function (arterial-venous oxygen difference). One metabolic equivalent (1 MET) refers to an oxygen consumption of 3.5 ml/kg/min (Garber et al., 2011). Patients with cardiovascular diseases demonstrate VO$_{2\text{peak}}$ values in the lower percentiles for age and sex due mainly to central hemodynamic dysfunction, but also in part to peripheral mechanisms (Hambrecht et al., 2000; Keteyian, 2011). Peripheral mechanisms include a reduced oxygen extraction from the arteries due to reduced capillary density and muscle oxidative capacity (Fleg & Lakatta, 1998; Gault & Willems, 2013; Ogawa et al., 1992). Further, women and men entering CR have estimated functional capacities of 14.5±3.9 ml/kg/min and 19.3±6.1 ml/kg/min, respectively (Ades et al., 2006). This indicates that low intensity activities of daily living require a higher exertion level for these patients than for healthy individuals, and thus increases susceptibility to ischemia, re-infarction, and hospitalizations (Ades et al., 2006). Moreover, improvements in functional capacity among heart disease patients in response to CR have been linked to improved QoL, lower incidences of cardiac events, reduced hospitalizations, and decreased mortality rates.
Effect of exercise on functional capacity

Substantial increases in VO$_2$peak along with null findings have been reported across numerous CR studies among heart disease patients. For example, VO$_2$peak improved from 14.8±2.5 ml/kg/min to 18.9±2.7 ml/kg/min (~ 4 ml/kg/min increase) in response to eight weeks of CR among heart failure patients who cycled an average of 40 minutes at 60% VO$_2$peak (Belardinelli et al., 2006). Conraads et al. (2015) demonstrated an improvement of 4.5 ml/kg/min (22.2±5.56 to 26.8±6.7 ml/kg/min) among 200 coronary artery disease (CAD) patients after 12 weeks of continuous moderate intensity exercise and a 5.1 ml/kg/min improvement in a high intensity interval group (23.5±5.7 to 28.6±6.7 ml/kg/min) (Conraads et al., 2015). Larger improvements have been demonstrated after a ten-week high intensity CR program where male and female CAD patients showed an increase of nearly 6 ml/kg/min (31.8±9.3 to 37.8±12.4 ml/kg/min) (Rognmo, Hetland, Helgerud, Hoff, & Slørdahl, 2004). Similarly, peak oxygen uptake increased approximately 7 ml/kg/min, or 2 METS, after 12 weeks of dynamic exercise CR training among a diverse disease population (CAD, CABG, and MI) (Vanhees, Fagard, Thijs, & Amery, 1995). All studies had a frequency of three days weekly for 10 to 26 weeks. These studies show that functional capacity can be substantially improved for a variety of cardiac disease states with different training prescription components.

Conversely, several research groups have reported only modest improvements in functional capacity among patients enrolled in CR. In the largest known CR study among
heart failure patients (HF-ACTION, n=1,620) a modest increase of 0.6 ml/kg/min was reported after 12 weeks of exercise (Swank et al., 2012). An increase of 2.7 ml/kg/min was demonstrated after a ten-week moderate intensity (50-60% VO₂peak) CR program among CAD patients (Rognmo et al., 2004). These two studies show an improvement in functional capacity by less than 1 MET. In elderly male CAD patients (≥65 age, n=39), functional capacity only changed from 22.8±3.4 ml/kg/min at baseline to 24.6±3.1 ml/kg/min (1.8 ml/kg/min increase) after six months of a moderate intensity (reported as RPE 12-13) program (Seki et al., 2008). In a follow-up study, the same group of researchers reported an increase of 0.8 ml/kg/min in VO₂peak among 111 elderly male CAD patients in response to a similar exercise program (6 months, moderate intensity) (Onishi et al., 2010). Likewise, Carlson et al. (2000) showed no change in functional capacity among eighty patients (66 men and 14 women) in response to 12 weeks of a moderate-vigorous (60 to 85% VO₂peak) exercise regimen (Carlson, Johnson, Franklin, & VanderLaan, 2000). These results highlight the discrepancies in functional capacity changes among patients who complete a CR program. Several factors (e.g., frequency, study length) may explain the disparities in functional capacity results among cardiac patients, and include disease condition (e.g., CAD, heart failure), or complications with the procedure, severity of myocardial damage, adherence to CR, compliance to medication, tolerance to exercise, safety concerns among exercise clinicians, and the components of the exercise prescription.
Why the effect of exercise training is different among various cardiac diseases

The improvement in functional capacity in response to CR may be affected by the complexities of the underlying disease states. In most conditions, central hemodynamics (cardiac function) is compromised due to the inefficiencies in oxygen supply to the contracting myocardium thus causing an ischemic insult, and possible myocardial damage. Continued occurrence of ischemia leads to treatment (e.g., stent, CABG), but also heightens the patient’s risk for future heart failure. The positive effects of exercise are influenced tremendously by the extent of myocardial damage and function. For example, while heart failure patients benefit from CR with increased QoL, a large body of evidence demonstrates only small increases in functional capacity (Swank et al., 2012). The heart failure condition is extremely complex, and patients not only suffer from central hemodynamic inefficiencies, but also commonly have co-morbidities (e.g., renal failure, edema, sleep apnea). Conversely, percutaneous transluminal coronary angioplasty (PTCA) patients have demonstrated more robust improvements in functional capacity in response to CR (Belardinelli et al., 2001). The PTCA population may be less complex in comparison to heart failure.

Effect of adherence on functional capacity

The magnitude of improvement in several CR primary outcomes, including functional capacity, is reported to be proportional to the number of exercise sessions completed (Martin et al., 2012). Adherence to CR is the number of sessions completed divided by the number prescribed (~36 sessions), and commonly reported as a percentage. Clinicians and researchers recommend 100%, but unfortunately, adherence
rates in large CR trials have been reported at nearly 50% (18 out of 36 sessions) (Ades et al., 2017; Colbert et al., 2015; Martin et al., 2012). Similar to medications and other treatments, the benefits of exercise among heart disease patients is dose dependent. For this reason, tremendous efforts have been developed and employed to increase adherence rates in CR (Ades et al., 2017).

To combat low adherence in CR, researchers have developed more aggressive exercise programs in the effort to improve outcomes within a shorter number of exercise sessions. These efforts have been shown to be effective, illustrated by higher attendance rates (82%) among patients enrolled in an interval-based exercise program (Moholdt et al., 2011). In addition, the interval group was more adherent to exercise after completion of CR, resulting in sustained improvements in functional capacity (Moholdt et al., 2011). However, it remains unclear if patients who participate in alternative types of rehabilitation (interval exercise or home-based rehabilitation) are more adherent.

*Prescription components affecting functional capacity improvement*

The development and administration of the exercise prescription is the foundation of the exercise component in CR. Guidelines (discussed later) have been developed and recommended to provide a framework for the clinical exercise physiologist in assembling appropriate exercise programs for a variety of patients. Traditional exercise programs prescribed by clinical exercise physiologists are more conservative in exercise parameters, including the intensity, duration, frequency, and the progression of exercise. In general, functional capacity, patient safety and QoL improvements have been demonstrated among patients prescribed to traditional CR exercise programming. However,
improvements in functional capacity ranged from +7 ml/kg/min (18 to 33%) to no improvement (Keteyian et al., 2014; Rognmo et al., 2004; Swank et al., 2012; Vanhees et al., 1995). Similar to the exercise dose response, adaptations to exercise are principled in overload training and progression, but the extent to which clinics follow exercise guidelines and progress patients is unknown. Cardiac rehabilitation research studies commonly report exercise prescription ranges among enrolled patients, and may include durations of 20-40 minutes and intensities ranging from 55-85% of HRR, HR_{max} or VO_{2peak} with a frequency goal of 3 times/week. However, progression of patients is rarely documented, and final exercise prescription achievements are seldom reported. For these reasons, functional capacity outcomes vary tremendously.

In response to unsatisfactory outcomes in traditional CR programming, a recent surge of research and practice has been placed on implementation of high intensity interval exercise (HIIT) in CR (Keteyian et al., 2014; Moholdt et al., 2009; Moholdt et al., 2011; Rognmo et al., 2004). While outcomes have been shown to be similar, and in some studies are superior to traditional exercise prescriptions, guidelines have yet to be established for HIIT (Keteyian et al., 2014; Rognmo et al., 2004). The emphasis on HIIT was initiated in an attempt to maximize exercise prescription variables (e.g., duration and intensity) due to common low frequencies of training in cardiac patients, and to also overload and progress patients with a more systematic approach. Interval training with 4-minute intervals of 85%-95% HR_{peak} with progression through increasing the number of intervals have been shown successful (Conraads et al., 2015; Rognmo et al., 2004). High intensity interval training was introduced to maximize intensity and exercise duration at higher intensities, and progression of a CR session, but again, discrepant findings have
been reported in regard to functional capacity changes (Keteyian et al, 2014; Rognmo et al., 2004). For this reason, there are no established or published HIIT prescription details for CR. Therefore, it is critical to further investigate effective exercise prescription models that employ specific intensity goals and progression.

**Exercise Recommendations for Cardiac Rehabilitation**

*What are the current guidelines for exercise prescription?*

The current exercise guidelines for CR patients published by the American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) (2013) recommend an exercise program including (1) 40-80% of HRR or VO₂peak with an exercise test and HRRest + 20 to 30 bpm or an RPE of 12-16 without an exercise test; in heart failure patients, the recommended intensity is 60-80% HRR or an RPE of 11-14; (2) 20-60 minutes duration of exercise; (3) 3-5 days per week; and (4) exercise mode of total body aerobic exercise (AACVPR, 2013). The AHA in conjunction with the AACVPR recommend a moderate-to-vigorous aerobic exercise program, in combination with dynamic resistance training to improve functional capacity, QoL and reduce cardiac risk factors (Price, Gordon, Bird, & Benson, 2016).

The guidelines published by these associations are, however, not the recommendations for CR worldwide. There is no consensus on exercise prescription as there seem to be many uncertainties. For example, Price et al. (2016) reported nearly twenty different sets of exercise guidelines from agencies worldwide. Table one shows the differences in prescribing aerobic endurance training in intensity, duration, frequency and program length that are published by regional heart associations worldwide.
Table 1: Aerobic exercise prescription guidelines for different regions worldwide
(Data from Price et al., 2016)

<table>
<thead>
<tr>
<th>Country/Continent</th>
<th>Intensity (VO(_2) or HR)</th>
<th>Duration (min)</th>
<th>Frequency (d/week)</th>
<th>Program length</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>40-80%</td>
<td>11-16</td>
<td>20-60</td>
<td>≤ 36 sessions</td>
</tr>
<tr>
<td></td>
<td>VO(_2)peak</td>
<td></td>
<td>3-5</td>
<td></td>
</tr>
<tr>
<td>Europe</td>
<td>50-80%</td>
<td>10-14</td>
<td>≥20-30</td>
<td>2-16 weeks</td>
</tr>
<tr>
<td></td>
<td>VO(_2)max</td>
<td></td>
<td>≥3</td>
<td></td>
</tr>
<tr>
<td>Canada</td>
<td>40-85%</td>
<td>N/A</td>
<td>20-40</td>
<td>≥ 12 weeks</td>
</tr>
<tr>
<td></td>
<td>HRR</td>
<td></td>
<td>3-5</td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td>40-60%</td>
<td>12-13</td>
<td>15-60</td>
<td>5 months</td>
</tr>
<tr>
<td></td>
<td>VO(_2)peak</td>
<td></td>
<td>1-3</td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td>Low- to moderate-intensity</td>
<td>N/A</td>
<td>30-60</td>
<td>3-12 weeks</td>
</tr>
</tbody>
</table>

According to the data shown in table one, it is evident that there is no worldwide agreement on the optimal exercise prescription modalities for CR, and these inconsistencies influence patient outcomes (e.g. functional capacity improvement). The unanswered questions include if intensity is the strongest predictor of improvement in aerobic functioning, or are duration of a session and/or frequency of exercise equally, or
The data in the table clearly indicates that there are several knowledge gaps that need to be answered to provide consistent CR guidelines throughout the world.

**Intensity**

The intensity of the exercise prescription is commonly determined from a baseline assessment where the percentage of maximal effort is used (e.g. \%HR_{max}, \%HRR, \%VO_2peak) (Seals, Hagberg, Hurley, Ehsani, & Holloszy, 1984; Thomas, Cunningham, Rechnitzer, Donner, & Howard, 1985). Subjective measure of perceived exertion (RPE) is commonly used when a baseline assessment is not performed (Nilsson, Westheim, & Risberg, 2008; Scherr et al., 2013; Swain & Franklin, 2002). Most continents/regions recommend 40% VO_2peak, HRR, or HR_{max} as the lowest intensity, but no consensus recommendation exists for higher intensity exercise in CR. Canada is the only nation that recommends exercise to be performed above 80% HRR. None of the guidelines recommends HIIT, which has been implemented in CR for the past decade. Some guidelines do not use RPE to determine intensity of training and the highest RPE on the 6-20 scale recommended is 16 in the United States, while an RPE of 10-14 is a more common guideline. However, in cardiac patients, RPEs are often reported as being lower than in healthy individuals for a given intensity (Pollock, Foster, Rod, & Wible, 1982). There is a large variability in reported RPEs between patients which leads to the question wether RPE is a precise enough method to use for exercise prescription in cardiac patients (Joo et al., 2004).

Moderate intensity or continuous training (CT) is recommended in all published guidelines for CR worldwide. In CT, the patient engages in moderate intensity exercise
for a duration of up to 60 minutes during CR. A study, analyzing the effectiveness of CT in heart failure patients, measured an improved functional capacity after eight weeks of three sessions weekly at 60% VO\textsubscript{2peak} of 1.4 METs (Belardinelli et al., 2006). In CABG patients, functional capacity increased after 4 weeks of CT at 70% HR\textsubscript{max} by 0.7 METs, on the other hand (Moholdt et al., 2009). An intensity of 50 to 60% VO\textsubscript{2peak} led to an improvement of 0.8 METs in CAD patients (Rognmo et al., 2004). An intensity based on RPE (12 to 13) was also not successful in improving functional capacity (0.2 METs and 0.5 METs, respectively) in elderly CAD patients (Onishi et al., 2010; Seki et al., 2008). In heart failure patients, an intensity of 50-70% VO\textsubscript{2peak} did not improve functional capacity by more than 0.1 METs (Freyssin et al., 2012; Sabelis et al., 2004). In a meta-analysis of heart failure patients including 35 studies, functional capacity significantly improved in the exercising groups with an effect size of 0.6 (van Tol, Huijsmans, Kroon, Schothorst, & Kwakkel, 2006). However, it appears that an intensity threshold needs to be achieved during continuous aerobic training to foster improvements in functional capacity among heart failure patients (Freyssin et al., 2012). This was also demonstrated by no change in functional capacity after exercise below the first ventilatory threshold. Moreover, higher exercise intensities performed in CR have been shown to be the strongest predictor for improvement in VO\textsubscript{2peak} in both CHD and HF patients (p<0.05) (Uddin et al., 2016).

High intensity interval training has gained popularity in the last decade for cardiac patients. In HIIT, several intervals of very high intensity (above 85% VO\textsubscript{2max}) for 30 seconds to 4 minutes are interspersed with rest/recovery intervals at a lower exercise intensity (~40-70% HR\textsubscript{peak}) (Keteyian et al., 2014; Moholdt et al., 2009; Rognmo et al.,
This routine of exercise interval to rest is repeated several times, and the total exercise session may be only 20 minutes (Keteyian et al., 2014; Moholdt et al., 2009; Rognmo et al., 2004; Tschentscher et al., 2016). Hence, an advantage of HIIT is the shorter duration for each exercise session, and the ability to sustain a higher intensity across the exercise session.

Comparative CR studies of CT versus HIIT training on functional capacity have been inconclusive (Keteyian et al., 2014; Moholdt et al., 2009; Rognmo et al., 2004). Keteyian et al. (2014) measured a 16% increase in VO$_2$peak after HIIT compared to an 8% increase after CT in a ten-week study (Keteyian et al., 2014). These findings are similar to the study by Rognmo et al. (2004) where the HIIT group increased VO$_2$peak by 17.9% and the CT group increased by 8% after ten weeks (Rognmo et al., 2004). While VO$_2$peak increased significantly from baseline after 4 weeks of CT and HIIT (with no significant difference between groups reported), only the HIIT group sustained the improvement at 6-month follow-up (Moholdt et al., 2009). Additionally, no differences were detected among heart failure patients who engaged in either HIIT or CT above 70% VO$_2$peak, further indicating that an intensity threshold (> 70%) might be required for CT (Tschentscher et al., 2016). Hence, HIIT versus CT in CR shows inconsistent results. This may be the reason for the lack of established guidelines for HIIT, but these studies also represent the importance of intensity in the CR exercise prescription. Therefore, the ideal intensity targets for CR for various cardiac disorders seems not to be conclusively identified and more emphasis should be placed on researching these.
Duration

There seems to be consistency in the recommendations for the duration of aerobic exercise session (see table one). All guidance from the various regions suggest a minimum of 20 minutes of aerobic exercise per CR session. The maximal duration recommended is 60 minutes (Australia, Japan, USA). Hartung et al. (1977) demonstrated that a duration of at least 15 minutes was effective for improving functional capacity, and that 25 minutes induced a greater VO$_2$max response with training (Hartung, Smolensky, Harrist, Rangel, & Skrovan, 1977). In a later work, Wenger et al. (1986) reported that a duration of 15 to 25 minutes was only effective when intensity exceeded 90% VO$_2$max, and lower intensity exercise was effective when duration was longer than 35 minutes (Wenger & Bell, 1986). In support of these findings, Kohrt et al. (1991) observed improvement in functional capacity among elderly subjects (>60 years of age) when exercise was at least 40 minutes per session regardless of intensity (Kohrt et al., 1991). It is important to mention that the studies by Hartung, Wenger, and Kohrt were published nearly 30 years ago, and conducted among non-cardiac disease patients. In a recent survey study among nearly 60 US CR clinics, aerobic exercise duration ranged from 30-60 minutes, with 40 minutes being reported among the majority of clinics (O'Neil et al., 2018). The 40-minute time frame may be ideal in CR because several research groups have reported minimal improvements in functional capacity when duration was set to 30 minutes among cardiac patients (McKelvie et al., 2002; Onishi et al., 2010; Seki et al., 2008; Smart & Steele, 2012). Hence, the optimal duration for cardiac patients has yet to be determined; however, it appears that durations of 15 to 45 minutes, depending on the intensity, are beneficial in improving functional capacity.
**Frequency**

The frequency of training varies tremendously between regions. While some guidelines recommend at least one session and up to three weekly, advise from CR organizations in other continents advocate for at least three and up to five sessions weekly which is similar to the American College of Sports Medicine (ACSM) guidelines for physical activity among healthy individuals (American College of Sports Medicine, 2017). Improvement in functional capacity has been consistently demonstrated among CAD, MI, CABG and heart failure patients who engaged in three sessions per week (Belardinelli et al., 2006; Conraads et al., 2015; Dorn, Naughton, Imamura, & Trevisan, 1999; Rognmo et al., 2004; Vanhees et al., 1995). While a frequency of three sessions has been shown to be successful, this has not been consistently demonstrated in all studies. Non-improvements have been reported in heart failure patients in response to two, three, and five weekly training sessions (Edelmann et al., 2011; Freyssin et al., 2012; McKelvie et al., 2002; Sabelis et al., 2004; Smart & Steele, 2012). Similar null findings were also reported among CAD patients who completed three weekly rehabilitations sessions, and in some studies using three weekly rehabilitation sessions in addition to two home-based sessions (Carlson et al., 2000; Onishi et al., 2010; Rognmo et al., 2004; Seki et al., 2008). Reasons stated for a non-improvement in functional capacity included low patient numbers, patients who did not start the at home program right away and the direct measurement of VO$_2$peak instead of an estimated value which was reported to be higher (Carlson et al., 2000).

In one of the few comparative studies, Le Bris et al. (2006) contrasted three versus five sessions per week of aerobic exercise on functional capacity among CAD
patients who completed 20 exercise sessions. The researchers demonstrated a greater increase in functional capacity in the five days a week group compared to three. In addition, it was reported that the high frequency subjects (5 days/wk) could tolerate exercise twice as long as the low frequency subjects (3 days/wk) (Le Bris, Ledermann, Topin, Messner-Pellenc, & Le Gallais, 2006). A limitation of the study by Le Bris et al. (2006) is the small number of subjects (4 in total). There is limited availability of studies investigating the effect of frequency on functional capacity. Therefore, more research is needed to determine the optimal training frequency for CR.

**Progression**

Rate of progression has not been mentioned in any of the published exercise guidelines (Price et al., 2016). Progressing cardiac patients throughout their rehabilitation is important to enhance improvement in functional capacity. The most mentioned form of progression in published research is the increase in duration followed by an increase in intensity, which corresponds with the ACSM exercising guidelines for healthy individuals (Edelmann et al., 2011; American College of Sports Medicine, 2017). As functional capacity is low in cardiac patients, exercise durations should be shorter at the beginning of CR (Ades et al., 2006). It is the goal of most clinical exercise physiologists to improve the duration of exercise before improving the intensity of exercise; however, in CR duration is limited due to the clinic scheduling. Frequency is often not altered in non-research-controlled settings, patients attend CR sessions whenever it fits their schedule which often is two or three days per week. In one study, heart failure patients performed two sessions per week at an intensity of 50-60% VO₂peak with a progression
in duration from 20 to 40 minutes across the first four weeks (Edelmann et al., 2011). Starting in week five, frequency was increased to three times weekly, and intensity was incrementally progressed to 70% \( VO_2 \text{peak} \) (Edelmann et al., 2011). Patients in the study improved functional capacity, maximal workload, and maximal exercising time in a symptom-limited exercise test. Intensity is another exercise variable that is used for progression in exercise among cardiac patients. In a ten-week HIIT study, intensity was increased from 80% \( VO_2 \text{max} \) after two weeks of training to 90% \( VO_2 \text{max} \) in CAD patients with an increase in functional capacity of 6 ml/kg/min over the course of the study (Rognmo et al., 2004). Similar results have been reported among heart failure patients who were progressed from 50% to 80% of maximal power achieved in an initial exercise test across eight weeks of interval exercise which improved functional capacity by nearly 1 MET (Freyssin et al., 2012). Duration and intensity are the two most used prescription components altered to change training for continuous improvement in functional capacity throughout CR. As the exercise capacity of cardiac patients is thought to improve throughout a rehabilitation program, progressing them is important to achieve the highest possible gains in functional capacity. However, the ideal timing and extent for progression are not well established.

**How CR Centers in the U.S.A. implement the current guidelines**

Recently, a research group explored exercise prescription practice among CR centers throughout the Midwest of the United States (O'Neil et al., 2018). The results for each exercise prescription variable are presented in table 2 below. These findings demonstrate the large variability in the administration of exercise guidelines. For
intensity, the majority of surveyed CR centers (84%) reported to use a rating of perceived exertion as their main intensity marker (O'Neil et al., 2018). These values are in accordance with a similar study performed in the Netherlands, where the usage of RPE was reported by 82% and 76% of CR centers for CAD and heart failure patients, respectively (Vromen et al., 2013). Exercise intensities of an RPE of 11 to 15, HRR of 30 to 80% and \( \text{HR}_{\text{max}} \) of 50-85% are used in US centers. While the RPE and HRR ranges are within the current AACVRP guidelines, a prescription of maximal heart rate is not mentioned in these but is used by 27% of clinics (O'Neil et al., 2018; AACVPR, 2013). The same is true for METs as intensity measurement which is also used by 27% of clinics (O'Neil et al., 2018). The third method mentioned in the guidelines for intensity prescription (\( \text{VO}_{2}\text{peak} \)) was only mentioned by 2% of the clinics as utilized method. In the Netherlands, \( \text{VO}_{2}\text{peak} \) is not used in CAD patients and in only 12% of heart failure patients (Vromen et al., 2013). Other methods used in the Netherlands include the Karvonen method and percentage workload (Vromen et al., 2013). While a stress test is recommended by the AACVPR and should be performed whenever possible, the majority of Midwestern CR centers (67%) did not perform or utilize baseline testing results to formulate exercise prescriptions (O'Neil et al., 2018). In a study in New York State, 90% of CR centers performed an initial exercise test (DeTurk & Scott, 2008). In the Netherlands, stress testing is performed by 76% and 64% of CR centers in CAD and heart failure patients. In the absence of an initial stress test, US rehabilitation centers prescribe exercise intensity based on an RPE of 11 to 14, 20-40 bpm above \( \text{HR}_{\text{rest}} \), or trial and error (O'Neil et al., 2018). In the Netherlands, an RPE (82 and 85%) as well as a \( \text{HR}_{\text{max}} \) (36 and 43%) measure for intensity was used in CAD and heart failure patients,
respectively. The RPE range used by these centers was in between the recommendation of 11-16 stated in the guidelines. Using $HR_{\text{rest}}$ plus 20-40 bpm as an intensity measure is recommended in the current ACSM exercise prescription guidelines (10\textsuperscript{th} ed.) (American College of Sports Medicine, 2017). A trial and error technique should not be utilized but was also common in the Netherland with 55\% in CAD and 64\% in heart failure patients (Vromen et al., 2013). These studies clearly show that more than the three methods given in the guidelines are used in CR centers.

According to table two, duration ranging from 30 to 60 minutes seemed the most common among US clinics with the majority of clinics targeting a duration of 40 minutes (41\%), which meets recommendations (O'Neil et al., 2018). Only 8\% of CR clinics prescribe exercise at the upper end of the guidelines (60 min) (O'Neil et al., 2018). In the study of Netherland CR centers, a duration of 30 minutes was common among CAD patients and 24 minutes in heart failure patients. These durations represent the lower end of the AACVPR guidelines (Vromen et al., 2013). Frequency of three days per week was the most common among the 58 CR centers that returned the survey; only three centers (6\%) said their patients would perform four to five sessions weekly (O'Neil et al., 2018). This indicates that most CR centers do follow the recommended frequency of training published by the AACVPR. Only 15\% of centers conducted two sessions weekly for their patients. In the Netherland, an average frequency of two days per week was reported by all CR centers (Vromen et al., 2013). This is less than the recommended frequency of at least three days weekly. As form of progression, intensity and duration have been named by US CR centers (94\% and 84\%, respectively) (O'Neil et al., 2018). Fourteen of the CR center (24\%) mentioned to progress from CT to interval training but without specification
on the intensity of intervals (O'Neil et al., 2018). Eight percent of the questioned CR centers answered that frequency is increased during the prescribed rehabilitation sessions.

While the study by O’Neil et al. (2018) looked at the utilization of the AACVPR guidelines by US CR centers, a similar study has been conducted in the Netherlands to investigate what prescription methods are used in the country. As research on the application of the guidelines is limited, more research is needed to evaluate if CR centers follow the current AACVPR guidelines or which adjustments have been made by CR providers.
Table 2: AACVPR cardiac rehabilitation prescription guidelines in comparison to actual prescription (Data from O’Neil et al., 2018)

<table>
<thead>
<tr>
<th>Variable / prescription</th>
<th>AACVPR guidelines</th>
<th>Actual prescription (reported as % of 58 clinics surveyed)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>HRR (34%)</td>
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<tr>
<td></td>
<td></td>
<td>VO₂R (2%)</td>
</tr>
<tr>
<td><strong>Intensity</strong></td>
<td>40-80% HRR</td>
<td>RPE (84%)</td>
</tr>
<tr>
<td><strong>Methods</strong></td>
<td>40-80% VO₂peak</td>
<td>Other reported techniques</td>
</tr>
<tr>
<td></td>
<td>11-16 RPE</td>
<td>METs (27%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HRₘₐₓ (27%)</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>20-60 min</td>
<td>30 min (29%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>40 min (41%)</td>
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<tr>
<td></td>
<td></td>
<td>35-50 min (22%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60 min (8%)</td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td>3-5 d/wk</td>
<td>2 d/wk (15%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 d/wk (98%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4-5 d/wk (6%)</td>
</tr>
<tr>
<td><strong>Progression</strong></td>
<td></td>
<td>Intensity (94%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Duration (84%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Frequency (8%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CT to interval training (24%)</td>
</tr>
<tr>
<td><strong>Exercise test</strong></td>
<td>Yes</td>
<td>Yes (n=19)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No (n=39)</td>
</tr>
</tbody>
</table>
The uncertainties of exercise prescription for CR

As has been stated above, there is no agreement on the ideal exercise prescription for cardiac patients entering CR. Continents and individual countries have published guidelines, which clearly show the many uncertainties of the ideal prescription for cardiac patients. Aerobic exercise training in CR has the greatest impact on decreasing mortality, risk for cardiac death, and recurrence of cardiac disease (Keteyian et al., 2008; Keteyian et al., 2018). However, the spectrum for duration, frequency and length of program is wide among the published guidelines. The intensity recommendations are all within a moderate intensity range, but no organization recommended HIIT, even so there is evidence that high intensity exercise might be more beneficial than moderate intensity exercise in improving functional capacity. Therefore, this database study hopes to determine the best possible training modalities, which provide the optimal health outcomes in terms of functional capacity.

Purpose of Study

The purpose of this study is to determine a prediction equation for improvement of peak METs from pre- to post-CR using intensity, duration, and frequency of exercise as parameters. Data collected from CR patients from the New Heart – Center for Wellness, Fitness and Cardiac Rehabilitation (NHCR) will be used. Patients will have completed CR, including a post CR assessment, in the previous five years. The primary aim of this study is to evaluate components of exercise prescriptions that contribute to the changes in functional capacity among patients who completed intake and post
assessments in CR. Independent variables analyzed will include exercise intensity, exercise duration, and exercise frequency.

Hypotheses

The following hypotheses will be tested in the study:

Set 1 of hypotheses to test that there is no effect or relationship between variables:

1. There will be no significant prediction of improvement in estimated peak METs by intensity, duration, frequency, and progression.

2. In the presence of the others, there will be no significant prediction of improvement in peak METs by intensity.

3. In the presence of the others, there will be no significant prediction of improvement in peak METs by duration.

4. In the presence of the others, there will be no significant prediction of improvement in peak METs by frequency.

Set 2 of hypotheses to test effectiveness of training

1. Functional capacity will increase in all patients who did complete the CR program no matter of the training prescription. Measured functional capacity increased two to ten percent from start to completion of CR (Kavanagh et al., 2003; Vanhees et al., 1995).

2. Functional capacity will be further increased in patients who exercised for 40 minutes compared to shorter durations at moderate intensity. CR for 30 minutes was not successful in all studies (McKelvie et al., 2002; O'Neil et al., 2018; Onishi et al., 2010; Seki et al., 2008). However, longer durations seem to enhance
increases in aerobic functioning and a duration of 40 minutes is widely used (O’Neil et al., 2018).

3. Functional capacity will be higher for individuals exercising at least three days per week compared to twice per week. Functional capacity increases with training volume. Training 3 days a week for 60 minutes compared to 2 days for 60 minutes provides a volume difference of 60 minutes per week and should therefore represent a difference in functional capacity (Belardinelli et al., 2006; Dorn et al., 1999; Edelmann et al., 2011; Le Bris et al., 2006; McKelvie et al., 2002; Sabelis et al., 2004; Smart & Steele, 2012; Vanhees et al., 1995).

4. Functional capacity will be elevated in patients exercising at higher intensities for shorter durations than for patients that exercise at moderate intensities for longer durations. Higher intensity exercise promotes a greater increase in functional capacity than exercise at lower intensities even when duration is longer. (Elliott, Rajopadhyaya, Bentley, Beltrame, & Aromataris, 2015; Liou, Ho, Fildes, & Ooi, 2016; Milanović et al., 2015; Rognmo et al., 2004; K. S. Weston, Wisløff, & Coombes, 2014; M. Weston, Weston, Prentis, & Snowden, 2016).

**Scope of Study**

**Database study**

Data from over 150 patients who completed CR including a post rehabilitation assessment at the NHCR in the past five years will be extracted from the NHCR and the AACVPR databases. The extracted data includes: blood pressure (BP) and heart rate (HR) at rest and during a graded exercise test along with speed and grade performance at intake. For each of the 36-exercise sessions to follow, data on the mode, intensity and
duration is given. Frequency of training will be determined based on sessions attended weekly. A resting BP and HR value pre and post exercise will be extracted from the database. A BP, HR and graded exercise test stages will be extracted from the post CR graded exercise test.

Patients will be cross-searched in the American Association for Cardiovascular and Pulmonary Rehabilitation database. From the (AACVPR) database, information on QoL, depression scores, and functional capacity (VO₂peak) will be extracted for each patient and converted to peak METs.

**Limitations**

We are limited to the data that was recorded or put into the database by employees of NHCR. As individuals have completed CR, we are not able to get any missing data from these individuals.
CHAPTER 2: REVIEW OF RELEVANT LITERATURE

This chapter presents a review and meta-analysis entitled “Comparison of Treadmill and Cycle Ergometer Exercise during Cardiac Rehabilitation: A meta-analysis” which will be send to review in the journal *The Journal of Cardiopulmonary Rehabilitation and Prevention*. It is authored by Stephanie Gerlach, Christine Mermier, Len Kravitz, Lance Dalleck, James Degnan, and Micah Zuhl. The manuscript follows the formatting guidelines of the journal. Figures and references are provided at the end of manuscript.
Original Investigation – Meta-analysis

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Running title: Comparing treadmill and cycling exercise in CR

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Keywords: (1) functional capacity; (2) cardiac rehabilitation; (3) continuous exercise

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All authors declare no conflicts of interest.
Abstract

**Purpose:** The primary exercise outcome in cardiac rehabilitation (CR) is an improvement in functional capacity. Treadmill walking is a common exercise mode; however, cycling is also a common alternative. Therefore, the purpose of this study was to compare treadmill versus cycling-based cardiac rehabilitation on functional capacity outcomes.

**Methods:** Several databases were searched for randomized studies using single modality continuous exercise. Studies implemented a continuous cycling or treadmill protocol. The effect of single modality exercise on FC (VO$_{2peak}$) was analyzed. Differences in the effect of CR on FC was assessed between the mode subgroup (cycling vs. treadmill) and disease state subgroup (CAD vs. CHF) within both the cycling and treadmill groups.

**Results:** Data were extracted from 23 studies including 600 patients (mean age 60yrs, 86% male). There was a significant difference in effect size between studies that used cycling, Hedges’ $g=0.85$ (95% CI, 0.52 – 1.17, $k=13$) and studies that used treadmill exercise, Hedges’ $g=0.46$ (95% CI, 0.22 – 0.70, $k=8$). Within cycling studies ($n=14$), FC was higher among coronary artery disease (CAD) patients compared to chronic heart failure (CHF) ($Z=23.95$, $p<0.001$). Conversely, among treadmill studies ($n=9$), FC was higher among CHF patients compared to CAD ($Z=-2.39$, $p<0.01$).

**Conclusion:** When cycling is the primary mode of exercise in CR there is a larger change in FC than treadmill only. In addition, CAD patients appeared to experience better gains if cycling was the primary mode of exercise in CR while CHF patients may benefit more from treadmill-based exercise.
Introduction

Among heart disease survivors, cardiac rehabilitation (CR) is the gold standard recommendation to reduce the mortality risk. Among heart disease survivors, cardiac rehabilitation (CR) is the gold standard recommendation to reduce the mortality risk. According to the American Heart Association, CR is a medically supervised program with the ultimate goal of restoring and maintaining patients’ optimal physical, psychological, social, and vocational status. An improvement in functional capacity, which is defined as the ability to perform activities of daily living such as walking or climbing stairs, is the primary exercise outcome of CR.

National (U.S.) and international exercise prescription guidelines for cardiac patients have been established by various groups (e.g., clinical organizations, government agencies) to guide clinical exercise physiologists. Regarding mode of exercise, the broad recommendation is for patients to perform whole body aerobic exercise (i.e., treadmill); however, localized lower body exercise (i.e., cycling) is also a common alternative. Limited research exists comparing the role of exercise mode in CR on functional capacity. Therefore, the purpose of this systematic review and meta-analysis was to compare treadmill versus cycling-based cardiac rehabilitation on functional capacity outcomes. In addition, we further aimed to identify if FC outcomes among coronary artery disease and heart failure patients is influenced by the modality (cycling or treadmill) of exercise in CR.

Methods

Search Strategy and Selection Criteria
Comparison of Treadmill and Cycle Ergometer Exercise during Cardiac Rehabilitation: A meta-analysis

A systemic literature review was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. PubMed, ScienceDirect, Cochrane Library, and Google Scholar were searched using the key words “cardiac rehabilitation”, “functional capacity”, “VO2max/peak”, “CAD”, “heart failure”, “treadmill”, “cycle/cycling”, “exercise” in various combinations. Studies published between 1980 and 2018 were included in the original search. In addition, reference lists of original and review articles were analyzed manually for studies not identified in the original search. After initial screening of titles and abstracts, studies were assessed for inclusion and quality for meta-analysis (Figure 1).

Studies were included if they met the following criteria: (1) specified if patients had coronary artery disease (CAD) or congestive heart failure (CHF); (2) patients performed continuous treadmill or cycling exercise (no other modes); (3) enrolled adult patients (<18 years of age). Exclusion criteria included (1) no distinction between exercise modalities; (2) no specification on cardiac disease; (3) functional capacity was not reported.

Only one study was located that compared cycling versus treadmill exercise on functional capacity among heart disease patients enrolled in CR. However, in this study patients in the treadmill group also performed cycling exercise, and therefore, only the cycling results were included. All other studies implemented either a continuous cycling or treadmill specific protocol and compared it to a control (non-exercise), or other exercise format (e.g., aerobic interval exercise). To perform an adequate comparison, only the continuous exercise training arms of studies (either cycling or
treadmill) were entered. Therefore, only a single arm of randomized studies were included.

Data Extraction and Outcome Assessment

Two reviewers independently reviewed and extracted data from 23 studies. The primary outcome was functional capacity change among heart disease patients enrolled in CR, and to further observe the primary mode of exercise (cycling or treadmill). For each study, patient characteristics (disease condition, sample size, age); study characteristics (publication year, country of origin), change in peak oxygen consumption (VO$_2$peak); and exercise characteristics were extracted. Patient disease conditions were categorized as either CAD or CHF.

The change in VO$_2$max was calculated for each study by subtracting the pre- from post-rehab measurement. In one study, pre and post VO$_2$peak were calculated based on peaked watts reported from a cycling test.$^{29}$ The Foster equation was used for the calculation.$^{32}$ Mode, intensity, duration, and length of CR program was extracted because these variables were reported across all studies. The mode was categorized as either cycle or treadmill. Exercise intensity varied among studies regarding prescription variables (e.g., %HR$_\text{max}$, RPE, %VO$_2$peak) and range of intensities (45-80%). Therefore, intensity was extracted as a percentage of the reported variable from each study. The average duration of each session (in minutes) reported in each study was extracted. The length of each study was reported in number of weeks and ranged from two to twenty-four weeks. Number of exercise sessions completed (i.e., adherence)
during rehabilitation program was also considered, but due to lack of reporting across studies, the variable was not included.

**Bias and limitations**

A bias assessment was performed using the Cochrane Collaboration’s tool for assessing risk of bias.\(^{33}\) We assessed the included studies for selection bias (sequence generation and allocation sequence concealment), performance bias (blinding of participants), detection bias (blinding of outcome assessors), attrition bias (incomplete outcome data), reporting bias (selective outcome reporting), and other biases.

**Statistical analysis**

Using a random-effects model, a meta-analysis was conducted using Meta Essentials for Microsoft Excel.\(^{34}\) Effect size (ES) for change in VO\(_2\)peak was determined as mean difference of pre- and post-CR divided by pooled standard deviation. Each mean ES was calculated as a weighted mean difference with 95% CIs. As the difference in pre- and post-intervention means reflect between-subjects’ effects, Hedges’ g was adjusted to account for the dependence between scores. For lack of correlation coefficients for included studies, a conservative estimate of \(r = 0.7\) was used, as recommended by Rosenthal.\(^{35}\) A combined ES was then calculated (Hedges’ g), weighting studies using a random effects model consistent with the pre–post analysis. Differences in effect of CR on VO\(_2\)peak was assessed between the mode subgroup (cycling vs. treadmill). To adequately assess which subgroup had a larger change on VO\(_2\)peak, a random effects subgroup analysis was performed using a Z-test to compare the two effects.\(^{36}\) The difference in effect of CR on functional capacity was assessed within the cycling and
treadmill studies for the disease condition subgroup (CAD vs. CHF). To compare the role of disease state, a random effects subgroup analysis was performed using a Z-test to compare the two effects (CAD vs. CHF). Heterogeneity was assessed using the $I^2$ test and was used for significant heterogeneity ($I^2 > 50\%$). Meta-regression analysis was performed within each subgroup independently using study duration (in weeks) as a moderator (i.e., independent variable). Statistical significance was set at $p < 0.05$.

Results

Literature Search and Publication Bias

A total of 23 studies involving 600 patients were included in the review. The study characteristics are summarized in Table 1. The mean age was 60 years and 86% of subjects were males. Average session duration was $32 \pm 6$ minutes (cycling = $30 \pm 4$ min and treadmill = $35 \pm 7$ min) and only one study had an exercise duration of less than 30 minutes. The data for thirteen studies was collected in Europe, four studies were completed in Asia, the results for three studies were gathered in North America, and the remaining studies were done in Australia and South America.

Overall, the quality of included studies was moderate to low. The random sequence generation was defined in two included trials. Randomization techniques were not disclosed in any other studies. No description of allocation concealment was discussed in any study, reflecting an unknown risk for bias. Due to the nature of the exercise intervention, the participants were unblinded for the intervention in all the included studies, indicating a high risk of bias. There was no blinding of the outcome assessment (VO$_2$peak); however, it is unlikely that this caused bias. All included studies
reported all the clinically relevant outcomes. We also found significant other bias due to small sample size. The likelihood of publication bias was also assessed using Egger regression test with the test being statistically significant ($p = 0.026$).
Comparison of Treadmill and Cycle Ergometer Exercise during Cardiac Rehabilitation: A meta-analysis

Table 1: Study characteristics

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample size</th>
<th>Population</th>
<th>Mode</th>
<th>Exercise program</th>
<th>Length (weeks)</th>
<th>Δ VO₂ (ml/kg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belardinelli et al. 2001</td>
<td>59</td>
<td>CAD</td>
<td>Cycle</td>
<td>30 min, 70%</td>
<td>24</td>
<td>5.1</td>
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<tr>
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<td>Tread</td>
<td>60 min, 45%</td>
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<tr>
<td>Cardozo et al. 2015</td>
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<td>Tread</td>
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<td>Conraads et al. 2015</td>
<td>89</td>
<td>CAD</td>
<td>Cycle</td>
<td>47 min, 70-75%</td>
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<td>Cycle</td>
<td>30 min, 60%</td>
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<td>CHF</td>
<td>Tread</td>
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</table>
Comparison of Treadmill and Cycle Ergometer Exercise during Cardiac Rehabilitation: A meta-analysis

<table>
<thead>
<tr>
<th>Author</th>
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<th>Mode</th>
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<th>Δ VO₂ (ml/kg/min)</th>
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<tr>
<td>Lee et al. 2008</td>
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<tr>
<td>Moholdt et al.</td>
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<td>Niewland et al.</td>
<td>18</td>
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<td>Cycle</td>
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<td>6</td>
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</tr>
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<td>Roditis et al.</td>
<td>10</td>
<td>CHF</td>
<td>Cycle</td>
<td>45 min, 50%</td>
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<td>Rognmo et al.</td>
<td>9</td>
<td>CAD</td>
<td>Tread</td>
<td>41 min, 50-60%</td>
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<tr>
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Comparison of Treadmill and Cycle Ergometer Exercise during Cardiac Rehabilitation: A meta-analysis

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample size</th>
<th>Population</th>
<th>Mode</th>
<th>Exercise program</th>
<th>Length (weeks)</th>
<th>Δ VO₂ (ml/kg/min)</th>
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<td>CHF</td>
<td>Tread</td>
<td>30 min, 75%</td>
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<tr>
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<td>CHF</td>
<td>Tread</td>
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<td>Zheng et al. 2008</td>
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</tr>
</tbody>
</table>

Abbreviations: CAD, coronary artery disease; CHF, chronic heart failure; tread, treadmill; Δ VO₂, average change in peak oxygen consumption in study participants from baseline to discharge.

*The effect of cardiac rehabilitation on VO₂peak change*

All studies reported both a pre- and post-CR VO₂peak value. Only studies reporting data from either treadmill only or cycle only exercise were analyzed. Therefore, a total of twenty-three mean, weighted ESs were derived from twenty-three studies (see figure 2). Overall, CR induced a significant increase in VO₂peak from pre- to post-CR (g = 0.72; 95% CI, 0.47 – 0.96; p < 0.0001) (Figure 2). Significant heterogeneity (I² = 86%) was identified, and reflects differences identified in samples.
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Subgroup analysis of cycling vs. treadmill

A subgroup analysis was performed to determine if the effect of cycling or treadmill exercise had a larger effect on VO$_2$peak. There was a significant difference in ES between studies that used cycling, Hedges’ g = 0.85 (95% CI, 0.52 – 1.17, k=13) and studies that used treadmill exercise, Hedges’ g = 0.46 (95% CI, 0.22 – 0.70, k=8) (Figure 3). However, this comparison should be interpreted with caution, as the studies in both the cycle and treadmill groups demonstrated high heterogeneity ($I^2 = 88\%$ and $I^2 = 62\%$, respectively). The test for the difference between the two groups (cycle vs. treadmill) was significant ($Z = 34.41$, $p < 0.001$). Note that if the studies were not weighted by variance (which essentially means ignoring differences in sample size), a p-value obtained by doing a t-test of the differences for the two groups gives a p-value of 0.0458. This suggests that the studies with the stronger weights (larger sample sizes) were especially supportive of the hypothesis that cycling studies showed bigger changes in VO$_2$peak than treadmill studies.

Subgroup analysis of disease condition

Subgroup analyses were performed within the cycling and treadmill studies independently to determine the role of disease condition (CAD vs. CHF). For the cycling studies, there were a total of 14 studies with ten CAD and five for CHF. The effect between studies that recruited patients with CAD, Hedges g= 1.03 (95% CI, 0.65 – 1.42, k=9) and studies that recruited CHF patients, Hedges g=0.40 (95% CI, 0.09 – 0.71, k=4) was different. The test between groups (CAD vs. CHF) in the cycling studies was
significant (Z=23.95, p<0.001) demonstrating that CAD patients functional change after participation in cycling exercise is larger than in CHF patients. In the treadmill studies (n=9), the subgroup for CAD included six studies and CHF included three studies. The effect between CAD studies, Hedges’ g=0.33 (95% CI, 0.19 – 0.47, k=5) and CHF studies, Hedges’ g=0.94 (95% CI, 0.23 – 1.65, k=2) was different. The test between groups (CAD vs. CHF) in the treadmill studies was also significant (Z=-2.39, p<0.01) demonstrating that CHF patients functional change after participation in treadmill only exercise is larger than in CAD patients. There was no moderating effect of study duration (in weeks) on functional capacity for either the cycling or treadmill studies.

**Discussion**

The primary finding from the meta-analytical review is that single modality exercise (either cycling or treadmill) during CR results in a significant improvement in functional capacity (reported as VO₂peak) among cardiac patients. The reported ES herein was 0.72, indicating a moderate to large effect of single modality exercise on functional capacity. In subgroup analysis we aimed to compare the effect of cycling versus treadmill only exercise on functional capacity changes in CR. In our review, the ES for cycling only studies was 0.85 and treadmill yielded an ES of 0.46. The comparison demonstrated that when cycling is the sole mode of exercise there is a larger change in VO₂peak than treadmill only. In addition, within each of the subgroups (cycling and treadmill) the effect of disease condition was analyzed. Based on the results, CAD had a larger effect on VO₂peak than CHF patients in cycling studies, and CHF patients had a larger effect in treadmill studies. This indicates that CAD patients
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may experience better gains if cycling is the primary mode of exercise in CR while CHF patients could benefit more from treadmill-based exercise.

Peak oxygen uptake (VO$_2$peak), or functional capacity, is an important prognostic indicator among heart disease patients. It is a predictor of all-cause mortality, re-hospitalizations, and disease progression.$^{37,38}$ Therefore, the principal exercise outcome among cardiac patients enrolled in CR is an improvement in functional capacity. Previous meta-analytical studies examining the effect of exercise-based CR on functional capacity among heart disease patients have reported ESs ranging from 0.60 – 0.96.$^{39-43}$ The results from the current study align with those from previous meta-analyses. The extracted studies in our review were all randomized control trials, but only the exercise arms were used for analysis. While previous meta-analytical studies compared multimodal exercise in CR to a non-exercise control group. The goal of the current review was to determine the role of mode on functional capacity in CR, and therefore, studies using multimodal options were excluded. Only one study compared modes (cycling vs. treadmill), but the treadmill group in this study also performed cycling exercise, which excluded the group from our analyses.$^{10}$ In addition, the studies identified in table 1 used various comparison groups, such as a high intensity interval training (n=14), other form of exercise (n=3), or a non-exercise control (n=6). For these studies, only the single modality continuous exercise arms were extracted for analysis. Due to the lack of comparative studies examining single modality exercise (e.g., treadmill vs. cycle ergometer), the current review was a single-arm analysis.
In the subgroup analysis, the data suggests that stationary cycling as part of a CR program increases functional capacity to a greater extent than treadmill walking. Eight cycling studies measured an increase in VO$_2$peak of over 1 MET (3.5 ml/kg/min) from pre- to post-CR,$^{10-14,19,20,29}$ compared to one treadmill study.$^{22}$ It is difficult to determine the exercise prescription factors that may moderate the effect between cycling and treadmill studies. Both exercise duration and intensity are important factors that influence functional capacity outcomes in CR.$^{39,41,43,44}$ However, the average exercise session duration was similar between cycling and treadmill studies (30 ± 4 min and 35 ± 7 min, respectively); and, we were unable to determine the role of exercise intensity as ranges were reported for the majority of studies. Adherence is also an important predictor of CR outcomes, but we were unable to extract adherence rates across targeted studies. This highlights the lack of reporting of exercise prescription techniques and outcomes in the exercise-based CR literature.

In healthy populations, treadmill exercise elicits greater improvements in functional capacity when compared to cycling.$^{45}$ The primary reason is that treadmill exercise requires recruitment of both upper and lower body muscle groups. However, among cardiac disease patients, cycling may offer a safer exercise experience, especially among patients who are unfamiliar with using a treadmill. It is also preferred among patients with gait and/or balance problems. The added safety may allow patients to achieve higher exercise intensities during training sessions. In addition, it is common for patients to use handrail support during treadmill exercise for safety and balance purposes, which reduces the exercise response.$^{46}$ Cycling exercise eliminates the need for
additional support, and may allow the patient to exercise freely. It is common for clinical exercise physiologist to prescribe a variety of exercise modes for cardiac patients during a CR session. This may be in effort to reduce patient boredom, improve adherence, and overall attendance. These results indicate that emphasizing cycling exercise may lead to higher functional capacity outcomes in CR.

In effort to understand the role of disease condition (CAD or CHF), separate subgroup comparisons were made within the cycling and treadmill only studies. Our findings show that cycling may be a more effective mode among CAD patients, and that CHF may benefit more from treadmill-based CR. This could imply that CHF patients require, or respond better to total body exercise that recruits upper and lower body limbs, such as treadmill exercise. Further increases in functional capacity may be reached if combined upper limb exercise is emphasized in CR. Conversely, results from targeted cycling studies showed that CAD patients improve more than CHF patients when primarily engaging in a cycling-based program. It is difficult to explain the cause for the difference between groups, and it might be a result of CAD patients being able to sustain lower body exercise compared the CHF patients. Localized muscle fatigue would lead to cessation of, or reducing the workload of exercise leading to a lessened overall functional capacity outcome.

Application to Practice

Even though all exercise as part of CR has been shown to improve functional capacity among cardiac patients, the findings of the meta-analysis suggest that clinical exercise physiologist should prescribe exercise as part of CR depending on the cardiac...
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disease of each patient. For example, a CAD patient, should be cycling for most of the time during, or the total duration of each CR session; a CHF patient, walking on the treadmill can benefit the improvement in functional capacity and hence decrease mortality risk to a greater extent than cycling.

Limitations

There are number of potential limitations. First, there are limited studies that reported single modality exercise in CR. The majority of identified studies described general aerobic-based exercise, and were excluded from analyses. Second, no adequate comparisons of treadmill versus cycling in CR could be located, and therefore, the results reported herein are from a single-arm analysis. Third, there was evidence of high levels of statistical heterogeneity within all analyses among the included trials. This may be explained by both exercise program characteristics (e.g., duration, intensity, adherence), and patient characteristics (e.g., severity of disease, baseline measures). Fourth, the studies were moderately biased based on lack of randomization details and allocation concealment.

Summary

There was a moderate to large ES for the difference in improvement in functional capacity between cycling and walking. This leads to conclude that cycling exercise might be more beneficial in cardiac patients to improve functional capacity. However, the effect is larger in CAD patients and for CHF patients, treadmill walking might lead to greater improvements in functional capacity.
References


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Figure 1: PRISMA diagram of study identification.
Figure 2: Forest plot of mean change in maximal oxygen consumption (VO\textsubscript{2}max in ml/kg/min) with 95% confidence intervals (CI’s) for each study. The black circles represent standardized effect size of the change in VO\textsubscript{2}max; the bars that pass through the circles represent the 95% confidence intervals (CIs). The estimated increase in VO\textsubscript{2}max as a result of continuous training during CR was 0.72 ml/kg/min (95% CI: 0.47 to 0.96 ml/kg/min; p<0.0001). * indicates statistical significance (p<0.0001).
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Figure 3: a. Forest plot for the identified cycling studies in the meta-analysis. The estimates reported for each study are the means and 95% confidence intervals for the change in VO\textsubscript{2}\text{max} in ml/kg/min. The estimated increase in VO\textsubscript{2}\text{max} as a result of
continuous cycling exercise was 0.85 ml/kg/min (95% CI: 0.52 to 1.17 ml/kg/min; p<0.01). **b. Forest plot for the identified treadmill studies in the meta-analysis.** The estimates reported for each study are the means and 95% confidence intervals for the change in VO₂max in ml/kg/min. The estimated increase in VO₂max as a result of continuous treadmill exercise was 0.46 ml/kg/min (95% CI: 0.22 to 0.70 ml/kg/min; p<0.01). * indicates statistical significance (p<0.01); α shows significantly greater than treadmill exercise (p<0.05).
CHAPTER 3: METHODOLOGY

Study overview

Patient data were extracted from two databases, including 1. New Heart Center for Wellness, Fitness and Cardiac Rehabilitation (NHCR) exercise prescription database; and 2. The American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) outcomes database. Each patient was cross referenced across both databases to gather exercise and outcome data. Only the NHCR patients were accessible in the AACVPR database. Data were exported in an Excel file which was transferred into IBM SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp) for data analysis. The study protocol was reviewed and approved by the University of New Mexico Institutional Review Board for Human Subject Research.

Patients

Data from 180 patients who completed pre- and post- assessments at NHCR were extracted from the facility’s database and from the AACVPR database. The NHCR performed post-CR exercise testing after 36 exercise sessions. All patients had a diagnosis of cardiovascular disease (CVD). This was a chart review study with no interaction between the patients and the research team.

Exercise testing

The submaximal modified Atterbom treadmill test was completed by each patient at intake and discharge (post 36 sessions) to predict functional capacity. In the ramp
type protocol, the workload increased every minute. The speed and incline for each
minute of the Atterbom exercise test can be found in table one.

Table 1: Atterbom exercise test protocol

<table>
<thead>
<tr>
<th>Minute</th>
<th>Speed (mph)</th>
<th>Incline (%)</th>
<th>METs</th>
</tr>
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<td>1</td>
<td>0.5</td>
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<tr>
<td>2</td>
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</tr>
<tr>
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<td>2</td>
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<tr>
<td>9</td>
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<td>9</td>
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</tr>
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</table>

The termination criteria for the modified Atterbom exercise test used by NHCR
was reaching 75\% of estimated maximal heart rate using the Karvonen method (HR_{target} =
HR_{max} – HR_{rest}) (HR_{max} = 220 - age), and/or a 5 (heavy) on the 0-10 RPE scale. The
protocol used by NHCR staff is presented in appendix c. Functional capacity is measured
in metabolic equivalents (METs). The results of the exercise test were entered into the
AACVPR database by the NHCR clinical staff.
Exercise Prescription and Training

The NHCR center conducts CR exercise sessions on Monday, Wednesday, and Friday of each week. Patients were encouraged to attend three sessions per week over a 12-week training program. However, it commonly takes patients up to 16 weeks to complete their program (data from New Heart). A medical doctor was present in the facility on these days to enhance the safety of training. Based on the pre-CR exercise test, an individual exercise prescription was developed for each patient. The NHCR center staff developed a progressive exercise prescription for each patient enrolled in the program. There were no set goals for each session; rather over the course of 36 CR sessions patients were encouraged to increase exercise duration and intensity for improvement in functional capacity. For most patients, a final total duration of 60 minutes was set as goal over the 36 CR sessions. Various modes of aerobic exercise (e.g. treadmill, cycle ergometer, Nustep) were available for patients. Duration, intensity, and mode of exercise were documented and entered into the New Heart database. Frequency of training was determined from the extracted data.

Data extraction

Overview

Patient records were searched, and data were exported into Excel for further analysis. A master datafile was created that included all exercise prescription and outcome data.
**AACVPR database**

New Heart administered several questionnaires at intake and after completion of their CR program. These included: a “Rate my plate” nutrition questionnaire, the PHQ-9 depression scale (0-27 severity score), and the Dartmouth COOP Quality of Life scale. All scales have been standardized and accepted by the American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR). The results from each questionnaire were entered into the AACVPR database by the New Heart clinical staff each week. Additionally, the functional capacity recorded as peak METs from the pre- and post-CR exercise tests was available from the AACVPR database. The data matching the patients identified in the New Heart database were extracted into an Excel file. All data was deidentified after extraction.

**New Heart database - Exercise prescription data**

New Heart staff updated the exercise prescription data regularly throughout the patients 36 CR sessions. The data included a pre- and post-exercising heart rate and blood pressure measurement. Also included were exercise prescription variables recorded throughout each exercise session. The data were entered into the NHCR database by staff from which it was extracted for analysis.

**Extracted data for analysis**

1. Functional capacity change— The change from pre- to post-CR peak METs represents the improvement in aerobic fitness over 36-CR sessions. It is calculated by post-CR peak MET value minus pre-CR peak MET value.
2. Exercise intensity – The pre-CR peak MET value was used as baseline for intensity calculation. Treadmill walking METs were calculated based on treadmill walking speed and incline for each exercise session. The ACSM metabolic equation, \( VO_2 = (0.1 \times \text{speed}) + (1.8 \times \text{speed} \times \text{grade}) + 3.5 \), was used to determine \( VO_2 \) and then converted to METs (1 MET = 3.5 ml.kg.min). The MET value for each exercise session was divided by the pre-CR peak METs to calculate intensity.

3. Exercise duration – Minutes of treadmill walking and total exercise time per session in minutes were recorded.

4. Exercise frequency – Number of sessions completed weekly.

5. Determination of exercise variables across CR - The first exercise session was established as the baseline workload. The increase in the workload from session one was calculated as a percent from pre-CR METs. Sessions 12, 24 and 36 were averaged from a total of three sessions. Specifically, sessions 11, 12, 13 were averaged to represent exercising values of session 12. Sessions 23, 24, 25 were averaged to represent session 24. Session 34, 35, and 36 were averaged to represent session 36.

Data utilization

Data were entered into an Excel spreadsheet from which the data were copied into SPSS for statistical analysis. Each column represented another variable (e.g., duration, speed, incline, exercising METs) and each row typified all the variables for one patient.
**Statistical Analysis**

A multiple regression analysis was performed in SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp) to establish a regression model able to estimate peak METs from treadmill walking intensity (as a percentage based on the functional capacity achieved in the initial exercise test), duration of treadmill walking in minutes, and frequency (number per sessions attended weekly). The confounding variables were age, measured in years, and sex (male or female). Before any data was analyzed, multiple regression diagnostics were performed to guarantee the assumptions of normality of residuals, multi-collinearity, homogeneity of variance, and independence were met. Statistical outliers were identified during diagnostic evaluation, and analyses were conducted with and without the outliers to gauge the influence of the values on the calculated regression weights. Intensity, duration, and frequency were the covariates in the regression model. All continuous variables were centered before any statistical analysis. The Pearson product-moment correlation coefficient (r) was used to evaluate multicollinearity between independent variables included in the model, while the coefficient of determination ($r^2$) was used to evaluate model fit. Statistical significance was set as $p < 0.05$. 
CHAPTER 4: RESULTS

Patient characteristics

A total of 180 patient records were extracted from both the NHCR and AACVPR databases. All patients completed 36 CR sessions. Patients with missing peak metabolic equivalents (METs) pre- or post-CR data; who did not walk on the treadmill; or participated in CR twice were excluded from the study (n=29). From the 151 included patients, 103 were male and 48 were female. The patient characteristics are located in table one. The average functional capacity at pre-CR was 4.4 ± 1.9 METs. At post-CR the average value was 6.7 ± 1.7 METs with a mean increase (post minus pre) of 2.25 ± 1.7 METs for all patients (p < 0.01). Patients attended on average 2.7 ± 0.49 exercise sessions per week, with most patients completing three sessions weekly (n=102) and only one patient exercised one day per week. Over the 36 sessions of CR, patients averaged 10.92 ± 3.58 minutes of treadmill exercise at an intensity of 92 ± 25.7% of pre-CR peak METs. On average the total exercise duration including all exercise modalities, was 45.5 ± 9.0 minutes among all patients. The maximal exercise duration was recorded as 75 minutes, and each patient completed a minimal duration of 22 minutes.

Data used for multiple linear regression model

Patient data were extracted from pre- and post-CR records. The dependent variable for the regression model was determined as ‘change in peak METs’ which represents the change (either up or down) between pre-CR peak METs to post-CR peak METs. Exercise information for sessions 11, 12 and 13; 23, 24, and 25; and 34, 35, and 36 were averaged together. To analyze the progression across rehabilitation, the data were
analyzed every 12 sessions (1-12, 12-24, 24-36). Therefore, data for sessions 11, 12, and 13 were averaged together, and recorded as session 12. Data for sessions 23, 24, and 25 were averaged together, and recorded as session 24. Data for sessions 34, 35, and 36 were averaged together and recorded as session 36. The data for day one was not averaged and represents the actual exercise prescription completed in the first CR session.

Inconsistent intensity data for the different modalities was reported for each patient throughout rehabilitation. For some exercise modalities, no intensity variable was recorded. Therefore, treadmill walking was included as the sole mode of exercise and intensity was calculated based on peak METs recorded pre-CR. For example, intensities at sessions 1, 12 (average of 11,12, 13), 24 (average of 23, 24, 25), and 36 (average of 34, 35, 36) were all recorded as a percentage from the pre-CR peak MET value. To maintain consistency for calculating intensity, only treadmill exercise was inputted into the model. The average intensity for each session (1, 12, 24, and 36) were averaged together for each patient, and then all patients were combined to get an overall average (see table 1). Also, only treadmill duration was used as the duration of exercise in the regression equation. Total exercise duration was not included in the regression equation due to unknown intensity data for modalities other than treadmill walking. Treadmill duration was averaged for sessions 1, 12 (average of 11,12, 13), 24 (average of 23, 24, 25), and 36 (average of 34, 35, 36). Frequency was determined based on weekly sessions attended. When patients did not attend the same number of sessions weekly, the number of weeks in which they attended two sessions as well as three sessions was counted. Based of these counts, frequency was determined using the frequency which they exercised in most weeks.
Multiple linear regression for peak MET change

A multiple regression model was constructed to estimate change in peak METs from pre-CR to post-CR from the independent variables age, sex, frequency, average treadmill duration and average treadmill intensity. The following multiple regression equation was calculated:

Eq. 4.1
\[
\Delta\text{METs} = -1.288 - (0.024*\text{age}) + (0.331 (*1 \ if \ men, \ *0 \ if \ women)) + (0.417*\text{frequency}) + (0.109*\text{average treadmill duration}) + (0.029*\text{average intensity}) \ (R = 0.536, \ \text{SEE} = 1.44).
\]

The outliers did not drive the change in peak METs. Average treadmill duration and average intensity were significant predictors of change in peak METs (p < 0.05). Therefore, according to our model, changes in treadmill duration and intensity of treadmill walking are important factors that impact functional capacity change in CR. The resultant regression model, calculated with the potential outliers included, can be found in table two. The results of the multiple linear regression suggest that a significant proportion of the total variation in change in peak METs was predicted by age, sex, frequency, average treadmill duration and average treadmill intensity, F(5,151) = 11.714 , p < 0.001. Multiple R² indicates that approximately 29% of the variation in change in peak METs was predicted by the model.

Comparing individual patients

The highest increase in functional capacity achieved by a patient was 7.5 METs. From 151 patients, four had no change in functional capacity over 36 CR sessions and six
patients had a decline in peak METs (max = -2.1 METs). Among the patients that improved functional capacity over 36 CR sessions (141), the minimum increase was 0.4 METs. A male patient (67 years) improved functional capacity by 6.2 METs over 36 CR sessions while attending two sessions weekly. This patient walked on average the longest and at the highest intensity among all patients (25 min, 172% peak METs). In comparison, the patient with the highest improvement in functional capacity (7.5 METs) was also a 67 years old male patient who exercised three days weekly. This patient walked on average for 16 minutes per session at an intensity of 89% peak METs. The patient with the largest decline (-2.1 METs) in functional capacity exercised for 3.5 minutes on the treadmill, which was the shortest among all patients, at an intensity of 57% peak METs.
Table 1: Descriptive characteristics of sample (n = 151)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Sample (n=151)</th>
<th>Male (n=103)</th>
<th>Female (n=48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>68.2 ±8.6</td>
<td>67.8 ±8.6</td>
<td>69.0 ±8.8</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>170.0 ±10.0</td>
<td>174.1 ±8.0</td>
<td>161.5 ±8.5</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79.8 ±17.2</td>
<td>85.1 ±16.5</td>
<td>68.7 ±12.8</td>
</tr>
<tr>
<td>Intake METs</td>
<td>4.4 ±1.9</td>
<td>4.7 ±2.0</td>
<td>3.9 ±1.7</td>
</tr>
<tr>
<td>Discharge METs</td>
<td>6.7 ±1.7</td>
<td>7.0 ±2.7</td>
<td>5.9 ±2.3</td>
</tr>
<tr>
<td>Change METs</td>
<td>2.3 ±1.7</td>
<td>2.4 ±1.9</td>
<td>2.0 ±1.2</td>
</tr>
<tr>
<td>Frequency (days per week)</td>
<td>2.7 ±0.5</td>
<td>2.7 ±0.4</td>
<td>2.5 ±0.5</td>
</tr>
<tr>
<td>Average Treadmill Duration (min)</td>
<td>10.9 ±36</td>
<td>10.9 ±3.6</td>
<td>11.0 ±3.2</td>
</tr>
<tr>
<td>Average Intensity (% intake METs)</td>
<td>91.5 ±25.7</td>
<td>89.6 ±20.7</td>
<td>95.4 ±27.3</td>
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Assumptions

It was assumed that age would negatively predict change in functional capacity and would affect intensity and duration negatively. Age was negatively correlated with all independent variables but frequency, and it was significantly negatively correlated with average treadmill duration ($r = -0.136, p = 0.048$). This indicates that average treadmill duration was influenced by age. There was a higher increase in functional capacity in men but the difference was not significant. Frequency (attendance of sessions/week) was predicted to enhance functional capacity, however it was not a significant predictor of change in peak METs but was significantly correlated with sex ($r = 0.179, p = 0.014$). Residuals were examined for normality, and visual inspection of the
P-P plot confirmed that the assumption was met. Homoscedasticity was also inspected using a scatterplot, and the assumption was met. Multicollinearity was met based on evaluation of the variance inflation factor (1.19-1.60).

*Interpretation of individual predictors*

To fully explain the impact of each predictor on functional capacity, the standardized coefficients (β) have been interpreted below. Standardized coefficients indicate how much the dependent variable varies with an independent variable when all other independent variables are held constant.

**Age.** According to the model, age is a negative predictor of change in peak METs. Each year increase in age, the change in peak METs decreases by 0.024. Age is not a significant predictor of the change in peak METs (p = 0.082). Interpretation of the standardized β (-0.128) value reveals that as age increases by one standard deviation (8.6 years), peak METs decrease by 0.21 METs.

**Sex.** According to the model, the change in peak METs is higher in males than in females by 0.331. However, sex is not a significant predictor of change in peak METs (p = 0.2).

**Frequency.** According to the model, frequency is not a significant predictor of change in peak METs (p = 0.096); however, for each additionally day a patient exercises per week, the peak MET change is 0.42, which can be considered clinically meaningful. For example, if a patient exercises twice weekly, over the course of CR, functional capacity will increase by 0.84 METs. On the other hand, when a patient exercising four days weekly, peak METs will increase by 1.68. Even so this is not a significant predictor,
has the greatest impact on change in peak METs. There was no significant difference in frequency of training between sex. Interpretation of the standardized $\beta$ (0.121) value reveals that as frequency increases by one standard deviation (0.50 days), peak METs increase by 0.20 METs.

**Duration.** According to the model, the average duration of treadmill exercise is a significant predictor of change in peak METs ($p = 0.001$). Each additional minute of treadmill exercise yields an increase of 0.109 METs. For example, an increase in treadmill exercise by 10 minutes predicts an increase in functional capacity by 1.09 METs. Interpretation of the standardized $\beta$ (0.233) value reveals that as duration increases by one standard deviation (3.50 minutes), peak METs increase by 0.38 METs.

**Intensity.** Intensity was calculated as a percentage based of pre-CR peak METs. According to the model, treadmill exercise intensity is a significant predictor of change in peak METs ($p < 0.001$). A one percent increase in average exercise intensity (as percentage of baseline peak METs) predicts a peak MET increase by 0.029. More practically, a 35% increase in average exercise intensity across cardiac rehabilitation predicts a 1 MET increase. This is the equivalent of increasing a patient’s treadmill exercise intensity from 50% to 85% of their baseline peak MET value. Interpretation of the standardized $\beta$ (0.446) value reveals that as average intensity across 36 sessions of CR increases by one standard deviation (25%), peak METs increase by 0.78 METs.
Table 2: Multiple regression analysis of MET change versus average treadmill duration, average intensity, frequency, age and sex

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<th>Variable</th>
<th>Estimate</th>
<th>Std Error</th>
<th>$\beta$</th>
<th>p-value</th>
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<td>-</td>
<td>.351</td>
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<tr>
<td>Average Treadmill Duration</td>
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<td>.233</td>
<td>.001</td>
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<tr>
<td>Average Intensity</td>
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<td>.446</td>
<td>.000</td>
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<td>Age</td>
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<td>.014</td>
<td>-.125</td>
<td>.082</td>
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</tbody>
</table>
CHAPTER 5: DISCUSSION

The primary aim of this retrospective study was to determine the role of exercise prescription variables on functional capacity change among coronary artery disease (CAD) patients who completed 36 sessions of cardiac rehabilitation (CR). Understanding how the exercise prescription components affect the change in peak METs over a 36-session CR program is important as functional capacity, commonly measured as peak METs, is a valid indicator of mortality risk among cardiac patients (Carroll et al., 2007; Dunlay et al., 2014; Kavanagh et al., 2003). According to our model, average treadmill intensity and treadmill walking duration were significant predictors of functional capacity improvement when exercise frequency, patient age, and sex are held constant. More specifically and practically, the increase in treadmill exercise duration by an average of 10 minutes per session across 36 sessions predicts a 1 MET increase in functional capacity. Intensity in the current study was based on a percentage of peak treadmill METs achieved at patient intake. Our model suggests that an average increase in exercise intensity of 35% across 36 sessions yields a 1 MET increase in functional capacity. Researchers have demonstrated that every 1 MET increase in functional capacity from the start of CR is associated with a 40% reduction in all-cause mortality (Bachmann et al., 2018; Brawner et al., 2016). The results reported highlight the importance of both exercise duration, intensity, and ultimately the progression of cardiac patients on improving functional capacity across 36 sessions of prescribed CR.

Average intensity was a significant predictor of change in peak METs in the current model (p < 0.001). The average intensity of exercise was based on the METs achieved at the pre-CR exercise test, and calculated as percentage of this initial value.
Intensity was the strongest single predictor of change in functional capacity which is in accordance with previous meta-analysis findings (Uddin et al., 2016; Valkeinen, Aaltonen, & Kujala, 2010). For each percent increase in intensity, the change in peak METs increases by 0.029. Intensity increased on average by 12 percent between each twelve sessions period (sessions 1-12, sessions 12-24, sessions 24-36). On days one, twelve, twenty-four, and thirty-six, patients exercised on average at 74, 86, 98 and 104% of pre-CR peak METs, respectively. The average intensity for all 36 sessions among men and women was 89.6 ± 20.6 and 95.4 ± 27.2% of peak METs, respectively. The training intensity of patients was above the 40-80% VO₂peak recommended by the AACVPR (2013). In previous treadmill studies in which patients exercised at 50 to 60% of VO₂peak, functional capacity improved by 0.8 METs (Rognmo et al., 2004); and, by 0.1 METs when patients exercised between 70 to 75% VO₂peak (Cardozo et al., 2015). In the present study, patients, who exercised at the lower end (<60% VO₂peak) of the recommended intensity range, improved functional capacity by less than 0.9 METs, which corresponds with the findings of Rognmo et al. (2004). The patients who demonstrated the largest improvement in functional capacity in the current study exercised at an average intensity of over 100% of their pre-CR peak METs throughout all 36 CR sessions. The results should be interpreted with caution as intensity in the current study was based on the initial submaximal exercise test and determined based on only treadmill exercise during each sessions, and, therefore does not represent the intensity for the total exercise session.

It has been previously reported that higher intensities can lead to greater improvement in functional capacity in both healthy individuals and cardiac patients.
(Helgerud et al., 2007; Uddin et al., 2016). The implementation of high intensity interval exercise in CR has further demonstrated the role of intensity (Bacon, Carter, Ogle, & Joyner, 2013). Higher intensity intervals have a larger positive effect on functional capacity changes (Bacon et al., 2013). In addition, the progression of exercise intensity (45% to 124% VO2max) among a cohort of elderly men (60-70 yrs) across 12 weeks improved functional capacity by 2.4 METs (Makrides, Heigenhauser, & Jones, 1990). Researchers have also reported that cardiac patients who exercise below 3.5 METs on a treadmill during CR represent a group of cardiac patients at the highest mortality risk (Brawner et al., 2016). In summary, intensity was the strongest predictor of functional capacity changes in the current model, which further highlights the importance of clinical exercise physiologists encouraging patients to exercise at higher workloads.

Average treadmill walking duration was a significant predictor of change in peak METs (p < 0.001). The average treadmill exercise duration per session for the present study was similar for male and female patients (10.9 and 11.0 minutes, respectively). The patient with the longest average treadmill walking duration (25.1 minutes), improved functional capacity by 6.2 METs. The treadmill duration often reported in CR studies ranged from 30 to 45 minutes, and it must be noted that these previous studies all examined walking as the sole mode of exercise in a CR program (Blumenthal et al., 1988; Moholdt et al., 2011; Moholdt et al., 2009; Rognmo et al., 2004). Blumenthal et al. (1988) showed that CAD patients who walked for 30 to 45 minutes, three times weekly for 12 weeks achieved an average improvement of 0.94 METs. Similarly, patients who walked for either 35 or 46 minutes in each session, improved functional capacity by 0.7 METs regardless of the minutes walked (Moholdt et al., 2009; Moholdt et al., 2011).
Further, Rognmo et al. (2004) reported a 0.77 increase in peak METs among CAD patients who walked for an average of 41 minutes over 30 sessions. Reasons for the larger functional capacity change in the current study (2.2 METs) compared to previous studies (0.7 METs), could be the higher reported intensity in the present study (90% peak METs) vs. 50-60% reported on average in previous studies. In addition, only patients who completed a full 36 sessions were extracted for analyses while previous studies did not report adherence outcomes (Ades et al., 2017; Colbert et al., 2015; Martin et al., 2012).

There is commonly an inverse relationship between exercise intensity and duration, where the higher the intensity, the lower duration required to gain exercise benefits. The faster a patient walks and the higher the incline, the shorter the exercising bout. Accordingly, walking duration should be prolonged at lower treadmill workloads.

As mentioned earlier, every additional ten minutes of walking predicted a 1 MET increase as does a 35% increase in intensity over 36 CR sessions. In theory, according to this study’s data, if a CAD patient, no matter the age or sex, walks once weekly for 20 minutes and increases intensity by 35% of peak METs over 36 CR-sessions, a 3.4 MET improvement in functional capacity should be achieved post-CR.

Progression of exercise is necessary for continuous improvements in functional capacity. There are several variables that can be changed in order to progress a patient. The first variable that should be progressed according to ACSM is duration (American College of Sports Medicine, 2017). Hence, a patient should increase walking duration first followed by exercise intensity. Depending on the initial condition of the patient, a progression from 5 to 20 minutes should be initiated by the clinical exercise physiologist.
over the first ~12 sessions. As the initial walking intensity is at a lower to moderate level, increased intensity with no decline in duration should follow. Over the remainder of CR, regular increases in intensity should be applied. The higher the average intensity of exercise throughout CR, the more improvement in functional capacity.

Each additional day of exercise as part of CR improved peak METs by 0.4. This demonstrates the clinical importance of exercise frequency in CR. Le Bris et al. (2006) reported that CAD patients who exercised five days weekly had a greater increase in VO$_2$peak than patients who exercised on three days. This corresponds with the current findings. According to the model, for a patient who exercises three times weekly, peak METs would increase by 1.2 over 36-sessions; further, a patient would improve functional capacity by 2.0 METs when exercising five days weekly. The average frequency among patients was $2.66 \pm 0.48$ days per week. The bulk of the patients in the current study exercised for three sessions per week ($n = 102$). But, frequency was not a significant predictor in the model. However, an increase of peak METs by 0.4 for each day of training is clinically meaningful.

Age was a negative predictor of change in peak METs in the current model. With each additional year in age, the total change in peak METs was -0.24. A study measuring the effect of cycling exercise on CAD patients in the age ranges of 45-65, 65-75, and >75 years of age, measured a smaller increase in total work capacity with increase in age (Marchionni et al., 2003). In addition, age has has been identified as a clinical negative determinant for peak METs, which shows that the increase would be lower in elderly individuals (Gathright et al., 2019).
Similarly, sex was not a significant predictor of functional capacity in the current model; however, the increase in peak METs was greater in men than in women. It has been reported that baseline MET values predict change in functional capacity among men and women. Specifically, Cannistra and colleagues (1992) reported that women and men with pre-CR peak MET values of 4.1 and 5.5, respectively, increased to 4.9 METs in women and 6.4 METs in men post-CR. However, the relative increase was higher in women (20%) compared to men (14%), but men had an overall higher absolute change (Cannistra et al., 1992).

Limitations

1. Exercise prescription based on modalities other than treadmill could not be included in the study due to missing information (Watts) or incorrect recording of completed exercise.

2. Some patients exercised at the same treadmill workload (speed and incline) throughout most of their 36 CR sessions and did not increase duration, speed and/or incline to progress their exercising workload.

3. Total exercise duration was not put into the equation due to the inconsistent/missing exercise intensity reporting across all exercise modalities in all patients. Therefore, additional exercise modalities and duration were not accounted for in the model.

4. The impact of each exercise modality on improvement of functional capacity cannot be determined due to the missing intensity information as explained under the previous point.
5. Need another explaining that external validity may be at risk because of the inconsistencies of exercise prescription practice reported across CR centers.

**Conclusions**

Exercising as part of CR is important to improve functional capacity and hence may lead to a decreased mortality risk. Treadmill walking is a common exercise mode in CR, which has an impact on the change in functional capacity. The results of this study demonstrate the importance of treadmill walking intensity and duration for improving functional capacity throughout CR. Therefore, increasing the average treadmill duration and intensity across 36 sessions of CR is important. Even though, frequency was not a significant predictor in the current study, CVD patients should be active most days of the week, similar to the exercising guidelines for healthy individuals. This study demonstrates the importance of treadmill walking in achieving the primary goal of CR, which is an improvement in functional capacity.

**Future direction**

Based on the findings of the literature review and this study, more research has to be done to identify the exercise prescription components for CR with the greatest impact for CVD patients. This study looked at the influence of treadmill walking on improvement of functional capacity; however, most clinics incorporate several exercise modalities into a CR program. Therefore, the influence of each modality as part of a CR program has to be investigated. Further, there seems to be a discrepancy between the ideal exercise modality based on the CVD. Hence, a study measuring the improvement in functional capacity comparing treadmill to cycling exercise in CAD and chronic heart
failure (CHF) patients is necessary. There is limited research available analyzing the effect of frequency on functional capacity. Hence, more research is needed to determine the ideal frequency. Even though, research suggests that frequency influences functional capacity outcomes; it is unclear if one day per week is enough, or if there is a difference between exercising two and three days, or between three and five days per week.

Additionally, similar to the current study, the influence of prescription components on improvement in functional capacity among CHF patients needs to be investigated. As previous research suggest, there is less of an improvement in functional capacity among CHF patients, and treadmill walking seems to increase functional capacity more than cycling, a comparable analysis as in the current study should be perform for CHF patients.
APPENDICES

A. IRB approval letter

B. Letter of support from New Heart Center for Wellness, Fitness, and Cardiac Rehabilitation

C. Modified Atterbom exercise test protocol
Appendix A. IRB approval letter

DATE: January 7, 2019

IRB #: 21718
IRBNet ID & TITLE: 1383222-1 Identifying exercise prescription components that predict improvements in functional capacity among participants enrolled in cardiac rehabilitation

PILOT RECORD: Miaoh Zhu, PhD

SUBMISSION TYPE: New Project

BOARD DECISION: APPROVED
EFFECITIVE DATE: January 7, 2019
EXPIRATION DATE: N/A
RISK LEVEL: MINIMAL RISK
PROJECT STATUS: ACTIVE - OPEN TO ENROLLMENT

DOCUMENTS:
- Application Form - Project Information (UPDATED: 1/21/2018)
- CV/Resume - CV Zhu (UPDATED: 1/21/2018)
- HIPAA Waiver - Hipaa Waiver Request Form (UPDATED: 1/21/2018)
- Other - Scientific Review (UPDATED: 1/21/2018)
- Other - Project Team (UPDATED: 1/21/2018)
- Protocol - Protocol 121113 (UPDATED: 1/21/2018)
- Training Certifications - CITI Gerlich (UPDATED: 1/21/2018)
- Training Certifications - CITI Zhu (UPDATED: 1/21/2018)

Thank you for your New Project submission. The UNM IRB has APPROVED your submission. This approval is based on an acceptable risk/benefit ratio and a project design wherein the risks to participants have been minimized. This project is not covered by UNM's Federally-Approved Assurance (FWA) and will not receive federal funding.

The IRB has determined the following:
- Informed consent has been waived
- HIPAA is waived for all aspects of this project

This determination applies only to the activities described in the submission and does not apply should any changes be made to this research. If changes are being considered, it is the responsibility of the Principal Investigator to submit an amendment to this project and receive IRB approval prior to implementing the changes. A change in the research may disqualify this research from the current review category. If federal funding will be sought for this project, an amendment must be submitted so that the project can be reviewed under relevant federal regulations.
All reportable events must be promptly reported to the UNM IRB, including UNANTICIPATED PROBLEMS involving risks to participants or others, SERIOUS or UNEXPECTED adverse events, NONCOMPLIANCE issues, and participant COMPLAINTS.

If an expiration date is noted above, a continuing review or closure submission is due no later than 30 days before the expiration date. It is the responsibility of the Principal Investigator to apply for continuing review or closure and receive approval for the duration of the project. If the IRB approval for the project expires, all research related activities must stop and further action will be required by the IRB.

Please use the appropriate reporting forms and procedures to request amendments, continuing review, closure, and reporting of events for this project. Refer to the IRB website for forms and guidance on submissions.

Please note that all IRB records must be retained for a minimum of three years after the closure of this project.

The Office of the IRB can be contacted through mail at MSC02 1SSS, 1 University of New Mexico, Albuquerque, NM 87131-0001, phone at 505.277.2044, email at irb@unm.edu or in-person at 1805 Sigma Rd. NE, Albuquerque, NM 87106. You can also visit the IRB website at irb.unm.edu.
Appendix B. Letter of support from New Heart Center for Wellness, Fitness and Cardiac Rehabilitation

New Heart
Center for Wellness, Fitness, and Cardiac Rehabilitation
601 Lomas Blvd NE
Albuquerque, NM 87102

Dear Dr. Zuhl,

I am pleased to provide you, and your research team access to the New Heart Cardiac Rehabilitation patient database in support of the research project titled "Identifying exercise prescription components that predict improvements in functional capacity among participants enrolled in cardiac rehabilitation."

Our staff will train your research team members on navigating the database to collect appropriate exercise information. The information available will include: patient demographics, exercise prescriptions, and patient outcomes (pre and post rehab results). Your research team will be responsible for de-identifying the information. In addition to the training, we will also provide you with office/desk space to complete your work.

I am happy to provide additional information upon request. Best of luck in achieving your research results.

Sincerely,

Dr. Barry Ramo, M.D.
Medical Director
New Heart
Center for Wellness, Fitness, and Cardiac Rehabilitation
Appendix C. Modified Atterbom exercise test protocol

<table>
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Test Results

MET<sub>mod</sub>: _____
MET<sub>max</sub>: _____

HR<sub>rest</sub>: _____ bpm
HR<sub>target</sub>: _____ - _____ bpm

Symptoms
- Chest Discomfort
- Dizziness
- Dyspnea
- Fatigue
- None
- Other: _____

Recovery
1
2
3

Comments: ____________________________________________
REFERENCES


Garber, C.E., Blissmer, B., Deschenes, M.R., Franklin, B.A., Lamonte, M.J., Lee, I.M.,


myocardial infarction and percutaneous coronary intervention. *Journal of Rehabilitation Medicine, 40*(9), 776-779.