Feasibility of an Aerobic Exercise Intervention in Rectal Cancer Patients During and After Neoadjuvant Chemoradiotherapy

by

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ABSTRACT

Background: Standard treatment for locally advanced rectal cancer includes long-course neoadjuvant chemoradiotherapy (NACRT) followed by definitive surgery. NACRT improves outcomes but it is also associated with significant toxicities and declines in physical fitness that may impede treatment response, symptom management, and post-surgical recovery. Exercise may improve these outcomes but the feasibility of exercise during NACRT has not been established. **Purpose:** The primary objective of this phase I study was to assess the safety and feasibility of an aerobic exercise intervention in rectal cancer patients during and immediately after NACRT. Changes in objective health-related fitness and patient-reported outcomes were also tracked. **Methods:** Rectal cancer patients scheduled to receive long-course NACRT followed by definitive surgery were recruited from the Cross Cancer Institute in Edmonton Alberta. All participants received a supervised moderate-intensity aerobic exercise program 3 days/week during NACRT followed by unsupervised aerobic exercise for ≥ 150 minutes/week after NACRT. Feasibility was determined by eligibility rate, recruitment rate, follow-up rate, exercise adherence and adverse events. Health-related fitness outcomes and patient-reported outcomes were assessed pre-NACRT, post-NACRT and pre-surgery. **Results:** Of 45 rectal cancer patients screened, 32 (71%) were eligible and 18 (56%) of those were recruited. Follow-up post-NACRT was 83% for health-related fitness outcomes and 94% for patient-reported outcomes. Attendance for the supervised exercise sessions was 74%. The mean total aerobic exercise minutes/week was 222 ± 155 minutes for the unsupervised exercise. There were no adverse events resulting from the exercise intervention. Most health-related fitness outcomes and patient-reported outcomes declined during NACRT and recovered from post-NACRT to pre-surgery. For example, estimated VO_2 max declined from pre- to post-NACRT (mean change, -

1.3 ml/kg/min; 95% CI, -3.6 to 1.7) and then increased from post-NACRT to pre-surgery (mean change +2.4 ml/kg/min; 95% CI, -0.9 to 5.7). **Conclusion:** Aerobic exercise is safe and feasible for rectal cancer patients during and after NACRT. Phase II randomized trials to establish the harms and benefits of aerobic exercise in this patient population are warranted.

PREFACE

This thesis is an original work by Andria Morielli. The research project, of which this thesis is a part, received research ethics approval from the Health Related Ethics Board of Alberta (HREBA) -Cancer Committee, Project Name “Feasibility and Efficacy of Aerobic Exercise in Rectal Cancer Patients Receiving Neoadjuvant Chemoradiotherapy”, No. 26200, March 22, 2014.

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CHAPTER ONE

INTRODUCTION

Colorectal cancer is the third most common cancer diagnosis in Canada [1]. It is the second most common cancer death for males and the third most common cancer death for females in Canada [1]. The Canadian Cancer Society estimates 25,100 new cases of colorectal cancer and 9,100 deaths from the disease in 2015. [1]. The Canadian Cancer Society does not distinguish between cancer of the colon and cancer of the rectum, however, according to the American Cancer Society approximately two thirds of colorectal cancers occur in the colon and one third occur in the rectum [2]. Colon and rectal cancer both present major health problems, however, the anatomical location of the primary tumor and the patterns of disease spread are different and result in unique treatments. Rectal cancers act differently than colonic tumors specifically in terms of local recurrence [3].

Standard treatment for locally advanced rectal cancer usually includes long-course neoadjuvant chemoradiotherapy (NACRT) [3]. The use of long-course NACRT for patients with locally advanced moderate-to-high-risk operable rectal cancer leads to improvement in local control when compared to surgery alone, preoperative radiation or postoperative chemoradiation [3-5]. Despite a reduction in local recurrence rates, NACRT has not consistently demonstrated improvements in overall survival [4, 5]. Moreover, NACRT is associated with acute side effects including diarrhea, hand-foot-syndrome, cardiotoxicity, haematological toxicity, radiation dermatitis and fatigue [6, 7]. Although the late adverse effects of rectal cancer treatment seem to mainly be a result of surgery they may be worsened by preoperative radiotherapy or combined chemotherapy and radiotherapy [8]. The reported late effects include bowel dysfunction, urinary

dysfunction, sexual dysfunction, second cancers, decreased levels of physical and social functioning, persistent fatigue, body dissatisfaction and a reduction in quality of life [8, 9]. Interventions to manage these side effects and improve treatment and survival outcomes are highly desirable.

Exercise is increasingly being researched as a possible complementary behavioral intervention to help improve health-related fitness and quality of life in cancer survivors [10]. Exercise has been shown to be safe, help manage treatment side effects and improve quality of life (QoL) in several cancer patient groups receiving adjuvant chemotherapy or radiation therapy however, none of these studies have focused on rectal cancer patients receiving combined chemoradiotherapy [11]. Moreover, limited research has suggested that exercise during chemotherapy may improve chemotherapy completion rates [12, 13], treatment response [12], and even long-term disease-free survival [14]. Still, this evidence is limited to breast cancer patients receiving adjuvant chemotherapy. Additionally, there is some evidence that pre-surgical exercise interventions in cancer patients may improve cardiorespiratory fitness, QoL, and postsurgical complications nevertheless, none of these studies included patients receiving neoadjuvant treatment [15, 16]. Furthermore, a small number of exercise intervention studies for colorectal cancer survivors have demonstrated a short-term improvement in physical fitness, however, these studies included mostly colon cancer patients, did not analyze the data separately for rectal cancer patients, and did not include patients on active treatment [17]. No study to date has focused on rectal cancer patients receiving NACRT prior to definitive surgery [18].

West et al [19] demonstrated that NACRT has a negative impact on cardiovascular fitness in rectal cancer patients and that pre-surgical cardiovascular fitness in rectal cancer patients may predict postsurgical complications. Moreover, in the first exercise intervention study to date in

this clinical setting, West et al [18] showed that rectal cancer patients were able to exercise after NACRT and improve their cardiovascular fitness prior to surgery. Although their exercise intervention was limited to the post-NACRT/pre-surgery phase, these promising findings raise the possibility that initiating an exercise program during NACRT may result in even greater benefits for rectal cancer patients such as preventing declines in cardiovascular fitness, managing side effects, and potentially even improving treatment completion, treatment response, post-operative recovery, quality of life and survival. Given the substantial toxicity and side effects of NACRT, however, it is unclear if rectal cancer patients are willing and able to complete an exercise program during this difficult treatment.

The purpose of my thesis is to determine the feasibility and safety of an aerobic exercise intervention for rectal cancer patients both during NACRT and immediately after (prior to definitive surgery). The thesis consists of four chapters. Chapter One provided a brief overview of rectal cancer and it's treatments and existing research including: exercise interventions in rectal cancer patients, exercise interventions in colorectal cancer survivors, pre-surgical exercise interventions in cancer patients and exercise interventions during adjuvant cancer treatment. Chapter Two provides a more detailed review of these topics. For my study, I completed a supervised aerobic exercise intervention during NACRT followed by a mostly unsupervised aerobic exercise intervention after the completion of NACRT and prior to definitive surgery in rectal cancer patients. In chapter Three (Paper) I report the feasibility and safety of an aerobic exercise intervention for rectal cancer patients during and after NACRT. Finally, a general discussion of the findings, the strengths and limitations of the study, future directions and conclusions for this thesis can be found in Chapter Four.

CHAPTER TWO

LITERATURE REVIEW

This section provides a more detailed description of the treatments for rectal cancer and a more in depth review of the exercise literature. As noted in my introduction, no study to date has examined exercise in rectal cancer patients during NACRT. Moreover, only one exercise intervention study and two observational studies have been conducted exclusively in rectal cancer patients receiving long-course NACRT. Consequently, I have expanded my literature review to include studies of exercise in colorectal cancer patients, studies that addressed the same timing as my exercise intervention (i.e. pre-surgery and during active treatment), and studies that were focused on the same treatment type (i.e. combined chemoradiotherapy). When available, published systematic reviews were reviewed. If a published systematic review was not available, then the individual published studies were reviewed. The reviewed exercise literature in this section includes: (1) a systematic review of exercise interventions for colorectal cancer survivors, (2) the only exercise intervention study during neoadjuvant cancer treatment, to date, and an observational study during neoadjuvant cancer treatment, (3) a systematic review of pre-surgical exercise interventions with cancer patients, (4) a systematic review of exercise interventions during adjuvant cancer treatments, (5) and a systematic review of the effects of pre-surgical exercise interventions on post-operative outcomes not limited to cancer patients was also included in the literature review.

Rectal Cancer Treatments

External beam radiation therapy is the primary radiation technique used for neoadjuvant rectal cancer treatment and delivers radiation to the rectal wall (where the primary tumor lays) as well as to the complete mesorectum [20]. The long-course regimen delivers 1.8-2.0 Gray's (Gy)/day over 25-28 days on weekdays with a total dose of 45-54 Gy. The goal of preoperative

radiotherapy is to reduce the size of the tumor before a new evaluation for surgery [21]. Chemotherapy is often administered concurrently with long-course radiotherapy. Concurrent chemotherapy during radiotherapy has the added benefit of improved tumor downstaging compared with radiation alone [22]. Neoadjuvant infusional fluorouracil (5-FU) based chemotherapy or capecitabine (an oral agent converted in tissues to 5-FU) are most commonly used. Approximately 6-8 weeks after NACRT, patients are usually offered a total mesorectum excision (usually with an abdominal perineal resection or low anterior resection) followed by adjuvant chemotherapy and radiotherapy [3]. The advantages of neoadjuvant treatment include: sterilization of the mesorectal lymphatic channels helping to prevent spreading of tumor cells during mesorectal dissection, reducing the tumor size, exclusion of the small bowel from the radiation field (the small bowel often becomes tethered in the pelvis after surgery and is then subject to radiation exposure), improved response of well-oxygenated tumor and better functioning of the neorectum (which is not subjected to radiation) [20].

Exercise and Rectal Cancer

To date, only 3 studies have examined physical fitness in rectal cancer patients undergoing NACRT [18, 19, 23]. None of these studies included a randomized design and only one of them included an exercise intervention component. Moreover, the exercise intervention was introduced after the completion of NACRT.

One observational cohort study identified a decline in objective physical fitness after NACRT in twenty five rectal cancer patients who underwent cardiopulmonary exercise testing (CPET) before and after NACRT [19]. VO_2 peak and VO_2 at lactate threshold decreased significantly ($p<0.001$) from pre-to-post NACRT. Furthermore, reduced physical fitness was associated with post-operative in hospital morbidity. In another study, West et al [23] examined

the relationship between objectively measured physical fitness and in-hospital morbidity after rectal cancer surgery however, the sample was not exclusive to patients undergoing NACRT. Ninety five rectal cancer patients underwent CPET 2 weeks prior to NACRT or major surgery. Sixty-eight (72%) of these received NACRT. Lower VO_2 peak ($p<0.001$), VO_2 at lactate threshold ($p<0.001$), work rate at lactate threshold ($p<0.001$) and oxygen pulse at lactate threshold ($p=0.004$) were independently associated with increased odds of in-hospital morbidity. In addition, 3 patient who were unable to attain lactate threshold sustained in-hospital morbidity and their discharge was delayed. The authors reported no difference in pre-operative physical fitness or post-operative morbidity for patients who underwent NACRT vs. surgery alone however, the data wasn't shown.

In the only exercise intervention study exclusively for rectal cancer patients, West et al [24] examined how objectively measured physical fitness changed with NACRT and a structured responsive exercise training program (SRETP) for the 6 weeks immediately following NACRT. A secondary aim of the study was to assess the feasibility and safety of the exercise program. Thirty nine rectal cancer patients scheduled to receive NACRT were enrolled, 22 in the exercise intervention group and 17 in a non-randomized, parallel control group. Patients were automatically allocated to the exercise intervention however, if they were unable to commit to the exercise intervention or lived too far away (> 15 miles) they were asked to act as controls. The exercise program consisted 3 supervised (hospital-based) aerobic exercise sessions per week for a duration of 6 weeks. Exercise sessions consisted of 40 minutes (including a 5 minutes warm-up and 5 minute cool-down) of interval training on an electromagnetically braked cycle ergometer. The intensity of the intervals alternated from moderate (6x3 minutes at 80% of work rate at VO_2 at lactate threshold) to severe (6x2 minutes at 50% of the difference in work rates

between VO_2 peak and VO_2 at lactate threshold). The intensity of the exercise intervention was individualized according to the patient's cardiopulmonary exercise test results and was preloaded onto a chip-and-pin card which executed the intervals automatically. Physical fitness was assessed by a cardiopulmonary exercise test performed on an electromagnetically braked cycle ergometer. The test involved 2 minutes rest, 2 minutes of freewheel pedalling followed by ramped incremental pedalling until volitional termination. The ramp gradient was set to 10–25W min^{-1} based on a calculation using predicted freewheel oxygen uptake (VO_2), predicted VO_2 at peak exercise, height, and age. Outcome measures included VO_2 peak and VO_2 at lactate threshold, adherence to CPET testing and adverse events. Measurement timepoints included; Pre-NACRT, Post-NACRT and Post-SRETP. VO_2 peak and VO_2 at lactate threshold decreased ($p < 0.001$) from pre-to-post NACRT in all patients. From post-NACRT to post-SRETP, VO_2 peak ($p=0.0005$) and VO_2 at lactate threshold ($p<0.0001$) improved in the exercise group whereas VO_2 peak ($p=0.19$) and VO_2 ($p=0.204$) at lactate threshold continued to worsen in the control group. The mean (SD) adherence to the supervised exercise was 96 (5) %. Mean (SD) adherence to the CPET testing was 92 (14) % in the exercise group and 60 (5) % in the control group. There were no reported adverse events. The authors did not report eligibility and recruitment rate.

Exercise Interventions in Colorectal Cancer Patients

A recent systematic review and meta-analysis of exercise interventions for colorectal cancer patients found evidence for short-term improvements in physical fitness ($p<0.01$) after participation in aerobic exercise interventions compared with controls, however, no evidence was found for effects on quality of life ($p=0.53$) and fatigue ($p=0.38$) [17]. This evidence was from a small number of randomized controlled trials including 238 patients and should be

interpreted with caution. Furthermore, none of the studies reported safety data. Moreover, limited data was available for rectal cancer patients: 1 study was conducted exclusively in colon cancer patients [25] and the four other studies reported the number of patients with rectal cancer, however, the number of rectal cancer patient was small (5/23 (22%) [26], 8/49 (16%)[27], 20/46 (45%)[28], and 30/102 (29%)[29]) and none of the authors reported testing for an interaction by cancer site (colon vs. rectum). None of the reviewed studies were conducted in patients on active treatment. Based on the insufficient evidence and lack of safety data, the authors concluded that no recommendations for exercise intervention for colorectal cancer patients could be made.

Exercise Interventions during Neoadjuvant Cancer Treatment

To date, only two studies have examined physical fitness before and after neoadjuvant treatment for cancers other than rectal [16, 30]. The study participants were esophageal, gastric and breast cancer patients. Furthermore, all patients were undergoing neoadjuvant chemotherapy rather than NACRT. Moreover, only one of the studies included an exercise intervention component. In an observational cohort study, Jack et al [30] reported a reduction in VO2 peak and VO2 at lactate threshold ($p \leq 0.001$) from pre-to-post neoadjuvant chemotherapy in thirty nine esophageal and gastric cancer patients. These reductions were associated with an increased mortality risk one year post neoadjuvant chemotherapy and surgery ($p=0.014$) in patients who completed their neoadjuvant chemotherapy. Hornsby et al [16] evaluated the safety and efficacy of a moderate-to-high intensity aerobic exercise intervention in breast cancer patients receiving neoadjuvant chemotherapy. Twenty patients were randomly assigned to a 12 week aerobic exercise intervention (n=10) or control group (n=10). Patients in the aerobic exercise group exercised 3 days per week at 60-100% of VO2 peak for 15-45 minutes on a cycle ergometer in a supervised setting. Outcome measures included adverse events, CEPT, adherence to the exercise

prescription, attendance and the FACT-B. Three adverse events were reported during CPET; oxygen desaturation (<84%), anxiety attack and dizziness. One adverse event occurred during exercise training; unexplained leg pain. Adherence to the exercise prescription was 82% and attendance was 66%. VO2 increased in the aerobic exercise group and decreased in the control group. The between group difference was significant (p=0.001). Scores for the FACT-B increased by 11.1 points in the aerobic exercise group and decreased by 1.5 point in the control group however, the within and between group changes were non-significant (p=0.685). The authors also reported the eligibility rate, 2.1% (30/1445) and, the recruitment rate, 73% (20/30).

Pre-Surgery Exercise Interventions for Cancer Patients

Singh et al.[15] conducted a systematic review of pre-surgical exercise interventions for cancer patients. The review included 18 studies with a total of 966 patients. Nine studies were randomized controlled trials, 3 were controlled trials and 6 were single-group trials. Ten studies involved lung cancer, four prostate and the remaining four studies involved colon, colorectal and mixed cancers. None of the studies included patients receiving neoadjuvant treatment. Most of the studies prescribed aerobic exercise, however, the mode, frequency, duration and intensity of the exercise varied across studies. Based on the limited data, the authors concluded that pre-surgical interventions have a positive effect on rate of continence, functional walking capacity, cardiorespiratory fitness, quality of life and length of hospital stay. Much more research is needed to determine the feasibility of pre-surgical exercise interventions in cancer patients and their potential to improve clinical outcomes.

Exercise Interventions during Adjuvant Cancer Treatment

Mishra et al [11] conducted a systematic review of exercise interventions during active cancer treatments. The review included 56 randomized controlled trials with 4826 participants with breast, prostate, gynecologic, hematologic and other cancer diagnosis. Only 36 of the trials were conducted in patients currently undergoing active treatment: 10 trials included a mix of patients during and post treatment and 10 trials were conducted in patients scheduled to receive active treatment. The reviewed trials were all conducted during adjuvant cancer treatment. Furthermore, none of the studies focused on combined chemoradiotherapy. The type of exercise varied and included: walking by itself or in combination with cycling, resistance training, or strength training; resistance training; strength training; cycling; yoga and; Qigong. The results of the review suggest that exercise has a positive impact on overall health-related quality of life, physical functioning, role functioning, social functioning and fatigue. Exercise interventions resulted in a greater reduction in anxiety for breast cancer survivors compared to those with other cancer types. On the contrary, reductions in depression, fatigue and sleep disturbances and improvements in quality of life, emotional well-being, physical function and role function for cancers other than breast were greater. Furthermore, moderate-to-vigorous exercise interventions resulted in greater improvements in quality of life, physical functioning and greater reductions in anxiety, fatigue and sleep quality when compared to exercise interventions of light intensity.

Pre-Surgery Exercise Interventions

Santa Mina et al [31] systematically reviewed the effects of pre-surgical exercise on peri- and post-surgical outcomes. The review included 21 studies and a total of 1371 participants. Seventeen of the trials were randomized controlled trials. Most of the studies were conducted in orthopedics, however, 1 study was conducted in colon cancer patients, one in colorectal cancer

patients and one in lung cancer patients. The majority of the studies were mixed modality (aerobic and strength) and the median duration of the exercise intervention was 6 weeks (range 1-8). The majority of the studies suggested improvements in physical function, length of hospital stay, and pain following surgery however, they were not consistently effective at showing improvements in health-related quality of life or aerobic fitness. The authors advised the cautious interpretation of these results due to the modest methodological quality and significant risk of bias across the studies.

CHAPTER THREE

PAPER

Aerobic Exercise in Rectal Cancer Patients Receiving Neoadjuvant Chemoradiotherapy

Introduction

Standard treatment for locally advanced rectal cancer usually includes long-course neoadjuvant chemoradiotherapy (NACRT) consisting of 5-6 weeks of radiotherapy (45-54 Gy) with concurrent chemotherapy (capecitabine or 5-flurouracil) [3]. Approximately 6-8 weeks after NACRT, patients are usually offered a total mesorectal excision (usually with an abdominal perineal resection or low anterior resection) followed by adjuvant chemotherapy [3]. NACRT leads to improved local control compared to surgery alone, preoperative radiation, or postoperative chemoradiation [3-5] although the improvements in overall survival are less clear [4, 5]. Unfortunately, NACRT is associated with acute side effects including fatigue, diarrhea, radiation dermatitis, haematological toxicity, hand-foot-syndrome, and cardiotoxicity [6, 7]. Interventions to manage these side effects and improve treatment outcomes are highly desirable.

Exercise has been shown to manage treatment side effects and improve quality of life (QoL) in several cancer patient groups receiving adjuvant chemotherapy or radiotherapy [11]. Moreover, limited research has suggested that exercise during chemotherapy may improve chemotherapy completion rates [12, 13], treatment response [12], and even long-term disease-free survival [14]. Additionally, pre-surgical exercise interventions in cancer patients may improve cardiorespiratory fitness, QoL, and postsurgical complications [15]. Few studies to date, however, have examined the benefits and risks of exercise in rectal cancer patients receiving NACRT prior to definitive surgery [18].

West et al [19] demonstrated that NACRT in rectal cancer patients has a negative impact on cardiovascular fitness which may predict postsurgical complications. Moreover, in the first exercise intervention study in this clinical setting, West et al [18] showed that an exercise program initiated immediately after NACRT was feasible and improved cardiovascular fitness.

These promising findings raise the question of whether initiating an exercise program during NACRT may have even greater benefits for rectal cancer patients such as preventing declines in cardiovascular fitness, managing side effects, and improving treatment outcomes. Given the substantial toxicity and side effects of NACRT, however, it is unclear if rectal cancer patients would be willing and able to complete an exercise program during NACRT.

The primary purpose of this phase I study was to test the safety and feasibility of an aerobic exercise intervention in rectal cancer patients during and immediately after long-course NACRT. A secondary purpose was to track changes in objective health-related fitness outcomes and patient-reported outcomes over the course of the intervention. We hypothesized that rectal cancer patient initiating NACRT would be willing and able to complete an aerobic exercise program. To demonstrate feasibility, our prespecified criteria included a recruitment rate of ≥20%, an adherence rate to the supervised exercise program during NACRT of ≥70%, and a follow-up assessment rate for the health-related fitness outcomes and patient-reported outcomes at post-NACRT of ≥80%.

Material and Methods

Setting and Participants

The study was conducted at the Cross Cancer Institute and the University of Alberta in Edmonton, Canada. The study was approved by the Health Research Ethics Board of Alberta-Cancer Committee. Written informed consent was obtained from participants. Eligibility criteria were: (1) rectal cancer patients scheduled to receive long-course NACRT followed by definitive surgery; (2) between the ages of 18 and 80; (3) no uncontrolled medical or psychiatric conditions; (4) cleared to participate in exercise as determined by the Physical Activity Readiness Questionnaire for Everyone (PAR-Q+), and (5) able to understand English.

Design and Procedures

The study was a prospective single group design with assessments at pre-NACRT; post-NACRT and pre-surgery. Between April and October 2014, potentially eligible patients were identified and screened by their radiation oncologist and the study coordinator at the time of their first radiation consultation. The study coordinator followed-up with eligible patients by phone and scheduled interested patients for pre-NACRT testing.

Exercise Intervention

The exercise intervention was divided into two phases: (1) during NACRT and (2) post-NACRT. During NACRT, all exercise sessions were supervised by an exercise specialist at the Behavioral Medicine Fitness Center within walking distance of the cancer centre. During NACRT, the primary goal of the exercise intervention was to provide 18 supervised aerobic exercise sessions (3 sessions/week for 6 weeks). A secondary goal was to determine if patients could reach 150 minutes of moderate intensity aerobic exercise in 3 training sessions per week (50 minutes/session). The exercise prescription was individually tailored to each patient based on the results of the pre-NACRT treadmill test (40-60% of estimated VO_2 reserve). Each training session consisted of a five minute aerobic warm-up and cool-down at low-intensity. The intensity of the exercise sessions was monitored via heart rate monitors and the Borg rating of perceived exertion scale. Exercise modalities included treadmill, upright bike, recumbent bike, elliptical and rower. For each supervised session, the exercise trainer recorded attendance, duration, intensity and any symptoms during or immediately after the exercise.

After NACRT, patients were provided the option of continuing with the supervised exercise program, completing an unsupervised exercise program, or a combination. During this phase, the goal of the exercise program was to maintain (or achieve) 150 minutes of moderate intensity aerobic exercise/week. The exercise prescription was individually tailored to each

patient based on the results of the post-NACRT treadmill test (40-60% of estimated VO_2 reserve). Patients completing unsupervised exercise were provided with a heart rate monitor and were asked to record exercise frequency, intensity, duration and modality. The study coordinator completed weekly telephone calls or email follow-ups to assist and support patients in meeting the exercise prescription.

Demographic, Behavioral and Medical Characteristics

Demographic and behavioral variables were assessed using self-report and medical data was extracted from medical records. Baseline exercise was assessed by the Godin Leisure Time Exercise Questionnaire (GLTEQ) [32].

Feasibility Outcomes

The feasibility outcomes included eligibility rate, recruitment rate, follow-up rate, adherence rate, and adverse events. Exercise adherence during NACRT was assessed as the number of sessions attended out of 18. Exercise adherence after NACRT was self-reported using the GLTEQ [32]. All serious adverse events were tracked.

Timing of Assessments

Our goal was to complete the pre-NACRT assessment on the same day as the radiation planning session. The post-NACRT assessment was planned for within 1 week of completing NACRT or the same day as the last radiation session for out-of-town patients. The pre-surgery assessment was planned for 1-2 weeks prior to surgery. For out-of-town patients, the goal was to do the pre-surgery test when they were in town for other pre-surgical appointments.

Health-related Fitness Outcomes

Cardiorespiratory fitness was assessed using a multistage submaximal aerobic exercise test (modified Balke[33]) with direct measures of gas exchange and ventilation on a calibrated metabolic measurement system (Parvo Medics TrueOne® 2400; Sandy, UT, USA). The test was terminated at the end of the stage during which the patient reached 85% of their age predicted maximal heart rate. Functional aerobic capacity (VO_2 max) was estimated using the heart rate and volume of oxygen consumption (VO_2) from two submaximal stages of the treadmill test during which patients achieved steady-state heart rate between 115 and 150 beats per minute. The slope was then determined by calculating the ratio of the difference between the two submaximal VO_2 measures and the corresponding heart rates [33, 34]. The Senior's Fitness Test (SFT) was used to assess physical functioning [35, 36]. Body composition was assessed by height, weight, waist and hip circumference [37, 38].

Patient-reported Outcomes

Health-related QoL was measured using the Medical Outcomes Study Short-Form 36 [39]. Cancer specific QoL was measured using the Functional Assessment of Cancer Therapy-Colorectal (FACT-C) [40], the FACT-D (diarrhea) [41], and the FACT-F (fatigue) [42]. Psychosocial functioning was assessed by the Centre for Epidemiology Studies Short Depression Scale (CES-D) [43], the Spielberger State Anxiety Scale (SSAS) [44], the Perceived Stress Scale (PSS) [45], the Rosenberg Self-Esteem Scale (RSES) [46], and the Pittsburgh Sleep Quality Index (PSQI) [47].

Statistical Analysis

For this phase I feasibility study, our goal was to recruit between 10 and 20 patients. Given the small sample size and the three assessment time points, we only report the descriptive

statistics of mean change and 95% confidence interval (CI) for the health-related fitness outcomes and patient-reported outcomes between each pair of time points (pairwise) and also for a complete case analysis (listwise). Data were analysed using IBM SPSS Statistics version 22.

Results

Flow of patients through the trial is summarized in Figure 1. Between April 17 and October 23, 2014, 45 rectal cancer patients were assessed for eligibility, 32 (71%) were eligible, and 18 (56%) of these were recruited. All patients completed health-related fitness testing and patient-reported outcomes pre-NACRT. For logistical reasons, 8 of the recruited patients (44%) completed their pre-NACRT fitness test immediately after their first radiation treatment.

The baseline demographic, behavioral and medical profiles of the patients are reported in Table 1. NACRT included 50.4 to 54 Gy in 28-30 fractions on weekdays. Two patients (11%) had a delay ≥ 5 days in their radiation treatment because of enteritis. The mean cumulative dose of chemotherapy was 88% (range 57 to 100%) of the planned dose. Four patients (22%) needed a dose reduction for a mean of 7 days (range 5-8 days) because of hand-foot syndrome (n=3; 17%) or enteritis (n=1; 6%). Six patients (33%), two of which had a previous dose reduction, stopped chemotherapy for a mean of 9.5 days (range 5-13 days) because of hand-foot syndrome (n=4; 22%), diarrhea (n=1; 6%), enteritis (n=1; 6%), or cardiotoxicity (n=1; 6%). The median duration of NACRT was 6.5 weeks (range 6-8 weeks) and the median time between the completion of NACRT and definitive surgery was 8 weeks (range 5 to 11 weeks).

Follow-up Completion Rate

At post-NACRT, 15 patients (83%) completed health-related fitness outcomes and 17 (94%) completed the patient-reported outcomes. At pre-surgery, 14 patients (78%) completed

health-related fitness testing and patient-reported outcomes. In total, 13 patients (72%) completed the health-related fitness outcomes and 14 patients (78%) completed the patient-reported outcomes at all three timepoints.

Exercise Program Adherence

Including all 18 patients who initiated the study, the average attendance was 13.3 (74%) of the 18 supervised exercise sessions during NACRT. The most common reasons for missed supervised exercise sessions were hand-foot-syndrome, not feeling well, poor sleep, diarrhea, nausea, fatigue and logistical reasons. The mean duration of the supervised exercise sessions was 40 minutes ± 9 minutes and the intensity goal (moderate) was met 100% of the time. The most frequently used modality was the treadmill (67.4% of sessions). No adverse events were experienced during the supervised exercise sessions.

After NACRT, 14 of the 16 patients (88%) still on trial chose to complete their exercise in an unsupervised format. Self-report exercise was collected from 14 of 18 patients (78%) at the pre-surgery timepoint. The mean total aerobic exercise minutes was 222 ± 155 minutes with 10 of 14 (71%) patients still on trial meeting the aerobic exercise goal of ≥150 minutes/week.

Health-related fitness outcomes

Descriptive statistics for changes in health-related fitness are reported in Table 2. Estimated VO_2 max showed a pattern of decline from pre- to post-NACRT (mean change, -1.3 ml/kg/min; 95% CI, -3.6 to 1.7), recovery from post-NACRT to pre-surgery (mean change +2.4 ml/kg/min; 95% CI, -0.9 to 5.7), resulting in an overall slight improvement from pre-NACRT to pre-surgery (mean change, +1.1 ml/kg/min; 95% CI, -1.7 to 3.9). The 6-minute walk distance improved across all three timepoints achieving a mean change of +47 [95% CI, 14 to 80] from pre-NACRT to pre-surgery.

Patient-reported Outcomes

Descriptive statistics for changes in health-related QoL are presented in Table 3. The observed pattern showed a decline from pre to post-NACRT, and improvement from post-NACRT to pre-surgery for almost all outcomes. Changes in cancer specific QoL are reported in Table 4. The pattern showed a decline for almost all outcomes from pre to post-NACRT, and improvement from post-NACRT to pre-surgery. Changes in psychosocial functioning are reported in Table 5. Perceived stress and sleep quality worsened from pre- to post-NACRT and returned to near pre-NACRT levels from post-NACRT to pre-surgery.

Discussion

The 71% eligibility rate in our study suggests that the majority of rectal cancer patients receiving NACRT are eligible for an aerobic exercise intervention. Although there are no studies with which we can directly compare our results, this eligibility rate is similar to the 67% eligibility rate for a supervised exercise intervention in colorectal cancer survivors receiving adjuvant chemotherapy [48]. Moreover, it is higher than the eligibility rate for supervised exercise trials in breast and prostate cancer patients receiving chemotherapy (33 to 41%) [12, 49, 50] or radiotherapy (37%) [51]. In the only other exercise intervention study targeting pre-surgical rectal cancer patients, West et al [18] did not report the eligibility rate. The main reasons for ineligibility in our study were medical conditions that are significant contraindications to exercise. These eligibility criteria are unlikely to be addressed in any future trials. Nevertheless, the 71% eligibility rate suggests a clear subpopulation of rectal cancer patients initiating NACRT who are eligible for an exercise intervention.

The recruitment rate of 56% is higher than the 26-49% recruitment rates reported for other studies recruiting cancer patients to exercise interventions during adjuvant treatment [12,

48-51]. Again, the West et al [18] study did not report the recruitment rate or reasons for refusal. In our study, patients mainly refused because they were afraid it would be "too much" during NACRT. This reason may be addressed based on our feasibility data. The over 50% recruitment rate suggests strong interest of rectal cancer patients in an exercise intervention during NACRT.

Follow-up assessment rates for the health-related fitness testing and questionnaires were excellent at the post-NACRT timepoint (83% and 94% respectively) and even the pre-surgical time point (78% for all assessments). Other exercise trials in cancer patients receiving adjuvant treatments have reported slightly higher rates [12, 49, 50]. Moreover, West et al [18] reported an excellent follow-up rate for fitness assessments of 100% in the exercise group; however, only 59% of the control group provided follow-up fitness assessments, perhaps because the control group consisted of patients who declined exercise and/or were from out of town. In our study, it was feasible to get the out-of-town patients back for the pre-surgery fitness testing. The main reason for missed fitness testing was acute medical contraindications. This is not unexpected in this high-risk patient group.

The intention-to-treat adherence rate of 74% for the supervised exercise sessions is promising and similar to that reported in other trials during chemotherapy [12, 48-50]. Our study is one of the first to examine exercise adherence during combined chemoradiotherapy. The two most frequently reported barriers to exercise during NACRT were hand-foot-syndrome and logistical issues. Hand-foot-syndrome has not been previously reported as a barrier to exercise but it should be addressed in future trials with this patient population because exercise has the potential to exacerbate this symptom. Logistical issues included the necessity of scheduling out-of-town patients for their health-related fitness test on the same day as their first/last radiation session, which reduced the number of supervised exercise sessions available.

In the post-NACRT phase, only 2 of 16 (13%) patients were interested in continuing with supervised exercise. This finding contrasts with West et al [18] who reported a 96% adherence rate to a hospital-based supervised exercise program for rectal cancer patients after NACRT. One difference between the studies is that West et al [18] only included local patients in the exercise intervention whereas out-of-town patients were assigned to the control group. Nevertheless, even our local patients did not express interest in continuing with the supervised exercise after NACRT. Fortunately, adherence to the unsupervised exercise in the post-NACRT phase was excellent with a mean of over 200 minutes of self-reported aerobic exercise and 10 of 14 (71%) patients meeting the goal of ≥ 150 minutes/week. These data suggest that an unsupervised exercise program after NACRT may be feasible.

Our study suggested a small decline in cardiovascular fitness from pre- to post-NACRT of 1.3 ml/kg/min despite the aerobic exercise intervention. Without an exercise intervention, West et al [18] observed a decline in cardiovascular fitness during NACRT of 2.5 ml/kg/min suggesting that our aerobic exercise intervention may have prevented some of the decline in fitness during NACRT. Moreover, our study suggested an improvement in cardiovascular fitness from post-NACRT to pre-surgery of 2.4 ml/kg/min. In the study by West et al [18], the post-NACRT supervised exercise intervention resulted in an improvement of 2.7 ml/kg/min (compared to a decline of 1.3 ml/kg/min in a non-randomized control group), suggesting that our unsupervised exercise intervention may be as effective as supervised exercise for improving cardiorespiratory fitness in the post-NACRT setting. Furthermore, in another observational study, West et al [19] observed a decline in cardiovascular fitness from pre-NACRT to pre-surgery of 1.4 ml/kg/min compared to our suggested improvement of 1.1 ml/kg/min.

The pattern of decline for many of the generic and cancer-specific QoL outcomes exceeded the 2 to 3 point clinically meaningful difference during NACRT despite the aerobic exercise intervention. Without a proper comparison group, however, we are unable to comment on whether exercise blunted or worsened these declines in QoL during NACRT. Most QoL outcomes recovered after NACRT and some even exceeded pre-NACRT levels at the pre-surgery timepoint. Again, however, we are unable to determine if the exercise intervention amplified or blunted these gains in QoL after NACRT.

Our study has important strengths and limitations. To our knowledge, it is the first study to test an exercise intervention in rectal cancer patients during NACRT. Moreover, we closely tracked eligibility and recruitment rates to determine the potential reach of our intervention. Furthermore, the exercise intervention during NACRT was supervised and all adverse events and reasons for missed exercise sessions were documented. Finally, we used validated measures to assess health-related fitness and patient reported-outcomes. One limitation of our study is the lack of a comparison group. Nevertheless, given that our study was the first to test an exercise intervention in rectal cancer patients during NACRT, we felt that it was prudent to conduct a phase I study to determine the safety and feasibility of exercise before embarking on randomized controlled trials.

In conclusion, our phase I study demonstrated acceptable eligibility, recruitment, adherence, and follow-up rates during and after NACRT. Our study suggests that a supervised aerobic exercise intervention in rectal cancer patients during NACRT followed by an unsupervised exercise program after NACRT is safe and feasible. Phase II randomized trials are needed to establish the risks and benefits of aerobic exercise in this clinical setting.

Table 1. Baseline characteristics of rectal cancer patients participating in an aerobic exercise intervention during and after neoadjuvant chemoradiotherapy in Edmonton, Alberta, Canada, April 2014- February 2015 (n=18)

Variable	No. (%)	Mean (SD)
Demographic Profile		
Age		57.5 (10.4)
Sex, male	12 (66.7)	
Married	12 (66.7)	
Completed university/college	8 (44.4)	
Annual family income ≥$60,000	10 (55.6)	
Employment status		
Employed full/part-time	8 (44.4)	
Disability/sick leave	6 (33.3)	
Retired	4 (22.2)	
Ethnicity, Caucasian	17 (94.4)	
Behavioral/Health Profile		
Number of comorbidities		
None	7 (38.9)	
1-2	7 (38.9)	
≥3	4 (22.2)	
Most common comorbidities[1]		
High blood pressure	6 (33.3)	
High cholesterol	6 (33.3)	
Arthritis	5 (27.8)	
Weight, kg		84.2 (16.1)
BMI, kg/m^2		28.7 (4.2)
Healthy weight	2 (11.1)	
Overweight	10 (55.6)	
Obese	6 (33.3)	
Smoking Status		
Current smoker	3 (16.7)	
Ex-smoker	8 (44.4)	
Exercise Status		
Current aerobic exerciser	5 (27.8)	
Current resistance exerciser	4 (22.2)	
Aerobic exercise minutes		97 (131)
Cancer Profile		
Disease Stage (Pre NACRT)		
IIA	2 (11.1)	
IIIB	13 (72.2)	
IIIC	1 (5.6)	
IVA	1 (5.6)	
Unknown	1 (5.6)	
Ostomy (Pre-NACRT)	2 (11.1)	
Radiation Dose, Gy		52.5 (1.8)
Chemotherapy Protocol		
Oral Capecitabine	17 (94.4)	
Intravenous 5-Fluororacil	1 (5.6)	

Table 2. Changes in health-related fitness outcomes in rectal cancer patients participating in an aerobic exercise intervention during and after neoadjuvant chemoradiotherapy in Edmonton, Alberta, Canada, April 2014- February 2015

Outcome	Pre-NACRT (n=18) Mean (SD)	Post-NACRT (n=15) Mean (SD)	Pre-surgery (n=14) Mean (SD)	Pre- to post-NACRT (n=15) Mean change [95% CI]	Post-NACRT to pre-surgery (n=13) Mean change [95% CI]	Pre-NACRT to pre-surgery (n=14) Mean change [95% CI]
Vo_2max[1], ml/kg/min	24.7 (6.1)	23.3 (5.9)	26.0 (7.5)	-1.5 [-3.6 to 0.7]	2.9 [-0.2 to 6.0]	0.8 [-1.6 to 3.1]
Complete cases (n=11)	25.4 (7.0)	24.1 (6.1)	26.5 (8.2)	-1.3 [-3.6 to 1.7]	2.4 [-0.9 to 5.7]	1.1 [-1.7 to 3.9]
Vo_2max[1], L/min	2.06 (0.53)	1.88 (0.58)	2.18 (0.63)	-0.13 [-0.32 to 0.07]	0.26 [0.03 to 0.48]	0.09 [-0.08 to 0.24]
Complete cases (n=11)	2.1 (0.6)	2.0 (0.6)	2.2 (0.7)	-0.10 [-0.30 to 0.10]	0.22 [-0.01 to 0.45]	0.12 [-0.07 to 0.30]
Six-minute walk[2], m	533 (85)	560 (98)	581 (73)	19 [-21 to 58]	16 [-22 to 54]	37 [5 to 69]
Complete cases (n=11)	545 (101)	576 (105)	592 (66)	31 [-17 to 79]	16 [-22 to 54]	47 [14 to 80]
30-second chair stands, n	15 (5)	17 (6)	18 (6)	1 [0 to 3]	1 [-1 to 3]	3 [1 to 4]
Complete cases (n=13)	16 (6)	17 (6)	18 (6)	1 [-1 to 3]	1 [-1 to 3]	3 [1 to 4]
30-second arm curls, n	19 (4)	20 (4)	22 (5)	1 [-1 to 3]	2 [1 to 4]	2 [0 to 5]
Complete cases (n=13)	19 (4)	20 (5)	22 (5)	0 [-2 to 3]	2 [1 to 4]	2 [0 to 5]
Sit-and-reach, cm	-7.1 (10.2)	-8.9 (9.4)	-6.4 (10.5)	-1.8 [-4.3 to 0.8]	2.9 [-0.8 to 6.5]	0.5 [-4.0 to 4.9]
Complete cases (n=13)	-6.8 (10.7)	-8.9 (9.3)	-6.0 (10.9)	-2.1 [-5.0 to 0.9]	2.9 [-0.8 to 6.5]	0.8 [-4.0 to 5.6]
Back scratch[3], cm	-8.8 (9.3)	-7.9 (9.0)	-8.5 (9.0)	1.0 [-2.0 to 4.0]	-1.1 [-2.8 to 0.6]	-1.4 [-3.7 to 0.9]
Complete cases (n=12)	-6.5 (9.2)	-6.7 (9.6)	-7.8 (9.6)	-0.2 [-2.8 to 2.5]	-1.1 [-3.0 to 0.8]	-1.3 [-3.9 to 1.3]
8-foot- up-and- go, s	4.5 (0.6)	4.3 (0.6)	4.1 (0.5)	-0.1 [-0.4 to 0.2]	-0.2 [-0.5 to 0.2]	-0.4 [-0.6 to -0.1]
Complete cases (n=13)	4.4 (0.6)	4.2 (0.6)	4.1 (0.5)	-2.0 [-0.5 to 0.1]	-0.2 [-0.5 to 0.2]	-0.4 [-0.6 to -0.1]
Weight, kg	84.2 (16.1)	82.8 (17.3)	85.1 (18.5)	-1.4 [-2.7 to -0.1]	1.2 [0.5 to 1.9]	0.0 [-1.6 to 1.6]
Complete cases (n=13)	84.0 (17.7)	82.8 (18.6)	83.9 (18.6)	-1.3 [-2.8 to 0.2]	1.2 [0.5 to 1.9]	-0.2 [-1.9 to 1.6]
Waist circumference, cm	100.5 (14.5)	99.3 (15.8)	101.2 (15.5)	-1.4 [-3.0 to 0.1]	0.8 [-0.9 to 2.5]	0.1 [-1.9 to 2.1]
Complete cases (n=13)	101.0 (16.8)	99.9 (16.9)	100.7 (16.0)	-1.1 [-2.8 to 0.6]	0.8 [-0.9 to 2.5]	-0.3 [-0.9 to 2.5]

[1]Pre-NACRT n=16, post-NACRT n=13, pre-surgery n=14, pre- to post-NACRT n=12, post-NACRT to pre-surgery n=12, pre-NACRT to pre-surgery n=13.
[2]Pre-NACRT n=18, post-NACRT n=14, pre-surgery n= 13, pre- to post-NACRT n=14, post-NACRT to pre-surgery n=11, pre-NACRT to pre-surgeryn=13.
[3]Pre-NACRT n=16, post-NACRT n=15, pre-surgery n=14, pre- to post-NACRT n=14, post-NACRT-pre-surgery n=13, pre-NACRT to pre-surgery n=13.

Table 3. Changes in health-related quality of life in rectal cancer patients participating in an aerobic exercise intervention during and after neoadjuvant chemoradiotherapy in Edmonton, Alberta, Canada, April 2014- February 2015

Outcome	Pre-NACRT (n=18) Mean (SD)	Post-NACRT (n=17) Mean (SD)	Pre-surgery (n=14) Mean (SD)	Pre- to post-NACRT (n=17) Mean change [95% CI]	Post-NACRT to pre-surgery (n=14) Mean change [95% CI]	Pre-NACRT to pre-surgery (n=14) Mean change [95% CI]
Physical functioning	49.2 (6.2)	45.9 (5.0)	52.5 (4.9)	-3.3 [-6.3 to -0.4]	7.1 [3.4 to 10.8]	2.4 [-1.3 to 6.1]
Complete cases (n=14)	50.1 (5.9)	45.5 (5.5)	52.5 (4.9)	-4.7 [-7.2 to -2.1]	7.1 [3.4 to 10.8]	2.4 [-1.3 to 6.1]
Role-physical[1]	44.9 (10.1)	35.2 (8.0)	47.1 (7.6)	-9.8 [-15.1 to -4.6]	10.5 [5.7 to 15.3]	0.5 [-5.7 to 6.7]
Complete cases (n=14)	46.5 (10.2)	36.6 (8.1)	47.1 (7.6)	-10.0 [-16.0 to -4.0]	10.5 [5.7 to 15.3]	0.5 [-5.7 to 6.7]
Bodily pain	51.2 (11.6)	45.5 (10.8)	53.6 (6.7)	-6.3 [-12.9 to 0.4]	7.7 [2.3 to 13.2]	0.5 [-4.6 to 5.7]
Complete cases (n=14)	53.0 (9.9)	45.9 (11.4)	53.6 (6.7)	-7.2 [-15.0 to 0.6]	7.7 [2.3 to 13.2]	0.5 [-4.6 to 5.7]
General health	47.3 (8.6)	43.2 (10.9)	49.9 (6.5)	-4.9 [-9.4 to -0.3]	5.4 [1.1 to 9.8]	1.6 [-3.8 to 7.0]
Complete cases (n=14)	48.3 (9.0)	44.5 (10.6)	49.9 (6.5)	-3.8 [-8.8 to 1.1]	5.4 [1.1 to 9.8]	1.6 [-3.8 to 7.0]
Vitality	49.7 (10.4)	44.4 (10.1)	57.4 (6.8)	-6.2 [-9.9 to -2.6]	10.9 [4.3 to 17.6]	5.3 [-0.9 to 11.6]
Complete cases (n=14)	52.1 (9.0)	46.5 (9.6)	57.4 (6.8)	-5.6 [-9.6 to -1.6]	10.9 [4.3 to 17.6]	5.3 [-0.9 to 11.6]
Social functioning	46.5 (9.5)	38.9 (11.4)	53.0 (5.8)	-7.4 [-14.0 to -0.8]	12.9 [6.0 to 19.7]	4.3 [-1.1 to 9.7]
Complete cases (n=14)	48.7 (8.2)	40.1 (11.8)	53.0 (5.8)	-8.6 [-16.5 to -0.7]	12.9 [6.0 to 19.7]	4.3 [-1.1 to 9.7]
Role-emotional[1]	41.1 (12.0)	45.6 (11.4)	53.7 (4.5)	4.7 [-3.2 to 12.7]	6.4 [1.1 to 11.7]	10.8 [3.1 to 18.5]
Complete cases (n=14)	42.8 (12.4)	47.3 (11.7)	53.7 (4.5)	4.4 [-4.5 to 13.4]	6.4 [1.1 to 11.7]	10.8 [3.1 to 18.5]
Mental health[1]	49.9 (9.7)	51.7 (9.6)	54.4 (6.4)	1.0 [-3.2 to 5.2]	-0.0 [-3.1 to 3.1]	1.2 [-2.0 to 4.4]
Complete cases (n=14)	53.2 (5.4)	54.4 (7.5)	54.4 (6.4)	1.2 [-2.8 to 5.2]	-0.0 [-3.1 to 3.1]	1.2 [-2.0 to 4.4]
Physical health component	49.4 (8.2)	40.3 (8.0)	49.7 (4.9)	-9.2 [-12.8 to -5.7]	9.5 [5.6 to 13.4]	-0.4 [-4.6 to 3.7]
Complete cases (n=14)	50.1 (8.3)	40.2 (8.1)	49.7 (4.9)	-9.9 [-14.2 to -5.7]	9.5 [5.6 to 13.4]	-0.4 [-4.6 to 3.7]
Mental health component	45.8 (8.9)	47.9 (11.0)	55.7 (4.4)	1.5 [-3.1 to 6.1]	5.0 [0.8 to 9.3]	7.0 [3.9 to 10.1]
Complete cases (n=14)	48.7 (5.9)	50.7 (9.2)	55.7 (4.4)	2.0 [-3.0 to 6.9]	5.0 [0.8 to 9.3]	7.0 [3.9 to 10.1]

[1]Pre-NACRT n=17, post-NACRT n=17, pre-surgery n= 14, pre- to post-NACRT n=16, post-NACRT to pre-surgery n=14, pre-NACRT to pre-surgery n=14.

Table 4. Changes in cancer-specific quality of life in rectal cancer patients participating in an aerobic exercise intervention during and after neoadjuvant chemoradiotherapy in Edmonton, Alberta, Canada, April 2014- February 2015

Outcome	Pre-NACRT (n=18) Mean (SD)	Post-NACRT (n=17) Mean (SD)	Pre-surgery (n=14) Mean (SD)	Pre- to post-NACRT (n=17) Mean change [95% CI]	Post-NACRT to pre-surgery (n=14) Mean change [95% CI]	Pre-NACRT to pre-surgery (n=14) Mean change [95% CI]
Physical well-being	22.9 (4.3)	17.5 (7.3)	25.9 (1.2)	-5.5 [-9.1 to -1.9]	8.3 [4.0 to 12.6]	2.3 [0.4 to 4.1]
Complete cases (n=14)	23.6 (4.1)	17.6 (8.0)	25.9 (1.2)	-6.0 [-10.1 to -1.9]	8.3 [4.0 to 12.6]	2.3 [0.4 to 4.1]
Social well-being	24.0 (3.7)	29.4 (5.7)	34.0 (2.2)	5.1 [2.8 to 7.3]	2.9 [0.8 to 4.9]	8.4 [6.7 to 10.1]
Complete cases (n=14)	25.5 (2.4)	31.1 (4.5)	34.0 (2.2)	5.6 [2.9 to 8.2]	2.9 [0.8 to 4.9]	8.4 [6.7 to 10.1]
Emotional well-being	19.0 (3.9)	13.6 (2.3)	14.1 (1.3)	-5.5 [-7.3 to -3.7]	0.1 [-1.2 to 1.3]	-6.1 [-7.5 to -4.7]
Complete cases (n=14)	20.2 (2.8)	14.0 (2.3)	14.1 (1.3)	-6.2 [-8.0 to -4.4]	0.1 [-1.2 to 1.3]	-6.1 [-7.5 to -4.7]
Functional well-being	21.6 (5.3)	17.5 (4.4)	23.2 (3.5)	-4.2 [-6.7 to -1.7]	4.2 [1.7 to 6.7]	-0.1 [-1.4 to 1.2]
Complete cases (n=14)	23.3 (4.3)	19.0 (4.6)	23.2 (3.5)	-4.3 [-7.3 to -1.3]	4.2 [1.7 to 6.7]	-0.1 [-1.4 to 1.2]
Colorectal subscale	21.3 (4.3)	17.8 (4.4)	23.9 (3.0)	-3.6 [-5.5 to -1.7]	5.3 [2.7 to 7.9]	2.0 [-0.9 to 4.9]
Complete cases (n=14)	21.6 (3.9)	18.6 (4.5)	23.9 (3.0)	-3.3 [-5.3 to -1.3]	5.3 [2.7 to 7.9]	2.0 [-0.9 to 4.9]
Diarrhea subscale	34.9 (7.1)	29.5 (9.5)	36.9 (7.6)	-5.0 [-9.0 to -0.9]	5.1 [0.5 to 9.8]	1.5 [-2.5 to 5.5]
Complete cases (n=14)	35.3 (6.3)	31.7 (8.2)	36.9 (7.6)	-3.6 [-8.2 to 0.9]	5.1 [0.5 to 9.8]	1.5 [-2.5 to 5.5]
Fatigue subscale	38.7 (9.1)	29.9 (9.5)	45.2 (5.2)	-9.4 [-14.0 to -4.7]	13.2 [4.9 to 21.5]	4.1 [-1.0 to 9.3]
Complete cases (n=14)	41.1 (8.4)	32.0 (14.7)	45.2 (5.2)	-9.1 [-14.7 to -3.4]	13.2 [4.9 to 21.5]	4.1 [-1.0 to 9.3]
FACT-C	108.8 (15.9)	95.8 (20.5)	121.0 (8.2)	-13.7 [-20.9 to -6.6]	20.7 [10.9 to 30.5]	6.5 [0.2 to 12.8]
Complete cases (n=14)	114.5 (11.6)	100.2 (19.7)	121.0 (8.2)	-14.2 [-22.5 to -5.9]	20.7 [10.9 to 30.5]	6.5 [0.2 to 12.8]
TOI-C	65.8 (11.3)	52.8 (15.2)	72.9 (6.1)	-13.3 [-19.1 to -7.4]	17.8 [9.5 to 26.1]	4.2 [-0.5 to 8.9]
Complete cases (n=14)	68.7 (9.7)	55.1 (15.6)	72.9 (6.1)	-13.6 [-20.4 to -6.8]	17.8 [9.5 to 26.1]	4.2 [-0.5 to 8.9]

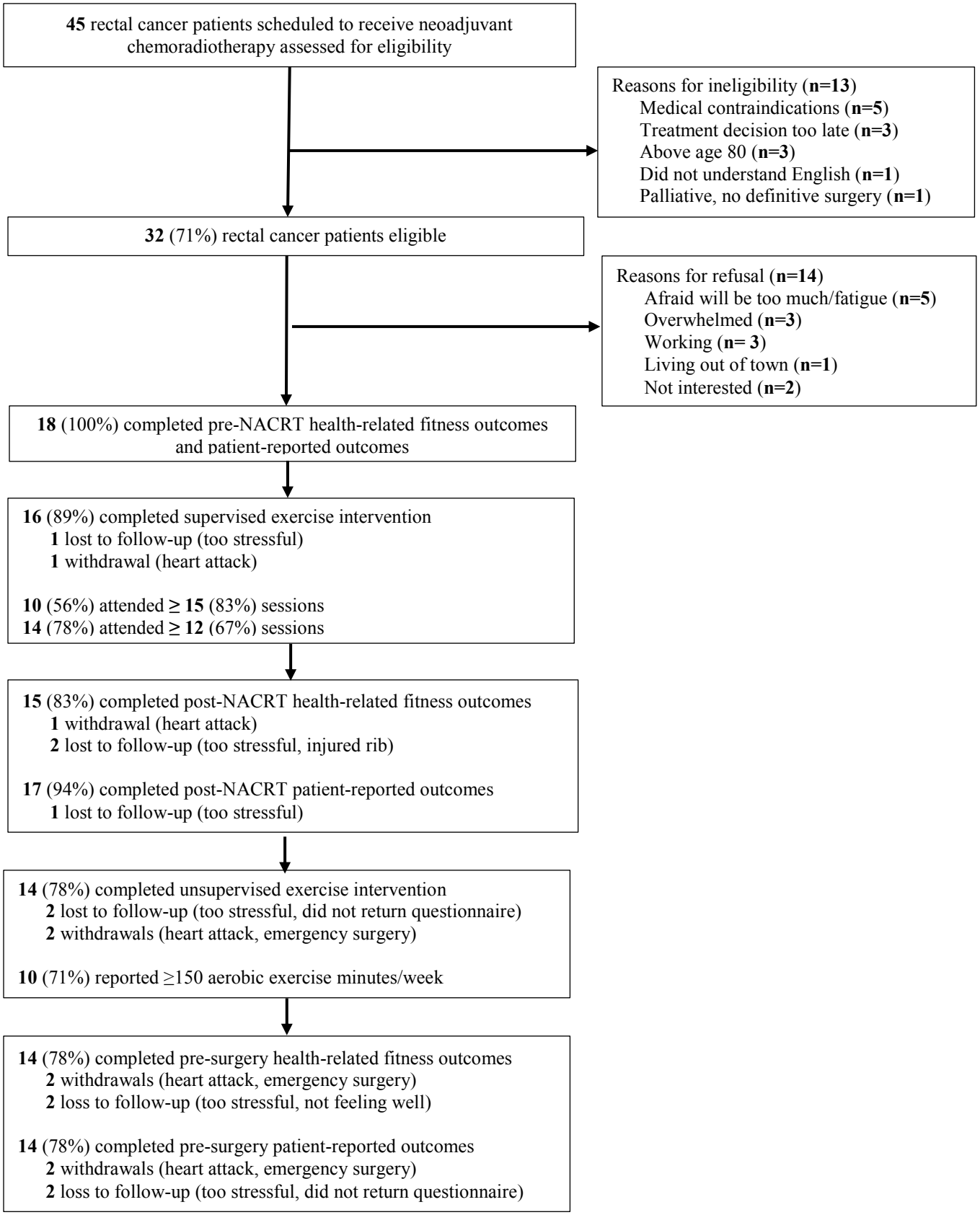
Abbreviations: FACT-C, Functional Assessment of Cancer Therapy – Colorectal Symptom Index; TOI-C, Trial Outcome Index- Colorectal

Table 5. Changes in psychosocial functioning in rectal cancer patients participating in an aerobic exercise intervention during and after neoadjuvant chemoradiotherapy in Edmonton, Alberta, Canada, April 2014- February 2015

Outcome	Pre-NACRT (n=18) Mean (SD)	Post-NACRT (n=17) Mean (SD)	Pre-surgery (n=14) Mean (SD)	Pre- to post-NACRT (n=17) Mean change [95% CI]	Post-NACRT to pre-surgery (n=14) Mean change [95% CI]	Pre-NACRT to pre-surgery (n=14) Mean change [95% CI]
Depression	4.8 (3.9)	5.7 (4.9)	2.6 (3.4)	1.2 [-0.2 to 2.5]	-1.9 [-3.5 to -0.4]	-0.8 [-1.6 to 0.0]
Complete cases (n=14)	3.4 (2.9)	4.5 (4.5)	2.6 (3.4)	1.1 [-0.4 to 2.7]	-1.9 [-3.5 to -0.4]	-0.8 [-1.6 to 0.0]
Anxiety	17.9 (7.1)	17.1 (6.2)	14.6 (4.5)	-0.1 [-2.4 to 2.2]	-0.9 [-3.1 to 1.3]	-0.7 [-1.9 to 0.4]
Complete cases (n=14)	15.4 (4.6)	15.6 (5.7)	14.6 (4.5)	0.2 [-2.0 to 2.4]	-0.9 [-3.1 to 1.3]	-0.7 [-1.9 to 0.4]
Perceived stress	16.0 (9.1)	17.5 (8.7)	11.9 (6.4)	2.5 [-1.0 to 6.0]	-3.9 [-8.1 to 0.3]	-0.7 [-3.8 to 2.4]
Complete cases (n=14)	12.6 (6.3)	15.9 (8.7)	11.9 (6.4)	3.2 [-0.6 to 7.0]	-3.9 [-8.1 to 0.3]	-0.7 [-3.8 to 2.4]
Self-esteem	34.3 (4.9)	35.0 (4.3)	37.1 (4.0)	0.3 [-0.8 to 1.4]	1.2 [-0.9 to 3.3]	1.4 [-0.8 to 3.7]
Complete cases (n=14)	35.6 (4.3)	35.9 (3.8)	37.1 (4.0)	0.2 [-1.2 to 1.6]	1.2 [-0.9 to 3.3]	1.4 [-0.8 to 3.7]
Sleep quality	6.1 (3.3)	9.0 (5.5)	5.6 (3.2)	2.8 [0.7 to 4.9]	-2.1 [-4.0 to -0.3]	0.1 [-1.6 to 1.7]
Complete cases (n=14)	5.6 (2.9)	7.8 (5.3)	5.6 (3.2)	2.2 [-0.1 to 4.5]	-2.1 [-4.0 to -0.3]	0.1 [-1.6 to 1.7]

FIGURE CAPTION

Figure 1. Flow of participants through the trial, Edmonton, Alberta, Canada, April 2014-February 2015


45 rectal cancer patients scheduled to receive neoadjuvant chemoradiotherapy assessed for eligibility
Reasons for ineligibility (**n=13**)
Medical contraindications (**n=5**)
Treatment decision too late (**n=3**)
Above age 80 (**n=3**)
Did not understand English (**n=1**)
Palliative, no definitive surgery (**n=1**)
32 (71%) rectal cancer patients eligible
Reasons for refusal (**n=14**)
Afraid will be too much/fatigue (**n=5**)
Overwhelmed (**n=3**)
Working (**n= 3**)
Living out of town (**n=1**)
Not interested (**n=2**)
18 (100%) completed pre-NACRT health-related fitness outcomes and patient-reported outcomes
16 (89%) completed supervised exercise intervention
1 lost to follow-up (too stressful)
1 withdrawal (heart attack)
10 (56%) attended ≥ **15** (83%) sessions
14 (78%) attended ≥ **12** (67%) sessions
15 (83%) completed post-NACRT health-related fitness outcomes
1 withdrawal (heart attack)
2 lost to follow-up (too stressful, injured rib)
17 (94%) completed post-NACRT patient-reported outcomes
1 lost to follow-up (too stressful)
14 (78%) completed unsupervised exercise intervention
2 lost to follow-up (too stressful, did not return questionnaire)
2 withdrawals (heart attack, emergency surgery)
10 (71%) reported ≥150 aerobic exercise minutes/week
14 (78%) completed pre-surgery health-related fitness outcomes
2 withdrawals (heart attack, emergency surgery)
2 loss to follow-up (too stressful, not feeling well)
14 (78%) completed pre-surgery patient-reported outcomes
2 withdrawals (heart attack, emergency surgery)
2 loss to follow-up (too stressful, did not return questionnaire)

CHAPTER FOUR

DISCUSSION

Overview

Many of the discussion points have already been addressed in Chapter Three, however, in this section I will expand on some of these discussion points, the strengths and limitations of the study, and future research directions. The primary purpose of this phase I study was to evaluate the feasibility and safety of an aerobic exercise intervention both during and after NACRT in high-risk rectal cancer patients. A secondary purpose was to track changes in objective health-related fitness outcomes and patient-reported outcomes over the course of the intervention. I hypothesized that rectal cancer patient initiating NACRT would be willing and able to complete an aerobic exercise program. To demonstrate feasibility, the prespecified criteria included a recruitment rate of ≥20%, an adherence rate to the supervised exercise program during NACRT of ≥70%, and a follow-up assessment rate for the health-related fitness outcomes and patient-reported outcomes at post-NACRT of ≥80%. The recruitment rate was 56%, adherence to the number of supervised exercise sessions was 74% and follow-up assessment rate at post-NACRT for the health-related fitness testing and the questionnaires were 83% and 94% respectively. Furthermore, no exercise related adverse events were reported. The predetermined study objectives were met and the study was deemed feasible and safe.

The 71% eligibility rate in the present study is excellent and suggests that the majority of rectal cancer patients receiving NACRT are eligible for an aerobic exercise intervention. Although there are no studies with which I can directly compare the results, this eligibility rate is similar to the 67% eligibility rate for a supervised exercise intervention in colorectal cancer

survivors receiving adjuvant chemotherapy [48]. Moreover, it is higher than the eligibility rate for supervised exercise trials in breast and prostate cancer patients receiving chemotherapy (33 to 41%) [12, 49, 50] or radiotherapy (37%) [51]. In the only other exercise intervention study targeting pre-surgical rectal cancer patients, West et al [18] did not report the eligibility rate. The main reasons for ineligibility in my study were medical conditions that are significant contraindications to exercise. These eligibility criteria are unlikely to be addressed in any future trials. Nevertheless, the 71% eligibility rate suggests a clear subpopulation of rectal cancer patients initiating NACRT who are eligible for an exercise intervention.

The recruitment rate of 56% is also excellent and higher than the 26-49% recruitment rates reported for other studies recruiting cancer patients to exercise interventions during adjuvant treatment [12, 48-51]. Again, in the study most similar to mine, West et al [18] study did not report the recruitment rate or reasons for refusal. In the present study, patients mainly refused because they were afraid it would be "too much" during NACRT. This reason may be addressed based on the feasibility data. In future trials, patients being recruited will be informed that other rectal cancer patients were able to exercise during NACRT. Nevertheless, the over 50% recruitment rate suggests strong interest of rectal cancer patients in an exercise intervention during NACRT.

Follow-up assessment rates for the health-related fitness testing and questionnaires were excellent at the post-NACRT timepoint (83% and 94% respectively) and even the pre-surgical time point (78% for all assessments). Other exercise trials in cancer patients receiving adjuvant treatments have reported slightly higher rates [12, 49, 50]. Moreover, West et al [18] reported an excellent follow-up rate for fitness assessments of 100% in the exercise group; however, only

59% of the control group provided follow-up fitness assessments, perhaps because the control group consisted of patients who declined exercise and/or were from out of town. In the present study, 3 of the 8 out-of-town patients did not complete the pre-surgery exercise intervention; 1 was withdrawn from the study due to emergency surgery, 1 was lost to follow-up and 1 was scheduled for fitness testing the day before surgery and became anxious. Overall, it was feasible to get the out-of-town patients back for the pre-surgery fitness testing; however, future trials should avoid scheduling patients too close to their surgery date. The other main reason for missed fitness testing in this study was acute medical contraindications. This is not unexpected in this high-risk patient group. Throughout the trial there were two adverse events that occurred, both were deemed by the medical team to be caused by the cancer treatment, not the exercise (cardiotoxicity and radiation fibrosis). Again, this is not unexpected in this high-risk patient group and future trials may consider powering their studies to account for some loss to follow-up due to severe treatment related toxicities.

The intention-to-treat adherence rate of 74% for the supervised exercise sessions is promising and similar to that reported in other trials during chemotherapy [12, 48-50] however, it is slightly lower than the reported 83% adherence during radiation therapy for prostate cancer [51]. Nevertheless, this study is one of the first to examine exercise adherence during combined chemoradiotherapy. The two most frequently reported barriers to exercise during NACRT were hand-foot-syndrome and logistical issues. Hand-foot-syndrome has not been previously reported as a barrier to exercise but it should be addressed in future trials with this patient population because exercise has the potential to exacerbate this symptom. Logistical issues included the necessity of scheduling out-of-town patients for their health-related fitness test on the same day

as their first/last radiation session, which reduced the number of supervised exercise sessions available. Based on my experience in this trial, future trials may consider standardizing the pre- and post-NACRT assessment timepoints to the same day as the first and last radiation session respectively.

In the post-NACRT phase, only 2 of 16 (13%) patients were interested in continuing with supervised exercise. This finding contrasts with West et al [18] who reported a 96% adherence rate to a hospital-based supervised exercise program for rectal cancer patients after NACRT. One difference between the studies is that West et al [18] only included local patients in the exercise intervention whereas out-of-town patients were assigned to the control group. Nevertheless, even the local patients in the current study did not express interest in continuing with the supervised exercise after NACRT. Fortunately, adherence to the unsupervised exercise in the post-NACRT phase was excellent with a mean of over 200 minutes of self-reported aerobic exercise and 10 of 14 (71%) patients meeting the goal of $\geq$ 150 minutes/week. These data suggest that a closely monitored unsupervised exercise program after NACRT may be feasible.

The current study suggested a small non-significant decline in cardiovascular fitness from pre- to post-NACRT of 1.3 ml/kg/min despite the aerobic exercise intervention. Without an exercise intervention, West et al [18] observed a decline in cardiovascular fitness during NACRT of 2.5 ml/kg/min suggesting that our aerobic exercise intervention may have prevented some of the decline in fitness during NACRT. Moreover, our study suggested an improvement in cardiovascular fitness from post-NACRT to pre-surgery of 2.4 ml/kg/min which resulted in a slight increase above baseline of 1.1 ml/kg/min. In the study by West et al [18], the post- NACRT supervised exercise intervention resulted in an improvement in cardiovascular fitness of 2.7

ml/kg/min (compared to a decline of 1.3 ml/kg/min in a non-randomized control group) returning the exercise group back to roughly pre-NACRT levels, suggesting that the unsupervised exercise intervention in the present study may be as effective as supervised exercise for improving cardiorespiratory fitness in the post-NACRT setting. Furthermore, in another observational study, West et al [19] observed a decline in cardiovascular fitness from pre-NACRT to pre-surgery of 1.4 ml/kg/min compared to the suggested improvement of 1.1 ml/kg/min observed in my study. The data from the current study suggest that initiating an exercise intervention during NACRT, and continuing it after NACRT, may not only prevent decline in cardiovascular fitness during NACRT but may also facilitate the recovery after NACRT.

The present study is the first to quantify changes in patient-reported outcomes in rectal cancer patients during NACRT and prior to definitive surgery. The pattern of decline for many of the generic and cancer-specific QoL outcomes exceeded the 2 to 3 point clinically meaningful difference during NACRT despite the aerobic exercise intervention. Without a proper comparison group, however, I cannot comment on whether exercise blunted or worsened these declines in QoL during NACRT. Most QoL outcomes recovered after NACRT and some even exceeded pre-NACRT levels at the pre-surgery timepoint. Again, however, I am unable to determine if the exercise intervention amplified or blunted these gains in QoL after NACRT.
Only randomized controlled trials with proper control groups are able to answer this question.

Strengths and Limitations

This study has important strengths and limitations. To the best of my knowledge, it is the first study to test an exercise intervention in rectal cancer patients during NACRT and the feasibility and safety of an exercise intervention during these difficult treatments was unknown. This is an important strength because the response to exercise may be different due to specific disease and treatment variables [52]. As such, we may not be able to generalize the benefits and harms of exercise in one patient population to another patient population. Moreover, the eligibility rate (and reasons for non-eligibility) and the recruitment rate (and reasons for refusal) were closely monitored in the current study. Tracking the eligibility and recruitment data is important to determine any selection bias in the sample and the generalizability of the findings. Many exercise trials do not closely track eligibility and recruitment rates which limits the feasibility of their application in day-to-day clinical practice. Furthermore, the exercise intervention during NACRT was supervised and objectively quantified. This is a strength of the study since relying on self-report data for assessing exercise has considerable limitations. In addition, all reasons for missed exercise sessions were documented and established specific barriers to supervised exercise which will help in the design of phase II trials in this patient cohort. Moreover, all adverse events were tracked and reported. Most exercise trials in cancer patients have not reported adverse events making it unclear if adverse events were not tracked or none occurred. Understanding the potential harms of exercise in cancer patients is just as important as understanding the benefits. Finally, validated measures were used to assess health-related fitness and patient reported-outcomes. Overall, this thesis provides us with important

insight into the practical day-to-day running of an exercise program for rectal cancer patients receiving NACRT.

This study does have limitations including the small sample size and non-randomized controlled design. Given that this study was part of two year master's thesis the recruitment period was limited to six months. As such, I only expected to recruit 10-20 patients, however, the small sample size is still a limitation in our study. The feasibility data may not be reliable and should be interpreted with caution. Another important limitation of this study is the lack of a comparison group. Consequently, I cannot distinguish how much of the observed changes in objective health-related fitness outcomes and patient-reported outcomes are attributable to the exercise program; changes during NACRT may be explained by the cancer treatments whereas changes post-NACRT may be explained by the natural recovery after treatment. Nevertheless, given that this study was the first to test an exercise intervention in rectal cancer patients during NACRT, I felt that it was prudent to conduct a phase I study to determine the safety and feasibility of exercise before embarking on randomized controlled trials. Another limitation of this study is the lack of post-surgical follow-up for outcomes including length of hospital stay, post-surgical outcomes and recovery. Again, given the limited timeframe of the master's thesis it was not feasible to include a longer-term follow-up. Another limitation is the single centre design which may limit the generalizability of the findings; the recruitment rate is biased by the radiation-oncologists and study coordinator at the site of the current study.

Another important limitation of the study was the estimation of VO2 max from submaximal heart rates and oxygen consumptions. I felt that it was prudent to use a submaximal treadmill test given that I was working with a high-risk patient cohort however, the pathogenesis

of the disease may affect heart rate response to exercise. West et al deemed it safe to maximally test rectal cancer patients receiving NACRT on a bike however, I was using a different testing modality and wanted to establish its safety before running maximal tests. I selected the treadmill for two main reasons: (1) our testing room was already set-up for its use and (2) I didn't think that exercising on a bike would be comfortable for patients due to the location of the tumor and the field of radiation. From my experience, some of the patients would not have been able to complete a post-NACRT test on the bike due to blisters and skin sensitivity on the buttocks. Conversely, in my trial, we had to delay two of our post-NACRT tests due to hand-foot syndrome. As such, future trials may consider using a maximal bike or treadmill test to assess cardiorespiratory function in rectal cancer patients however, they should allow for a 1 week delay in testing due to side effects. Furthermore, based on my experience, I would recommend an adequate warm-up period on the treadmill to ensure that the patient is comfortable and safe prior to starting the test.

Another limitation of the study was the use of a self-report measure to capture exercise adherence to the unsupervised exercise. Participants were loaned heart rate monitors so that they could monitor the intensity of their exercise. Perhaps future trials may consider setting up the heart rate monitor so that it logs all of the patients exercise sessions.

Future Directions

Randomized controlled trials with a proper comparison group are needed to establish the efficacy of moderate intensity aerobic exercise in preventing declines in health-related and patient reported outcomes including; cardiorespiratory function, physical function, QoL, depression, anxiety, stress, self-esteem and sleep quality. Future trials should also consider the

addition of other outcomes including; treatment toxicity, treatment completion, treatment response, post-surgical complications and post-surgical recovery. Further research may also examine the relationship of cardiorespiratory fitness with other novel outcomes including biological mechanisms and survival. Furthermore, future trials should also consider manipulating the intensity, duration and frequency and setting (supervised vs. unsupervised) of the aerobic exercise to determine the optimal dose for improving clinical and patient-reported outcomes. Additionally, future trials may want to explore the benefits of a strength training program or combined strength and aerobic training program in this clinical population. Much more research is needed before exercise recommendations for rectal cancer patients receiving NACRT can be made.

Conclusions

In conclusion, a supervised aerobic exercise intervention in high-risk rectal cancer patients during NACRT followed by an unsupervised, but closely monitored, exercise program after NACRT appears to be feasible, safe, and well-received by the participants. This phase I study demonstrated acceptable eligibility, recruitment, adherence, and follow-up rates during and after NACRT. This phase I study provides important information to inform future trial development. Phase II trials in rectal cancer patients during and after NACRT with proper comparison groups are needed to examine the effects of aerobic exercise on health-related fitness, patient-reported outcomes, and treatment outcomes. If positive, these trials could establish exercise as a new intervention to manage treatment side effects and improve outcomes in rectal cancer patients.

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Appendix A. Methods

Exercise Intervention

The exercise intervention was divided into two components: (1) during NACRT and (2) post-NACRT (prior to surgery). During NACRT, all exercise sessions were supervised by an exercise specialist at the Behavioral Medicine Fitness Centre on the University of Alberta Campus within a five minute walk of the Cross Cancer Institute. Patients were not allowed to exercise immediately before radiation as they were required to have a full bladder for their radiation session and exercise may have interfered with this requirement. During NACRT, the primary goal of the exercise intervention was to attend 18 supervised aerobic exercise sessions (3 sessions per week for the 6 weeks during which patients were undergoing NACRT). A secondary goal was to determine if patients could reach (and maintain) 150 minutes of moderate intensity aerobic exercise in 3 training sessions per week (50 minutes/session). The exercise prescription was individually tailored to each patient based on the results of the baseline treadmill test (40-60% of estimated VO_2 reserve). Prior to each session, an exercise specialist assessed blood pressure and heart rate and asked patients to report any immediate symptoms. Each training session consisted of a five minute aerobic warm-up and cool-down at low-intensity. The intensity of the exercise sessions was monitored via heart rate monitors and the Borg rating of perceived exertion scale. Exercise modalities included treadmill, upright bike, recumbent bike, elliptical and rower. For each supervised session, the exercise trainer recorded attendance, duration, intensity and any symptoms during or immediately after the exercise.

After NACRT, patients were provided the option of continuing with the supervised exercise program, completing an unsupervised exercise program, or a combination. The option

of unsupervised exercise was provided because patients were no longer coming daily to the cancer center for radiation and many of the patients were from out of town. During this phase, the goal of the exercise program was to maintain (or achieve) 150 minutes of moderate intensity aerobic exercise per week in bouts of 10 minutes or more. The exercise prescription was individually tailored to each patient based on the results of the post-NACRT treadmill test (40-60% of estimated VO_2 reserve). Patients completing unsupervised exercise were provided with a heart rate monitor and were asked to record exercise frequency, intensity (heart rate and rating of perceived exertion), duration and modality in the provided exercise log. The study coordinator completed weekly telephone calls or email follow-ups to assist and support patients in meeting the exercise objective. Adherence to the unsupervised exercise program was assessed at the end of the intervention by self-report using the Godin Leisure Time Exercise Questionnaire (GLTEQ) [1]. Patients were asked to recall their average weekly frequency and duration of light, moderate and vigorous physical activity that lasted more than 10 minutes and was done during free time since completing NACRT.

Demographic, Behavioral and Medical Characteristics

Demographic and behavioral variables were assed using self-report and included: age, sex, marital status, education level, annual income, employment status, ethnicity, smoking behavior and co-morbidities. Medical data was extracted from medical records and included: disease stage, treatments, and important medical dates. Measurements of height and weight obtained during the pre-NACRT test were used to compute body mass index. Baseline exercise was assessed by the GLTEQ [1]. Patients were asked to recall their level of physical activity

since their cancer diagnosis. We computed "aerobic exercise minutes" as moderate plus two times the vigorous minutes. Current aerobic exercisers were defined as achieving ≥150 aerobic exercise minutes per week and current resistance exercisers were defined as achieving ≥ 2 days/week of resistance training.

Health-related Fitness Outcomes

Cardiorespiratory fitness was assessed using a multistage submaximal aerobic exercise test with direct measures of gas exchange and ventilation on a calibrated metabolic measurement system (Parvo Medics TrueOne® 2400; Sandy, UT). Briefly, the test was administered in three minute stages, the first stage was at 2.5 mph, the second stage was at 3.0 mph and for every subsequent stage the speed remained constant and the grade increased by 5%. If a patient achieved a grade of 15% then the speed was increased for every subsequent stage and the grade remained constant. The test was terminated at the end of the stage during which the patient reached 85% of their age predicted maximal heart rate (220-age). Heart rate was monitored continuously and recorded every minute and blood pressure, oxygen saturation and the participant's rating of perceived exertion (RPE; 0-10) were taken in the last minute of every stage. Patients did a 5 minute active cool-down at 2.5 mph and 0% grade. Heart rate and blood pressure were recorded after 2 minutes of recovery. Functional aerobic capacity (VO_2 max) was estimated using the heart rate and volume of oxygen consumption (VO_2) from two submaximal stages of the treadmill test during which patients achieved steady-state heart rate between 115 and 150 beats per minute. The slope was then determined by calculating the ratio of the difference between the two submaximal VO_2 measures and the corresponding heart rates: [2, 3]

$$b = (VO_{2b}\text{-}VO_{2a}) / (HR_b\text{-}HR_a)$$

$$VO_2\,max = VO_{2b} + b\,(HRmax\text{-}HRb)$$

The Senior's Fitness Test (SFT) was used to assess physical functioning [4, 5]. The SFT consists of six items: (1) chair stand (number of unassisted chair stands performed in 30 seconds); (2) arm curl (number of arm curls performed with a weight in 30 seconds; 5 pounds for women and 8 pounds for men); (3) chair sit-and-reach (number of cm between extended fingers and tip of toe); (4) back scratch (number of cm between extended middle fingers); (5) 8-foot up-and-go (number of seconds to get out of chair, walk eight-feet, turn around a pylon and return to seated position); (6) six-minute walk (distance covered in meters around a 30 meter course) [4, 5].

Body composition was assessed by height, weight, waist and hip circumference. Height was measured using a stadiometer and recorded to the nearest 0.1 centimeter (cm). Weight was measured using a balance beam scale and recorded to the nearest 0.1 kilogram (kg). Body mass index (BMI) was calculated by dividing body weight in kilograms by height in meters squared (kg/m^2). Waist circumference was measured at the most superior edge of the iliac crest and hip circumference was measured at the maximal circumference of the buttocks with the patient standing with their feet together [6, 7]. Both measures were taken to the nearest 0.1 cm and repeated twice (a third trial was allowed if the measurements were not within 0.5 cm). The average of the two recorded measurements for both waist and hip were used.

Patient-reported Outcomes

Health-related QoL was measured using the Medical Outcomes Study Short-Form 36 (SF-36) [8]. This is a validated instrument that has been extensively used in clinical trials assessing QoL in cancer patients. The SF-36 contains 36 items that yield 8 heath domains: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health. Scores for each subscale ranged from 0-100 and were computed into norm-based scores according to the specifications of Quality Metric with higher scores indicating higher functioning [8]. The physical and mental component summary measures were computed by aggregating the standardized subscales and transforming them into norm-based scores.

Cancer specific QoL was measured using the well-validated Functional Assessment of Cancer Therapy-Colorectal (FACT-C) [9]. The FACT-C includes the 27 items from the FACT-General (FACT-G) and the 11-item colorectal subscale. The FACT-G is divided into four primary QoL domains: physical well-being (PWB), social/family well-being (SWB), emotional well-being (EWB) and functional well-being (FWB). In addition, the 11-item FACT-D (diarrhea) subscale was used to measure symptoms of diarrhea and the 13-item FACT-F (fatigue) subscale was used to measure symptoms of fatigue [10, 11]. The PWB, FWB and colorectal subscales were summed to form the Trial Outcome Index-Colorectal.

Depression was measured using the 10-item Centre for Epidemiology Studies Short Depression Scale (CES-D) [12]. Anxiety was measured using the 10-item Spielberger State

Anxiety Scale (SSAS) [13]. Stress was measures using the 14-item Perceived Stress Scale (PSS) [14]. Self-esteem was measured using the 10-item Rosenberg Self-Esteem Scale (RSES) [15]. The Pittsburgh Sleep Quality Index (PSQI) was used to measure sleep quality [16].

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Appendix B. Data Collection Sheet

Date: **BL / 6 WK / 12 WK**

Trial - Fitness Testing

Participant Information

Initials:	Study ID:
Age:	Birth Month:

Resting HR (bpm): _____	Resting BP (mmHg): _____
Post-exercise HR (bpm): _____	Post-exercise BP (mmHg): _____

Anthropometric Assessments

Waist Circumference 1 (cm): _____	Hip Circumference 1 (cm): _____
Waist Circumference 2 (cm): _____	Hip Circumference 2 (cm): _____
Wait Circumference 3 (cm): _____ *(If needed)*	Hip Circumference 3 (cm): _____ *(If needed)*
Waist Circumf Ave (cm): _____	Hip Circumf Ave.(cm): _____

Height (cm): _____	Weight (kg): _____

Measure to the nearest:

- Height: 0.1cm
- Weight: 0.1kg
- Waist: 0.1cm *
- Hip: 0.1cm *

*Within 0.5 cm

One-Leg Stance

	Trial 1 (0.1 sec)	**Trial 2** (0.1 sec)
Eyes Open Right		
Eyes Open Left		
Eyes Closed Right		
Eyes Closed Left		

Stopping criteria:

- Arms are uncrossed
- The raised foot is moved towards/away from the standing limb or touches the floor
- The weight-bearing foot is moved to maintain balance
- Maximum of 45 seconds has elapsed

Allow for a second trial if patient loses balance in the first 3 seconds of the eyes-closed test

Submaximal Exercise Test

Predicted Heart Rate Max = (220–Age) = 220 – _____ yrs = _____ **beats/min**

85% of Heart Rate Max = (HRmax ×0.85) = _____ **beats/min**

Minutes Standing: 1 min 2 min

Stage	Time (Min)	Speed (mph)	% Grade	Heart Rate	BP	RPE	O2 Sat
Exercise	1	2.5	0				
	2	2.5	0				
	3	2.5	0				
	4	3.0	0				
	5	3.0	0				
	6	3.0	0				
	7	3.0	2.5				
	8	3.0	2.5				
	9	3.0	2.5				
	10	3.0	5.0				
	11	3.0	5.0				
	12	3.0	5.0				
	13	3.0	7.5				
	14	3.0	7.5				
	15	3.0	7.5				
	16	3.0	10.0				
	17	3.0	10.0				
	18	3.0	10.0				
	19	3.0	12.5				
	20	3.0	12.5				
	21	3.0	12.5				
	22	3.0	15.0				
	23	3.0	15.0				
	24	3.0	15.0				
	25	3.4	15.0				
	26	3.4	15.0				
	27	3.4	15.0				
	28	3.7	15.0				
	29	3.7	15.0				
	30	3.7	15.0				

	31	4.1	15.0				
	32	4.1	15.0				
	33	4.1	15.0				
	34	4.5	15.0				
	35	4.5	15.0				
	36	4.5	15.0				
Recovery	1						
	2						
	3						
	4						
	5						

Treadmill Time to 85% of HRmax (min:sec): _____

Reason for ending test prematurely: _____

Pre O2: _____	Pre CO2: _____
Post O2: _____	Post CO2: _____

Correction needed? Yes No

Temperature: _____ Humidity: _____ Pressure:_____

Last Stage Completed	**Measured VO2:_____**	**HR:_____**
2nd Last Stage Completed	**Measured VO2:_____**	**HR:_____**

Physical Function Test

30 second Chair Stand	**# of full stands: _____**
Arm Curls Test Hand: RIGHT LEFT Weight: 5 lbs (WOMEN) 8 lbs (MEN)	**# of repetitions: _____**
Chair Sit & Reach Test Leg: RIGHT LEFT	Trial 1: + / −_____ cm Trial 2: + / −_____ cm **Best trial: _____ cm**
Back Scratch Test Hand: RIGHT LEFT	Trial 1: + / −_____ cm Trial 2: + / −_____ cm **Best trial: _____ cm**
8ft Up & Go	Trial 1: _____ sec Trial 2: _____ sec **Best trial: _____ sec**
6-minute Walk Lap Distance: _____ m # of Full Laps Completed: _____ Partial Lap Distance: _____ m	**Total Distance: _____ m**

Appendix C. Exercise Log

Week	**1**						**2**					
Session	**1**		**2**		**3**		**4**		**5**		**6**	
Date												
Pre-Exercise Assessments												
Resting HR												
Resting BP												
Exercise Session												
Mode												
Grade/Speed/ Wattage & duration												
Heart Rate Range												
Step Count												
Exercise Assessment												
Exercise RPE												
Other												
Post- Exercise Assessments												
Post HR												
Post BP												
Comments												

Appendix D. Baseline Questionnaire

Identification #:_____
Date: _____

Aerobic exercise in rectal cancer patients receiving neoadjuvant chemoradiotherapy

Investigators: Andria Morielli, MSc Student, University of Alberta; Nawaid Usmani, MD, Cross Cancer Institute; Normand G. Boulé, PhD, University of Alberta; Kerry S. Courneya, PhD, University of Alberta

BASELINE QUESTIONNAIRE

Instructions

Thank you for agreeing to participate in this study. In this questionnaire, we are going to ask you a series of questions about yourself. Many of the questions ask you about your physical and mental health, and some may be viewed as personal. It is important to answer as many of these questions as possible, however, if you feel uncomfortable answering certain questions please leave them blank. All responses are completely confidential and will never be used in any way that could link them to you. Many of the questions may seem similar but it is important to treat each question separately and provide an answer for each. There are no right or wrong answers and all we ask is that you provide responses that are as honest and accurate as possible. The questionnaire should take about 30-45 minutes of your time to complete. If you have any questions about completing the questionnaire, please contact Andria Morielli (Research Coordinator) at (780) 492-2829 (call collect from out of town) or morielli@ualberta.ca.

This set of questions asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Answer every question by marking a single answer. If you are unsure about how to answer a question please give the best answer you can.

1. In general, would you say your health is:

1	2	3	4	5
Excellent	Very good	Good	Fair	Poor

2. Compared to one year ago, how would you rate your health in general now?

1	2	3	4	5
Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

		Yes, limited a lot	Yes, limited a little	No, not limited at all
a.	**Vigorous Activities**, such as running, lifting heavy objects, participating in strenuous sports	1	2	3
b.	**Moderate Activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	1	2	3
c.	Lifting or carrying groceries	1	2	3
d.	Climbing **several** flights of stairs	1	2	3
e.	Climbing **one** flight of stairs	1	2	3
f.	Bending, kneeling or stooping	1	2	3
g.	Walking **more than a mile**	1	2	3
h.	Walking **several hundred yards**	1	2	3
i.	Walking **one hundred yards**	1	2	3
j.	Bathing or dressing yourself	1	2	3

4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down on the **amount of time** you spent on work or other activities	1	2	3	4	5
b. **Accomplished less** than you would like	1	2	3	4	5
c. Were **limited** in the **kind** of work or other activities	1	2	3	4	5
d. Had **difficulty** performing the work or other activities (e.g., it took extra effort)	1	2	3	4	5

5. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down on the **amount of time** you spent on work or other activities	1	2	3	4	5
b. **Accomplished less** than you would like	1	2	3	4	5
c. Did work or other activities **less carefully than usual**.	1	2	3	4	5

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

1	2	3	4	5
Not at all	Slightly	Moderately	Quite a bit	Extremely

7. How much bodily pain have you had during the past 4 weeks?

1	2	3	4	5	6
None	Very mild	Mild	Moderate	Severe	Very severe

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

1	2	3	4	5
Not at all	A little bit	Moderately	Quite a bit	Extremely

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give one answer that comes closest to the way you have been feeling.
How much of the time during the past 4 weeks…

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of life?	1	2	3	4	5
b. Have you been very nervous?	1	2	3	4	5
c. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5
d. Have you felt calm and peaceful?	1	2	3	4	5
e. Did you have a lot of energy?	1	2	3	4	5
f. Have you felt downhearted and depressed?	1	2	3	4	5
g. Did you feel worn out?	1	2	3	4	5
h. Have you been happy?	1	2	3	4	5
i. Did you feel tired?	1	2	3	4	5

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

1	2	3	4	5
All of the time	Most of the time	Some of the time	A little of the time	None of the time

11. How TRUE or FALSE is each of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. I seem to get sick a little easier than other people	1	2	3	4	5
b. I am as healthy as anybody I know	1	2	3	4	5
c. I expect my health to get worse	1	2	3	4	5
d. My health is excellent	1	2	3	4	5

Below is a list of statements that other people with cancer have said are important to their quality of life. Please indicate the extent to which you have experienced each of the statements during the past 7 days by circling the appropriate number using the following scale.

0	1	2	3	4
not at all	a little bit	somewhat	quite a bit	very much

During the PAST WEEK:

1. I have a lack of energy	0	1	2	3	4
2. I have nausea	0	1	2	3	4
3. Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
4. I have pain	0	1	2	3	4
5. I am bothered by side effects of treatment	0	1	2	3	4
6. I feel sick	0	1	2	3	4
7. I am forced to spend time in bed	0	1	2	3	4
8. I feel close to my friends	0	1	2	3	4
9. I get emotional support from my family	0	1	2	3	4
10. I get support from my friends	0	1	2	3	4
11. My family has accepted my illness	0	1	2	3	4
12. I am satisfied with family communication about my illness	0	1	2	3	4
13. I feel close to my partner (or the person who is my main support)	0	1	2	3	4
14. I am satisfied with my sex life	0	1	2	3	4
15. I feel sad	0	1	2	3	4
16. I am satisfied with how I am coping with my illness	0	1	2	3	4

During the PAST WEEK;

0 not at all	1 a little bit	2 somewhat	3 quite a bit	4 very much

17. I am losing hope in the fight against my illness	0	1	2	3	4
18. I feel nervous	0	1	2	3	4
19. I worry about dying	0	1	2	3	4
20. I worry that my condition will get worse	0	1	2	3	4
21. I am able to work (include work at home)	0	1	2	3	4
22. My work (include work at home) is fulfilling	0	1	2	3	4
23. I am able to enjoy life	0	1	2	3	4
24. I have accepted my illness	0	1	2	3	4
25. I am sleeping well	0	1	2	3	4
26. I am enjoying the things I usually do for fun	0	1	2	3	4
27. I am content with the quality of my life right now	0	1	2	3	4
28. I have swelling or cramps in my stomach area	0	1	2	3	4
39. I am losing weight	0	1	2	3	4
30. I have control of my bowels	0	1	2	3	4
31. I can digest my food well	0	1	2	3	4
32. I have diarrhea (diarrhoea)	0	1	2	3	4
33. I have a good appetite	0	1	2	3	4
34. I like the appearance of my body	0	1	2	3	4

35. Do you have an ostomy appliance?	Yes	No			
If yes, please answer the next two items					
36. I am embarrassed by my ostomy appliance	0	1	2	3	4
37. Caring for my ostomy appliance is difficult	0	1	2	3	4

During the PAST WEEK:

0	1	2	3	4
not at all	a little bit	somewhat	quite a bit	very much

DIARRHEA SYMPTOMS

1. I have control of my bowels	0	1	2	3	4
2. I move my bowels more frequently than usual	0	1	2	3	4
3. I am afraid to be far from a toilet	0	1	2	3	4
4. I have to limit my social activity because of diarrhea	0	1	2	3	4
5. I have to limit my physical activity because of diarrhea	0	1	2	3	4
6. I have to limit my sexual activity because of diarrhea	0	1	2	3	4
7. I am embarrassed by having diarrhea	0	1	2	3	4
8. I have abdominal cramps or discomfort due to my diarrhea	0	1	2	3	4
9. My problem with diarrhea keeps/wakes me up at night	0	1	2	3	4
10. I must move my bowels frequently to avoid accidents	0	1	2	3	4
11. I wear pads or protection to prevent soiling my underwear	0	1	2	3	4

During the PAST WEEK:

0	1	2	3	4
not at all	a little bit	somewhat	quite a bit	very much

FATIGUE/ANEMIA SYMPTOMS

1. I feel fatigued	0	1	2	3	4
2. I feel weak all over	0	1	2	3	4
3. I feel listless ("washed out")	0	1	2	3	4
4. I feel tired	0	1	2	3	4
5. I have trouble starting things because I am tired	0	1	2	3	4
6. I have trouble finishing things because I am tired	0	1	2	3	4
7. I have energy	0	1	2	3	4
8. I have trouble walking	0	1	2	3	4
9. I am able to do my usual activities	0	1	2	3	4
10. I need to sleep during the day	0	1	2	3	4
11. I feel lightheaded (dizzy)	0	1	2	3	4
12. I get headaches	0	1	2	3	4
13. I have been short of breath	0	1	2	3	4
14. I have pain in my chest	0	1	2	3	4
15. I am too tired to eat	0	1	2	3	4
16. I am interested in sex	0	1	2	3	4
17. I am motivated to do my usual activities	0	1	2	3	4
18. I need help doing my usual activities	0	1	2	3	4
19. I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
20. I have to limit my social activities because I am tired	0	1	2	3	4

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month.

1. During the past month, when have you usually gone to bed at night?

USUAL BED TIME _____

2. During the past month, how long has it usually taken you to fall asleep each night?

NUMBER OF MINUTES _____

3. During the past month, when have you usually gotten up in the morning?

USUAL GETTING UP TIME _____

4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spend in bed.)

HOURS OF SLEEP PER NIGHT _____

For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past month, how often have you had trouble sleeping because you . . .

a) Cannot get to sleep within 30 minutes

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

b) Wake up in the middle of the night or early morning

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

c) Have to get up to use the bathroom

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

d) Cannot breathe comfortably

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

e) Cough or snore loudly

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

f) Feel too cold

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

g) Feel too hot

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

h) Had bad dreams

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

i) Have pain

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

j) Other reason(s), please describe_____
_____

How often during the past month have you had trouble sleeping because of this?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

6. During the past month, how would you rate your sleep quality overall?

Very good_____ Fairly good_____ Fairly bad_____ Very bad_____

7. During the past month, how often have you taken medicine to help you sleep (prescribed or "over the counter")?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

No problem at all _____

Only a very slight problem _____

Somewhat of a problem _____

A very big problem _____

10. Do you have a bed partner or room mate?

No bed partner or room mate _____

Partner/room mate in other room _____

Partner in same room, but not same bed _____

Partner in same bed _____

If you have a room mate or bed partner, ask him/herhow often in the past month you have had . . .

a) Loud snoring

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

b) Long pauses between breaths while asleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

c) Legs twitching or jerking while you sleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

d) Episodes of disorientation or confusion during sleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

e) Other restlessness while you sleep; please describe_____
_____

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

Below is a list of statements concerning how you might have felt or behaved in the past week. Please use the following scale to indicate how often you felt or behaved in these ways in the past week.

0	1	2	3
Rarely or none of the time (< 1 day)	Some of the time (1-2 days)	Much of the time (3-4 days)	Most or all of the time (5-7 days)

During the PAST WEEK:

1. I felt depressed.	0	1	2	3
2. I felt that everything I did was an effort.	0	1	2	3
3. My sleep was restless.	0	1	2	3
4. I was happy.	0	1	2	3
5. I felt lonely.	0	1	2	3
6. People were unfriendly.	0	1	2	3
7. I enjoyed life.	0	1	2	3
8. I felt sad.	0	1	2	3
9. I felt that people disliked me.	0	1	2	3
10. I could not get "going".	0	1	2	3

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number that best indicates how you have felt during the past week. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer that best describes how you felt.

During the PAST WEEK:

	not at all	somewhat	moderately so	very much so
1. I felt calm	1	2	3	4
2. I was tense	1	2	3	4
3. I felt at ease	1	2	3	4
4. I worried over possible misfortunes	1	2	3	4
5. I felt frightened	1	2	3	4
6. I felt self-confident	1	2	3	4
7. I was jittery	1	2	3	4
8. I was relaxed	1	2	3	4
9. I was worried	1	2	3	4
10. I felt steady	1	2	3	4

The questions in this scale ask you about your feelings and thoughts during the last month. Although some of the questions are similar, there are differences between them and you should treat each one as a separate question. The best approach is to answer each one fairly quickly. For each question, please choose from the following alternatives:

	0 never	1 almost never	2 some-times	3 fairly often	4 very often
In the last month, how often have you…					
1. been upset because of something that happened unexpectedly	0	1	2	3	4
2. felt that you were unable to control the important things in your life	0	1	2	3	4
3. felt nervous and stressed	0	1	2	3	4
4. dealt successfully with irritating life hassles	0	1	2	3	4
5. felt that you were effectively coping with important changes that were occurring in your life	0	1	2	3	4
6. felt confident about your ability to handle your personal problems	0	1	2	3	4
7. felt that things were going your way	0	1	2	3	4
8. found that you could not cope with all the things that you had to do	0	1	2	3	4
9. been able to control irritations in your life	0	1	2	3	4
10. felt that you were on top of things	0	1	2	3	4
11. been angered because of things that happened that were outside of your control	0	1	2	3	4
12. found yourself thinking about things that you have to accomplish	0	1	2	3	4
13. been able to control the way you spend your time	0	1	2	3	4
14. felt difficulties were piling up so high that you could not overcome them	0	1	2	3	4

The following questions concern the general perceptions that you currently have about yourself. Please circle the number that best reflects your current view of yourself using the following scale as a guide for your responses.

	Strongly Disagree	disagree	agree	strongly agree
1. On the whole I am satisfied with myself.	1	2	3	4
2. At times I think that I am no good at all.	1	2	3	4
3. I feel that I have a number of good qualities.	1	2	3	4
4. I am able to do things as well as most other people.	1	2	3	4
5. I feel I do not have much to be proud of.	1	2	3	4
6. I certainly feel useless at times.	1	2	3	4
7. I feel that I am a person of worth, at least on an equal plane with others.	1	2	3	4
8. I wish I could have more respect for myself.	1	2	3	4
9. All in all, I am inclined to feel that I am a failure.	1	2	3	4
10. I take a positive attitude toward myself.	1	2	3	4

For this next question, we would like you to recall the amount of exercise you have done SINCE you were diagnosed with rectal cancer.

When answering these questions please:

- only count exercise sessions that lasted 10 minutes or longer in duration.
- only count exercise that was done during free time (i.e., not occupation or housework).
- note that the main difference between the first three categories is the intensity of the endurance (aerobic) exercise and the fourth category is for strength (resistance) exercise.
- please write the average frequency on the first line and the average duration on the second.
- if you did not do any exercise in one of the categories, please write in "0".

Considering a typical week (7 days) how many times on the average did you do the following kinds of exercise SINCE you were diagnosed with rectal cancer?

	Times Per Week	Average Duration
a. VIGOROUS/STRENUOUS EXERCISE (HEART BEATS RAPIDLY, SWEATING) (e.g., running, aerobics classes, cross country skiing, vigorous swimming, vigorous bicycling).	_____	_____
b. MODERATE EXERCISE (NOT EXHAUSTING, LIGHT PERSPIRATION) (e.g., fast walking, tennis, easy bicycling, easy swimming, popular and folk dancing).	_____	_____
c. LIGHT/MILD EXERCISE (MINIMAL EFFORT, NO PERSPIRATION) (e.g., easy walking, yoga, bowling, lawn bowling, shuffleboard).	_____	_____
d. RESISTANCE/STRENGTH EXERCISE (e.g., lifting weights, push ups, sit ups, therabands).	_____	_____

The following questions ask you to relate how you feel about doing exercise during your upcoming chemoradiotherapy treatment. Please pay careful attention to the words and descriptions for each scale and circle the number that best represents how you feel.

1. How beneficial do you think it will be for you to exercise during your chemoradiotherapy?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

2. How enjoyable do you think it will be for you to exercise during your chemoradiotherapy?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

3. How supportive do you think your family/friends will be of you exercising during your chemoradiotherapy?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

4. How motivated are you to exercise during your chemoradiotherapy?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

5. How difficult do you think it will be for you to exercise during your chemoradiotherapy?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

This part of the questionnaire is needed to help understand the characteristics of the people participating in the study. For this reason it is very important information. All information is held in strict confidence and its presentation to the public will be group data only.

1. Age: _____

2. Sex: Male _____ Female_____

3. Current Marital Status: Never Married _____ Married _____ Common Law _____
Separated _____ Widowed _____ Divorced _____

4. Education (Please check highest level attained):

_____ Some High School _____ Completed High School _____ Some University/College

_____ Completed Univ/Coll _____ Some Graduate School _____ Completed Grad School

5. Annual Family Income: < 20,000 _____ 20-39,999 _____ 40-59,999 _____

60-79,999 _____ 80-99,999 _____ > 100,000 _____

6. Current Employment Status: Disability _____ Retired _____ Part Time _____
Homemaker _____ Full Time _____ Sick Leave _____

7. What is your primary ethnic origin or race (please circle)?

White Black Hispanic Asian Aboriginal Other _____

8. Which of the following best describes your current smoking status?

____ Never Smoked ____ Ex-Smoker ____ Current Smoker

9. Has a doctor or nurse ever told you that you had any of the following conditions? (check all that apply):

High blood pressure	_____No	_____Yes	High cholesterol	_____No	_____Yes
Heart attack	_____No	_____Yes	Stroke	_____No	_____Yes
Emphysema	_____No	_____Yes	Chronic bronchitis	_____No	_____Yes
Diabetes	_____No	_____Yes	Other cancer	_____No	_____Yes
Angina (chest pains)	_____No	_____Yes	Arthritis	_____No	_____Yes

Any other long term health condition? _____

10. In the past month, was your ability to exercise limited by a health condition, injury, or disability?

1	2	3	4	5
No, Not at All	A Little	Somewhat	Quite a lot	Completely

11. Are you currently taking any medications for health problems? (e.g., for anxiety, depression, blood pressure, constipation, pain, to help with sleep, etc.).

What is the medication?	What is it for? (e.g., blood pressure, anxiety)
1. _____	_____
2. _____	_____
3. _____	_____

Others? _____

Anything else you would like to tell us? On this final page, please feel free to make any comments concerning your rectal cancer, your treatments, the questionnaire, the exercise program, or anything else you think may be helpful to us. All comments are welcome.

Thank you very much for your participation in this research project.

Please place the completed questionnaire in the envelope provided and bring it to your scheduled fitness test.

Appendix E. Post-treatment Questionnaire

Identification #:_____
Date: _____

Aerobic exercise in rectal cancer patients receiving neoadjuvant chemoradiotherapy

Investigators: Andria Morielli, MSc Student, University of Alberta; Nawaid Usmani, MD, Cross Cancer Institute; Normand G. Boulé, PhD, University of Alberta; Kerry S. Courneya, PhD, University of Alberta

POST-TREATMENT QUESTIONNAIRE

Instructions

Thank you for your continued participation in this study. Now that you have completed your pre-surgical chemoradiotherapy treatment, we are going to ask you many of the same questions as in the first questionnaire. However, it is important to answer these questions based on what you are thinking and feeling right now and not on how you answered the questions last time. This will give us important information about how your thoughts and feelings have changed. Many of the questions may seem similar but it is important to treat each question separately and provide an answer for all the questions if possible. However, if you feel uncomfortable answering certain questions please leave them blank. All responses are completely confidential and will never be used in any way that could link them to you. There are no right or wrong answers and all we ask is that you provide responses that are as honest and accurate as possible. The questionnaire should take about 30-45 minutes of your time to complete. If you have any questions about completing the questionnaire, please contact Andria Moriellli (Research Coordinator) at (780) 492-2829 (call collect from out of town) or morielli@ualberta.ca.

This first set of questions asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Answer every question by marking a single answer. If you are unsure about how to answer a question please give the best answer you can.

1. In general, would you say your health is:

1	2	3	4	5
Excellent	Very good	Good	Fair	Poor

2. Compared to one year ago, how would you rate your health in general now?

1	2	3	4	5
Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

		Yes, limited a lot	Yes, limited a little	No, not limited at all
a.	**Vigorous Activities**, such as running, lifting heavy objects, participating in strenuous sports	1	2	3
b.	**Moderate Activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	1	2	3
c.	Lifting or carrying groceries	1	2	3
d.	Climbing **several** flights of stairs	1	2	3
e.	Climbing **one** flight of stairs	1	2	3
f.	Bending, kneeling or stooping	1	2	3
g.	Walking **more than a mile**	1	2	3
h.	Walking **several hundred yards**	1	2	3
i.	Walking **one hundred yards**	1	2	3
j.	Bathing or dressing yourself	1	2	3

4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down on the **amount of time** you spent on work or other activities	1	2	3	4	5
b. **Accomplished less** than you would like	1	2	3	4	5
c. Were **limited** in the **kind** of work or other activities	1	2	3	4	5
d. Had **difficulty** performing the work or other activities (e.g., it took extra effort)	1	2	3	4	5

5. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down on the **amount of time** you spent on work or other activities	1	2	3	4	5
b. **Accomplished less** than you would like	1	2	3	4	5
c. Did work or other activities **less carefully than usual**.	1	2	3	4	5

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

1	2	3	4	5
Not at all	Slightly	Moderately	Quite a bit	Extremely

7. How much bodily pain have you had during the past 4 weeks?

1	2	3	4	5	6
None	Very mild	Mild	Moderate	Severe	Very severe

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

1	2	3	4	5
Not at all	A little bit	Moderately	Quite a bit	Extremely

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give one answer that comes closest to the way you have been feeling.
How much of the time during the past 4 weeks…

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of life?	1	2	3	4	5
b. Have you been very nervous?	1	2	3	4	5
c. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5
d. Have you felt calm and peaceful?	1	2	3	4	5
e. Did you have a lot of energy?	1	2	3	4	5
f. Have you felt downhearted and depressed?	1	2	3	4	5
g. Did you feel worn out?	1	2	3	4	5
h. Have you been happy?	1	2	3	4	5
i. Did you feel tired?	1	2	3	4	5

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

1	2	3	4	5
All of the time	Most of the time	Some of the time	A little of the time	None of the time

11. How TRUE or FALSE is <u>each</u> of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. I seem to get sick a little easier than other people	1	2	3	4	5
b. I am as healthy as anybody I know	1	2	3	4	5
c. I expect my health to get worse	1	2	3	4	5
d. My health is excellent	1	2	3	4	5

Below is a list of statements that other people with cancer have said are important to their quality of life. Please indicate the extent to which you have experienced each of the statements during the past 7 days by circling the appropriate number using the following scale.

0	1	2	3	4
not at all	a little bit	somewhat	quite a bit	very much

During the PAST WEEK:

1. I have a lack of energy	0	1	2	3	4
2. I have nausea	0	1	2	3	4
3. Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
4. I have pain	0	1	2	3	4
5. I am bothered by side effects of treatment	0	1	2	3	4
6. I feel sick	0	1	2	3	4
7. I am forced to spend time in bed	0	1	2	3	4
8. I feel close to my friends	0	1	2	3	4
9. I get emotional support from my family	0	1	2	3	4
10. I get support from my friends	0	1	2	3	4
11. My family has accepted my illness	0	1	2	3	4
12. I am satisfied with family communication about my illness	0	1	2	3	4
13. I feel close to my partner (or the person who is my main support)	0	1	2	3	4
14. I am satisfied with my sex life	0	1	2	3	4
15. I feel sad	0	1	2	3	4
16. I am satisfied with how I am coping with my illness	0	1	2	3	4

During the PAST WEEK;

0	1	2	3	4
not at all	a little bit	somewhat	quite a bit	very much

17. I am losing hope in the fight against my illness	0	1	2	3	4
18. I feel nervous	0	1	2	3	4
19. I worry about dying	0	1	2	3	4
20. I worry that my condition will get worse	0	1	2	3	4
21. I am able to work (include work at home)	0	1	2	3	4
22. My work (include work at home) is fulfilling	0	1	2	3	4
23. I am able to enjoy life	0	1	2	3	4
24. I have accepted my illness	0	1	2	3	4
25. I am sleeping well	0	1	2	3	4
26. I am enjoying the things I usually do for fun	0	1	2	3	4
27. I am content with the quality of my life right now	0	1	2	3	4
28. I have swelling or cramps in my stomach area	0	1	2	3	4
39. I am losing weight	0	1	2	3	4
30. I have control of my bowels	0	1	2	3	4
31. I can digest my food well	0	1	2	3	4
32. I have diarrhea (diarrhoea)	0	1	2	3	4
33. I have a good appetite	0	1	2	3	4
34. I like the appearance of my body	0	1	2	3	4
35. Do you have an ostomy appliance?	Yes	No			
If yes, please answer the next two items					
36. I am embarrassed by my ostomy appliance	0	1	2	3	4
37. Caring for my ostomy appliance is difficult	0	1	2	3	4

During the PAST WEEK;

0	1	2	3	4
not at all	a little bit	somewhat	quite a bit	very much

DIARRHEA SYMPTOMS

1. I have control of my bowels	0	1	2	3	4
2. I move my bowels more frequently than usual	0	1	2	3	4
3. I am afraid to be far from a toilet	0	1	2	3	4
4. I have to limit my social activity because of diarrhea	0	1	2	3	4
5. I have to limit my physical activity because of diarrhea	0	1	2	3	4
6. I have to limit my sexual activity because of diarrhea	0	1	2	3	4
7. I am embarrassed by having diarrhea	0	1	2	3	4
8. I have abdominal cramps or discomfort due to my diarrhea	0	1	2	3	4
9. My problem with diarrhea keeps/wakes me up at night	0	1	2	3	4
10. I must move my bowels frequently to avoid accidents	0	1	2	3	4
11. I wear pads or protection to prevent soiling my underwear	0	1	2	3	4

During the PAST WEEK:

0	1	2	3	4
not at all	a little bit	somewhat	quite a bit	very much

FATIGUE/ANEMIA SYMPTOMS

1. I feel fatigued	0	1	2	3	4
2. I feel weak all over	0	1	2	3	4
3. I feel listless ("washed out")	0	1	2	3	4
4. I feel tired	0	1	2	3	4
5. I have trouble starting things because I am tired	0	1	2	3	4
6. I have trouble finishing things because I am tired	0	1	2	3	4
7. I have energy	0	1	2	3	4
8. I have trouble walking	0	1	2	3	4
9. I am able to do my usual activities	0	1	2	3	4
10. I need to sleep during the day	0	1	2	3	4
11. I feel lightheaded (dizzy)	0	1	2	3	4
12. I get headaches	0	1	2	3	4
13. I have been short of breath	0	1	2	3	4
14. I have pain in my chest	0	1	2	3	4
15. I am too tired to eat	0	1	2	3	4
16. I am interested in sex	0	1	2	3	4
17. I am motivated to do my usual activities	0	1	2	3	4
18. I need help doing my usual activities	0	1	2	3	4
19. I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
20. I have to limit my social activities because I am tired	0	1	2	3	4

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month.

1. During the past month, when have you usually gone to bed at night?

USUAL BED TIME _____

2. During the past month, how long has it usually taken you to fall asleep each night?

NUMBER OF MINUTES _____

3. During the past month, when have you usually gotten up in the morning?

USUAL GETTING UP TIME _____

4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spend in bed.)

HOURS OF SLEEP PER NIGHT _____

For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past month, how often have you had trouble sleeping because you . . .

a) Cannot get to sleep within 30 minutes

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

b) Wake up in the middle of the night or early morning

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

c) Have to get up to use the bathroom

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

d) Cannot breathe comfortably

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

e) Cough or snore loudly

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

f) Feel too cold

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

g) Feel too hot

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

h) Had bad dreams

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

i) Have pain

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

j) Other reason(s), please describe_____
_____

How often during the past month have you had trouble sleeping because of this?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

6. During the past month, how would you rate your sleep quality overall?

Very good_____ Fairly good_____ Fairly bad_____ Very bad_____

7. During the past month, how often have you taken medicine to help you sleep (prescribed or "over the counter")?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

No problem at all _____

Only a very slight problem _____

Somewhat of a problem _____

A very big problem _____

10. Do you have a bed partner or room mate?

No bed partner or room mate _____

Partner/room mate in other room _____

Partner in same room, but not same bed _____

Partner in same bed _____

If you have a room mate or bed partner, ask him/her how often in the past month you have had . . .

a) Loud snoring

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

b) Long pauses between breaths while asleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

c) Legs twitching or jerking while you sleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

d) Episodes of disorientation or confusion during sleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

e) Other restlessness while you sleep; please describe_____
_____

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

Below is a list of statements concerning how you might have felt or behaved in the past week. Please use the following scale to indicate how often you felt or behaved in these ways in the past week.

0	1	2	3
Rarely or noneof the time (< 1 day)	Some of the time (1-2 days)	Much of the time (3-4 days)	Most or all of the time (5-7 days)

During the PAST WEEK:

1. I felt depressed.	0	1	2	3
2. I felt that everything I did was an effort.	0	1	2	3
3. My sleep was restless.	0	1	2	3
4. I was happy.	0	1	2	3
5. I felt lonely.	0	1	2	3
6. People were unfriendly.	0	1	2	3
7. I enjoyed life.	0	1	2	3
8. I felt sad.	0	1	2	3
9. I felt that people disliked me.	0	1	2	3
10. I could not get "going".	0	1	2	3

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number that best indicates how you have felt during the past week. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer that best describes how you felt.

During the PAST WEEK:

	not at all	somewhat	moderately so	very much so
1. I felt calm	1	2	3	4
2. I was tense	1	2	3	4
3. I felt at ease	1	2	3	4
4. I worried over possible misfortunes	1	2	3	4
5. I felt frightened	1	2	3	4
6. I felt self-confident	1	2	3	4
7. I was jittery	1	2	3	4
8. I was relaxed	1	2	3	4
9. I was worried	1	2	3	4
10. I felt steady	1	2	3	4

The questions in this scale ask you about your feelings and thoughts during the last month. Although some of the questions are similar, there are differences between them and you should treat each one as a separate question. The best approach is to answer each one fairly quickly. For each question, please choose from the following alternatives:

	0 never	1 almost never	2 some-times	3 fairly often	4 very often
In the last month, how often have you…					
1. been upset because of something that happened unexpectedly	0	1	2	3	4
2. felt that you were unable to control the important things in your life	0	1	2	3	4
3. felt nervous and stressed	0	1	2	3	4
4. dealt successfully with irritating life hassles	0	1	2	3	4
5. felt that you were effectively coping with important changes that were occurring in your life	0	1	2	3	4
6. felt confident about your ability to handle your personal problems	0	1	2	3	4
7. felt that things were going your way	0	1	2	3	4
8. found that you could not cope with all the things that you had to do	0	1	2	3	4
9. been able to control irritations in your life	0	1	2	3	4
10. felt that you were on top of things	0	1	2	3	4
11. been angered because of things that happened that were outside of your control	0	1	2	3	4
12. found yourself thinking about things that you have to accomplish	0	1	2	3	4
13. been able to control the way you spend your time	0	1	2	3	4
14. felt difficulties were piling up so high that you could not overcome them	0	1	2	3	4

The following questions concern the general perceptions that you currently have about yourself. Please circle the number that best reflects your current view of yourself using the following scale as a guide for your responses.

	Strongly Disagree	disagree	agree	strongly agree
1. On the whole I am satisfied with myself.	1	2	3	4
2. At times I think that I am no good at all.	1	2	3	4
3. I feel that I have a number of good qualities.	1	2	3	4
4. I am able to do things as well as most other people.	1	2	3	4
5. I feel I do not have much to be proud of.	1	2	3	4
6. I certainly feel useless at times.	1	2	3	4
7. I feel that I am a person of worth, at least on an equal plane with others.	1	2	3	4
8. I wish I could have more respect for myself.	1	2	3	4
9. All in all, I am inclined to feel that I am a failure.	1	2	3	4
10. I take a positive attitude toward myself.	1	2	3	4

For this next question, we would like you to recall any exercise you have done during your chemoradiotherapy treatment that was not part of the exercise program you did for this study. This means any exercise you did that was in addition to what you did for this study.

When answering these questions please:

- only count exercise sessions that lasted 10 minutes or longer in duration.
- only count exercise that was done during free time (i.e., not occupation or housework).
- note that the main difference between the first three categories is the intensity of the endurance (aerobic) exercise and the fourth category is for strength (resistance) exercise.
- please write the average frequency on the first line and the average duration on the second.
- if you did not do any exercise in one of the categories, please write in "0".

Considering a typical week (7 days) during your chemoradiotherapy treatment, how many times on the average did you do the following kinds of exercise that were not part of the exercise you did for this study?

	Times Per Week	Average Duration
a. VIGOROUS/STRENUOUS EXERCISE (HEART BEATS RAPIDLY, SWEATING) (e.g., running, aerobics classes, cross country skiing, vigorous swimming, vigorous bicycling).	_____	_____
b. MODERATE EXERCISE (NOT EXHAUSTING, LIGHT PERSPIRATION) (e.g., fast walking, tennis, easy bicycling, easy swimming, popular and folk dancing).	_____	_____
c. LIGHT/MILD EXERCISE (MINIMAL EFFORT, NO PERSPIRATION (e.g., easy walking, yoga, bowling, lawn bowling, shuffleboard).	_____	_____
d. RESISTANCE EXERCISE (e.g., lifting weights, push ups, sit ups, therabands).	_____	_____

The following questions ask you to rate how you felt about the exercise program that you were asked to do during your chemoradiotherapy treatment. Please pay careful attention to the words and descriptors for each scale and circle the number that best represents how you feel.

1. How beneficial was the exercise program during your chemoradiotherapy?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

2. How enjoyable was the exercise program during your chemoradiotherapy?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

3. How supportive were your family/friends of the exercise program during your chemoradiotherapy?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

4. How motivated were you to do the exercise program during your chemoradiotherapy?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

5. How difficult was it for you to do the exercise program during your chemoradiotherapy?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

We are interested in knowing about any benefits or harms you feel resulted from participating in the exercise program during your chemoradiotherapy treatment. Please use the following scale to guide your responses.

1	2	3	4	5	6	7
very much worse	somewhat worse	slightly worse	no change	slightly improved	somewhat improved	very much improved

What affect, if any, did the exercise program have on each of the following for you during your chemoradiotherapy treatment?

(a) cardiovascular endurance	1	2	3	4	5	6	7
(b) physical functioning	1	2	3	4	5	6	7
(c) balance	1	2	3	4	5	6	7
(d) muscular strength	1	2	3	4	5	6	7
(e) overall quality of life	1	2	3	4	5	6	7
(f) fatigue	1	2	3	4	5	6	7
(g) sleep quality	1	2	3	4	5	6	7
(h) depressed feelings	1	2	3	4	5	6	7
(i) anxious feelings	1	2	3	4	5	6	7
(j) stress	1	2	3	4	5	6	7
(k) self-esteem	1	2	3	4	5	6	7
(l) body weight or shape	1	2	3	4	5	6	7
(m) diarrhea	1	2	3	4	5	6	7
(n) pain/cramps in belly	1	2	3	4	5	6	7
(o) skin irritation at irradiated site	1	2	3	4	5	6	7
(p) tingling/numbness/peeling (hands & feet)	1	2	3	4	5	6	7
(q) nausea/vomiting	1	2	3	4	5	6	7
(r) ability to complete chemoradiotherapy	1	2	3	4	5	6	7
(s) illness or injury	1	2	3	4	5	6	7

Any other positive or negative effects you experienced?_____

We are also interested in knowing what, if any, barriers you felt made it difficult for you to do the exercise program during your chemoradiotherapy treatment. Please use the scale below to guide your responses.

1 not at all | 2 | 3 somewhat | 4 | 5 a fair bit | 6 | 7 very much

How much of a barrier was each of the following factors for you in trying to do the exercise program during your chemoradiotherapy treatment?

(a) medical appointments	1	2	3	4	5	6	7
(b) lack of motivation	1	2	3	4	5	6	7
(c) travelling to the fitness centre	1	2	3	4	5	6	7
(d) too busy and had limited time	1	2	3	4	5	6	7
(e) feeling tired or fatigued	1	2	3	4	5	6	7
(f) side effects of chemoradiotherapy	1	2	3	4	5	6	7
(g) diarrhea	1	2	3	4	5	6	7
(h) pain/cramps in belly	1	2	3	4	5	6	7
(i) skin irritation at irradiated site	1	2	3	4	5	6	7
(j) tingling/numbness/peeling (hands & feet)	1	2	3	4	5	6	7
(k) nausea/vomiting	1	2	3	4	5	6	7
(l) pain or soreness	1	2	3	4	5	6	7
(m) feeling sick/not feeling well	1	2	3	4	5	6	7
(n) illness or injury	1	2	3	4	5	6	7
(o) Do you have an ostomy appliance?			Yes	No			
If yes, how much of a barrier was it in trying to do the exercise program?	1	2	3	4	5	6	7
(p) Do you/did you have a PICC line?			Yes	No			
If yes, how much of a barrier was it in trying to do the exercise program?	1	2	3	4	5	6	7

Any other barriers you experienced? _____

The following questions ask you to rate how you felt about the exercise program you were asked to do during your chemoradiotherapy treatment.

1. Was exercising 3 days/week:

_____ too few

_____ about right

_____ too many

2. Was exercising for a duration of 50 minutes:

_____ too short

_____ about right

_____ too long

3. Was exercising at a moderate intensity:

_____ too easy

_____ about right

_____ too hard

This next set of questions asks you about how you would have liked to receive the exercise program during your chemoradiotherapy. **You may check more than one response.**

1. What combination of frequency and duration would you have preferred during chemoradiotherapy?
   - _____ 30 minutes/5 days week
   - _____ 40 minutes/4 days week
   - _____ 50 minutes/3 days week

2. What intensity of exercise would you have preferred during chemoradiotherapy?
   - _____ light intensity
   - _____ moderate intensity
   - _____ vigorous intensity

3. What type of exercise would you have preferred during chemoradiotherapy?
   - _____ aerobic (endurance)
   - _____ resistance (strength)
   - _____ both aerobic & resistance

4. How much of the exercise would you have liked to have been supervised during chemoradiotherapy?
   - _____ all supervised
   - _____ all unsupervised (on your own)
   - _____ combination supervised & unsupervised

5. Who would you have preferred to exercise with during chemoradiotherapy?
   - _____ alone
   - _____ other rectal cancer patients
   - _____ spouse
   - _____ friend

6. Where would you have preferred to do your exercise during chemoradiotherapy?
   - _____ outside around my neighbourhood
   - _____ in my home
   - _____ at the Cross Cancer Institute
   - _____ at a community fitness center
   - _____ at the fitness center where you did the supervised exercise

7. When would you have liked to exercise in relation to your chemoradiotherapy?
   - _____ right before radiotherapy
   - _____ right after radiotherapy
   - _____ well before radiotherapy (in the morning)
   - _____ well after radiotherapy (in the evening)

The following questions ask you to rate how you feel about exercising over the next six to eight weeks prior to your surgery. Please pay careful attention to the words and descriptions for each scale and circle the number that best represents how you feel.

1. How beneficial do you think it will be for you to exercise over the next 6 to 8 weeks before surgery?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

2. How enjoyable do you think it will be for you to exercise over the next 6 to 8 weeks before surgery?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

3. How supportive do you think your family/friends will be of you exercising over the next 6 to 8 weeks before surgery?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

4. How motivated are you to exercise over the next 6 to 8 weeks before surgery?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

5. How difficult do you think it will be for you to exercise over the next 6 to 8 weeks before surgery?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

Anything else you would like to tell us? On this final page, please feel free to make any comments concerning your rectal cancer, your treatments, the questionnaire, the exercise program, or anything else you think may be helpful to us. All comments are welcome.

Thank you very much for your continued participation in this research project. Please place the completed questionnaire in the envelope provided and bring it to your scheduled fitness test.

Appendix F. Pre-surgery Questionnaire

Identification #:_____
Date: _____

Aerobic exercise in rectal cancer patients receiving neoadjuvant chemoradiotherapy

Investigators: Andria Morielli, MSc Student, University of Alberta; Nawaid Usmani, MD, Cross Cancer Institute; Normand G. Boulé, PhD, University of Alberta; Kerry S. Courneya, PhD, University of Alberta

POSTINTERVENTION QUESTIONNAIRE

Instructions

Thank you for your continued participation in this study. At this postintervention assessment, we are going to ask you many of the same questions as in the previous questionnaires. However, it is important to answer these questions based on what you are thinking and feeling right now and not on how you answered the questions last time. This will give us important information about how your thoughts and feelings have changed. Many of the questions may seem similar but it is important to treat each question separately and provide an answer for each. Also, if at all possible, it is important to answer all questions. However, if you feel uncomfortable answering certain questions please leave them blank. All responses are completely confidential and will never be used in any way that could link them to you. There are no right or wrong answers and all we ask is that you provide responses that are as honest and accurate as possible. The questionnaire should take about 30-45 minutes of your time to complete. If you have any questions about completing the questionnaire, please contact Andria Moriellli (Research Coordinator) at (780) 492-2829 (call collect from out of town) or morielli@ualberta.ca.

This first set of questions asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Answer every question by marking a single answer. If you are unsure about how to answer a question please give the best answer you can.

1. In general, would you say your health is:

1	2	3	4	5
Excellent	Very good	Good	Fair	Poor

2. Compared to one year ago, how would you rate your health in general now?

1	2	3	4	5
Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

		Yes, limited a lot	Yes, limited a little	No, not limited at all
a.	**Vigorous Activities**, such as running, lifting heavy objects, participating in strenuous sports	1	2	3
b.	**Moderate Activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	1	2	3
c.	Lifting or carrying groceries	1	2	3
d.	Climbing **several** flights of stairs	1	2	3
e.	Climbing **one** flight of stairs	1	2	3
f.	Bending, kneeling or stooping	1	2	3
g.	Walking **more than a mile**	1	2	3
h.	Walking **several hundred yards**	1	2	3
i.	Walking **one hundred yards**	1	2	3
j.	Bathing or dressing yourself	1	2	3

4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down on the **amount of time** you spent on work or other activities	1	2	3	4	5
b. **Accomplished less** than you would like	1	2	3	4	5
c. Were **limited** in the **kind** of work or other activities	1	2	3	4	5
d. Had **difficulty** performing the work or other activities (e.g., it took extra effort)	1	2	3	4	5

5. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down on the **amount of time** you spent on work or other activities	1	2	3	4	5
b. **Accomplished less** than you would like	1	2	3	4	5
c. Did work or other activities **less carefully than usual**.	1	2	3	4	5

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

1	2	3	4	5
Not at all	Slightly	Moderately	Quite a bit	Extremely

7. How much bodily pain have you had during the past 4 weeks?

1	2	3	4	5	6
None	Very mild	Mild	Moderate	Severe	Very severe

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

1	2	3	4	5
Not at all	A little bit	Moderately	Quite a bit	Extremely

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give one answer that comes closest to the way you have been feeling.
How much of the time during the past 4 weeks…

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of life?	1	2	3	4	5
b. Have you been very nervous?	1	2	3	4	5
c. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5
d. Have you felt calm and peaceful?	1	2	3	4	5
e. Did you have a lot of energy?	1	2	3	4	5
f. Have you felt downhearted and depressed?	1	2	3	4	5
g. Did you feel worn out?	1	2	3	4	5
h. Have you been happy?	1	2	3	4	5
i. Did you feel tired?	1	2	3	4	5

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

1	2	3	4	5
All of the time	Most of the time	Some of the time	A little of the time	None of the time

11. How TRUE or FALSE is <u>each</u> of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. I seem to get sick a little easier than other people	1	2	3	4	5
b. I am as healthy as anybody I know	1	2	3	4	5
c. I expect my health to get worse	1	2	3	4	5
d. My health is excellent	1	2	3	4	5

Below is a list of statements that other people with cancer have said are important to their quality of life. Please indicate the extent to which you have experienced each of the statements during the past 7 days by circling the appropriate number using the following scale.

0	1	2	3	4
not at all	a little bit	somewhat	quite a bit	very much

During the PAST WEEK:

1. I have a lack of energy	0	1	2	3	4
2. I have nausea	0	1	2	3	4
3. Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
4. I have pain	0	1	2	3	4
5. I am bothered by side effects of treatment	0	1	2	3	4
6. I feel sick	0	1	2	3	4
7. I am forced to spend time in bed	0	1	2	3	4
8. I feel close to my friends	0	1	2	3	4
9. I get emotional support from my family	0	1	2	3	4
10. I get support from my friends	0	1	2	3	4
11. My family has accepted my illness	0	1	2	3	4
12. I am satisfied with family communication about my illness	0	1	2	3	4
13. I feel close to my partner (or the person who is my main support)	0	1	2	3	4
14. I am satisfied with my sex life	0	1	2	3	4
15. I feel sad	0	1	2	3	4
16. I am satisfied with how I am coping with my illness	0	1	2	3	4

During the PAST WEEK;

0	1	2	3	4
not at all	a little bit	somewhat	quite a bit	very much

17. I am losing hope in the fight against my illness	0	1	2	3	4
18. I feel nervous	0	1	2	3	4
19. I worry about dying	0	1	2	3	4
20. I worry that my condition will get worse	0	1	2	3	4
21. I am able to work (include work at home)	0	1	2	3	4
22. My work (include work at home) is fulfilling	0	1	2	3	4
23. I am able to enjoy life	0	1	2	3	4
24. I have accepted my illness	0	1	2	3	4
25. I am sleeping well	0	1	2	3	4
26. I am enjoying the things I usually do for fun	0	1	2	3	4
27. I am content with the quality of my life right now	0	1	2	3	4
28. I have swelling or cramps in my stomach area	0	1	2	3	4
29. I am losing weight	0	1	2	3	4
30. I have control of my bowels	0	1	2	3	4
31. I can digest my food well	0	1	2	3	4
32. I have diarrhea (diarrhoea)	0	1	2	3	4
33. I have a good appetite	0	1	2	3	4
34. I like the appearance of my body	0	1	2	3	4
35. Do you have an ostomy appliance?	Yes	No			
If yes, please answer the next two items					
36. I am embarrassed by my ostomy appliance	0	1	2	3	4
37. Caring for my ostomy appliance is difficult	0	1	2	3	4

During the PAST WEEK;

0	1	2	3	4
not at all	a little bit	somewhat	quite a bit	very much

DIARRHEA SYMPTOMS

1. I have control of my bowels	0	1	2	3	4
2. I move my bowels more frequently than usual	0	1	2	3	4
3. I am afraid to be far from a toilet	0	1	2	3	4
4. I have to limit my social activity because of diarrhea	0	1	2	3	4
5. I have to limit my physical activity because of diarrhea	0	1	2	3	4
6. I have to limit my sexual activity because of diarrhea	0	1	2	3	4
7. I am embarrassed by having diarrhea	0	1	2	3	4
8. I have abdominal cramps or discomfort due to my diarrhea	0	1	2	3	4
9. My problem with diarrhea keeps/wakes me up at night	0	1	2	3	4
10. I must move my bowels frequently to avoid accidents	0	1	2	3	4
11. I wear pads or protection to prevent soiling my underwear	0	1	2	3	4

During the PAST WEEK:

0	1	2	3	4
not at all	a little bit	somewhat	quite a bit	very much

FATIGUE/ANEMIA SYMPTOMS

1. I feel fatigued	0	1	2	3	4
2. I feel weak all over	0	1	2	3	4
3. I feel listless ("washed out")	0	1	2	3	4
4. I feel tired	0	1	2	3	4
5. I have trouble starting things because I am tired	0	1	2	3	4
6. I have trouble finishing things because I am tired	0	1	2	3	4
7. I have energy	0	1	2	3	4
8. I have trouble walking	0	1	2	3	4
9. I am able to do my usual activities	0	1	2	3	4
10. I need to sleep during the day	0	1	2	3	4
11. I feel lightheaded (dizzy)	0	1	2	3	4
12. I get headaches	0	1	2	3	4
13. I have been short of breath	0	1	2	3	4
14. I have pain in my chest	0	1	2	3	4
15. I am too tired to eat	0	1	2	3	4
16. I am interested in sex	0	1	2	3	4
17. I am motivated to do my usual activities	0	1	2	3	4
18. I need help doing my usual activities	0	1	2	3	4
19. I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
20. I have to limit my social activities because I am tired	0	1	2	3	4

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month.

1. During the past month, when have you usually gone to bed at night?

USUAL BED TIME _____

2. During the past month, how long has it usually taken you to fall asleep each night?

NUMBER OF MINUTES _____

3. During the past month, when have you usually gotten up in the morning?

USUAL GETTING UP TIME _____

4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spend in bed.)

HOURS OF SLEEP PER NIGHT _____

For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past month, how often have you had trouble sleeping because you . . .

a) Cannot get to sleep within 30 minutes

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

b) Wake up in the middle of the night or early morning

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

c) Have to get up to use the bathroom

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

d) Cannot breathe comfortably

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

e) Cough or snore loudly

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

f) Feel too cold

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

g) Feel too hot

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

h) Had bad dreams

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

i) Have pain

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

j) Other reason(s), please describe_____

_____

How often during the past month have you had trouble sleeping because of this?

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

6. During the past month, how would you rate your sleep quality overall?

Very good_____ Fairly good_____ Fairly bad_____ Very bad_____

7. During the past month, how often have you taken medicine to help you sleep (prescribed or "over the counter")?

Not during the past month_____ Less than once a week_____ Once or twice a week_____ Three or more times a week_____

8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

No problem at all _____

Only a very slight problem _____

Somewhat of a problem _____

A very big problem _____

10. Do you have a bed partner or room mate?

No bed partner or room mate _____

Partner/room mate in other room _____

Partner in same room, but not same bed _____

Partner in same bed _____

If you have a room mate or bed partner, ask him/her how often in the past month you have had . . .

a) Loud snoring

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

b) Long pauses between breaths while asleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

c) Legs twitching or jerking while you sleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

d) Episodes of disorientation or confusion during sleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

e) Other restlessness while you sleep; please describe_____
_____

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

Below is a list of statements concerning how you might have felt or behaved in the past week. Please use the following scale to indicate how often you felt or behaved in these ways in the past week.

0	1	2	3
Rarely or none of the time (< 1 day)	Some of the time (1-2 days)	Much of the time (3-4 days)	Most or all of the time (5-7 days)

During the PAST WEEK:

1. I felt depressed.	0	1	2	3
2. I felt that everything I did was an effort.	0	1	2	3
3. My sleep was restless.	0	1	2	3
4. I was happy.	0	1	2	3
5. I felt lonely.	0	1	2	3
6. People were unfriendly.	0	1	2	3
7. I enjoyed life.	0	1	2	3
8. I felt sad.	0	1	2	3
9. I felt that people disliked me.	0	1	2	3
10. I could not get "going".	0	1	2	3

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number that best indicates how you have felt during the past week. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer that best describes how you felt.

During the PAST WEEK:

	not at all	somewhat	moderately so	very much so
1. I felt calm	1	2	3	4
2. I was tense	1	2	3	4
3. I felt at ease	1	2	3	4
4. I worried over possible misfortunes	1	2	3	4
5. I felt frightened	1	2	3	4
6. I felt self-confident	1	2	3	4
7. I was jittery	1	2	3	4
8. I was relaxed	1	2	3	4
9. I was worried	1	2	3	4
10. I felt steady	1	2	3	4

The questions in this scale ask you about your feelings and thoughts during the last month. Although some of the questions are similar, there are differences between them and you should treat each one as a separate question. The best approach is to answer each one fairly quickly. For each question, please choose from the following alternatives:

	0 never	1 almost never	2 some-times	3 fairly often	4 very often
In the last month, how often have you…					
1. been upset because of something that happened unexpectedly	0	1	2	3	4
2. felt that you were unable to control the important things in your life	0	1	2	3	4
3. felt nervous and stressed	0	1	2	3	4
4. dealt successfully with irritating life hassles	0	1	2	3	4
5. felt that you were effectively coping with important changes that were occurring in your life	0	1	2	3	4
6. felt confident about your ability to handle your personal problems	0	1	2	3	4
7. felt that things were going your way	0	1	2	3	4
8. found that you could not cope with all the things that you had to do	0	1	2	3	4
9. been able to control irritations in your life	0	1	2	3	4
10. felt that you were on top of things	0	1	2	3	4
11. been angered because of things that happened that were outside of your control	0	1	2	3	4
12. found yourself thinking about things that you have to accomplish	0	1	2	3	4
13. been able to control the way you spend your time	0	1	2	3	4
14. felt difficulties were piling up so high that you could not overcome them	0	1	2	3	4

The following questions concern the general perceptions that you currently have about yourself. Please circle the number that best reflects your current view of yourself using the following scale as a guide for your responses.

	Strongly Disagree	disagree	agree	strongly agree
1. On the whole I am satisfied with myself.	1	2	3	4
2. At times I think that I am no good at all.	1	2	3	4
3. I feel that I have a number of good qualities.	1	2	3	4
4. I am able to do things as well as most other people.	1	2	3	4
5. I feel I do not have much to be proud of.	1	2	3	4
6. I certainly feel useless at times.	1	2	3	4
7. I feel that I am a person of worth, at least on an equal plane with others.	1	2	3	4
8. I wish I could have more respect for myself.	1	2	3	4
9. All in all, I am inclined to feel that I am a failure.	1	2	3	4
10. I take a positive attitude toward myself.	1	2	3	4

For this next question, we would like you to recall all the exercise you did since completing your chemoradiotherapy treatment. This means any exercise you did that was for the study and any exercise you did in addition to what you did for the study.

When answering these questions please:

- only count exercise sessions that lasted 10 minutes or longer in duration.
- only count exercise that was done during free time (i.e., not occupation or housework).
- note that the main difference between the first three categories is the intensity of the endurance (aerobic) exercise and the fourth category is for strength (resistance) exercise.
- please write the average frequency on the first line and the average duration on the second.
- if you did not do any exercise in one of the categories, please write in "0".

Considering a typical week (7 days) since you completed your chemoradiotherapy, how many times on the average did you do the following kinds of exercise?

	Times Per Week	Average Duration
b. VIGOROUS/STRENUOUS EXERCISE (HEART BEATS RAPIDLY, SWEATING) (e.g., running, aerobics classes, cross country skiing, vigorous swimming, vigorous bicycling).	_____	_____
b. MODERATE EXERCISE (NOT EXHAUSTING, LIGHT PERSPIRATION) (e.g., fast walking, tennis, easy bicycling, easy swimming, popular and folk dancing).	_____	_____
c. LIGHT/MILD EXERCISE (MINIMAL EFFORT, NO PERSPIRATION (e.g., easy walking, yoga, bowling, lawn bowling, shuffleboard).	_____	_____
d. RESISTANCE EXERCISE (e.g., lifting weights, push ups, sit ups, therabands).	_____	_____

The following questions ask you to rate how you felt about the exercise program that you were asked to do after the completion of your chemoradiotherapy treatment and prior to your surgery. Please pay careful attention to the words and descriptors for each scale and circle the number that best represents how you feel.

1. How beneficial was the exercise program after the completion of your chemoradiotherapy and prior to surgery?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

2. How enjoyable was the exercise program after the completion of your chemoradiotherapy and prior to surgery?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

3. How supportive were your family/friends of the exercise program after the completion of your chemoradiotherapy and prior to surgery?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

4. How motivated were you to do the exercise program after the completion of your chemoradiotherapy and prior to surgery?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

5. How difficult was it for you to do the exercise program after the completion of your chemoradiotherapy and prior to surgery?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

We are interested in knowing about any benefits or harms you feel resulted from participating in the exercise program after the completion of your chemoradiotherapy treatment and prior to your surgery. Please use the following scale to guide your responses.

1	2	3	4	5	6	7
very much worse	somewhat worse	slightly worse	no change	slightly improved	somewhat improved	very much improved

What affect, if any, did the exercise program have on each of the following for you after the completion of your chemoradiotherapy and prior to surgery?

(a) cardiovascular endurance	1	2	3	4	5	6	7
(b) physical functioning	1	2	3	4	5	6	7
(c) balance	1	2	3	4	5	6	7
(d) muscular strength	1	2	3	4	5	6	7
(e) overall quality of life	1	2	3	4	5	6	7
(f) fatigue	1	2	3	4	5	6	7
(g) sleep quality	1	2	3	4	5	6	7
(h) depressed feelings	1	2	3	4	5	6	7
(i) anxious feelings	1	2	3	4	5	6	7
(j) stress	1	2	3	4	5	6	7
(k) self-esteem	1	2	3	4	5	6	7
(l) body weight or shape	1	2	3	4	5	6	7
(m) diarrhea	1	2	3	4	5	6	7
(n) pain/cramps in belly	1	2	3	4	5	6	7
(o) skin irritation at irradiated site	1	2	3	4	5	6	7
(p) tingling/numbness/peeling (hands & feet)	1	2	3	4	5	6	7
(q) nausea/vomiting	1	2	3	4	5	6	7
(r) illness or injury	1	2	3	4	5	6	7
(s) preparation for surgery	1	2	3	4	5	6	7

Any other positive or negative effects you experienced?_____

We are also interested in knowing what, if any, barriers you felt made it difficult for you to do the exercise program after the completion of your chemoradiotherapy treatment and prior to your surgery. Please use the scale below to guide your responses.

1	2	3	4	5	6	7
not at all		somewhat		a fair bit		very much

How much of a barrier was each of the following factors for you in trying to do the exercise program after the completion of your chemoradiotherapy and prior to surgery?

(a) vacation	1	2	3	4	5	6	7
(b) bad weather	1	2	3	4	5	6	7
(c) medical appointments	1	2	3	4	5	6	7
(d) lack of motivation	1	2	3	4	5	6	7
(e) lack of exercise supervision	1	2	3	4	5	6	7
(f) too busy and had limited time	1	2	3	4	5	6	7
(g) feeling tired or fatigued	1	2	3	4	5	6	7
(h) lingering side effects of chemoradiotherapy	1	2	3	4	5	6	7
(i) diarrhea	1	2	3	4	5	6	7
(j) pain/cramps in belly	1	2	3	4	5	6	7
(k) skin irritation at irradiated site	1	2	3	4	5	6	7
(l) tingling/numbness/peeling (hands & feet)	1	2	3	4	5	6	7
(m) nausea/vomiting	1	2	3	4	5	6	7
(n) pain or soreness	1	2	3	4	5	6	7
(o) feeling sick/not feeling well	1	2	3	4	5	6	7
(p) illness or injury	1	2	3	4	5	6	7
(q) do you have an ostomy appliance?			Yes	No			
If yes, how much of a barrier was it in trying to do the exercise program?	1	2	3	4	5	6	7

Any other barriers you experienced? _____

The following questions ask you to rate how you felt about the exercise program you were asked to do after the completion of your chemoradiotherapy treatment and prior to your surgery.

1. Was exercising 3 days/week:

_____ too few

_____ about right

_____ too many

2. Was exercising for a duration of 50 minutes:

_____ too short

_____ about right

_____ too long

3. Was exercising at a moderate intensity:

_____ too easy

_____ about right

_____ too hard

This next set of questions asks you about how you would have liked to receive the exercise program after the completion of your chemoradiotherapy treatment and prior to your surgery.

1. What combination of frequency and duration would you have preferred after the completion of chemoradiotherapy and prior to surgery?

_____ 25 minutes/ 6 days week
_____ 30 minutes/5 days week
_____ 40 minutes/4 days week
_____ 50 minutes/3 days week
_____ other (please specify) _____

2. What intensity of exercise would you have preferred after the completion of chemoradiotherapy and prior to surgery?

_____ light intensity (minimal effort, no perspiration)
_____ moderate intensity (not exhausting, light perspiration)
_____ vigorous intensity (heart beats rapidly, sweating)

3. What type of exercise would you have preferred after the completion of chemoradiotherapy and prior to surgery?

_____ aerobic (endurance)
_____ resistance (strength)
_____ both aerobic & resistance
_____ other (please specify)
_____

4. What type of aerobic exercise would you have preferred after the completion of chemoradiotherapy and prior to surgery? Examples: Walking, biking, swimming, hiking, step class, tennis, skiing, yoga, golf etc. Please list any.

_____

_____

5. How much of the exercise would you have liked to have been supervised after the completion of chemoradiotherapy and prior to surgery?

_____ all supervised
_____ all unsupervised (on your own)
_____ combination supervised & unsupervised

6. Who would you have preferred to exercise with after the completion of chemoradiotherapy and prior to surgery?

_____ alone
_____ spouse
_____ friend
_____ other rectal cancer patients
_____ other

7. Where would you have preferred to do your exercise after the completion of chemoradiotherapy and prior to surgery?

_____ outside around my neighbourhood
_____ at the Cross Cancer Institute
_____ in my home
_____ at a community fitness center
_____ at the fitness center where you did the supervised exercise

You may check more than one response.

The next set of questions on this page relate to how you felt about taking part in this study.

Please answer each one as honestly as possible using the following scale:

1	2	3	4	5	6	7
not at all		somewhat		a fair bit		very much

1. How much of a burden was it for you to complete each of the following assessments in this study?

(a) the treadmill fitness test	1	2	3	4	5	6	7
(b) the physical function test	1	2	3	4	5	6	7
(c) the balance test	1	2	3	4	5	6	7
(d) the questionnaires	1	2	3	4	5	6	7

2. How much of a burden was it for you to complete each of the following?

(a) the supervised exercise sessions during your chemoradiotherapy	1	2	3	4	5	6	7
(b) the exercise sessions during the break period prior to surgery	1	2	3	4	5	6	7

3. With hindsight, how do you feel about participating in this study?

(a) rewarding	1	2	3	4	5	6	7
(b) a waste of my time	1	2	3	4	5	6	7
(c) useful for research helping others	1	2	3	4	5	6	7
(d) useful for me personally	1	2	3	4	5	6	7
(e) something that I would recommend to other rectal cancer patients	1	2	3	4	5	6	7

The following questions ask you to rate how you feel about exercising after you have recovered from your surgery. Please pay careful attention to the words and descriptions for each scale and circle the number that best represents how you feel.

2. How beneficial do you think it will be for you to exercise after you have recovered from surgery?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

2. How enjoyable do you think it will be for you to exercise after you have recovered from surgery?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

3. How supportive do you think your family/friends will be if you try to exercise after you have recovered from surgery?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

4. How motivated are you to exercise after you have recovered from surgery?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

5. How difficult do you think it will be for you to exercise after you have recovered from surgery?

1	2	3	4	5
not at all	a little bit	somewhat	quite a bit	very much

Anything else you would like to tell us? On this final page, please feel free to make any comments concerning your rectal cancer, your treatments, the questionnaire, the exercise program, or anything else you think may be helpful to us. All comments are welcome.

Any suggestions on how to improve the exercise program?

Thank you very much for your continued participation in this research project. Please place the completed questionnaire in the envelope provided and bring it to your scheduled fitness test.

Appendix G. Consent Form

Cross Cancer Institute

11560 University Avenue, Edmonton, AlbertaT6G 1Z2 Tel 780.432.8771

Feasibility and Efficacy of aerobic exercise in rectal cancer patients receiving neoadjuvant chemoradiotherapy

CONSENT FORM

This form is part of the process of informed consent. It is designed to explain this research study and what will happen to you if you choose to be in this study.

If you would like to know more about something mentioned in this consent form, or have any questions at any time regarding this research study, please be sure to ask your doctor or contact the Principal Investigator or Trial Coordinator (Contact information on page). Read this consent form carefully to make sure you understand all the information it provides. You will get a copy of this consent form to keep.

Your doctor has given us permission to ask you to be in this study. Your participation in this study is entirely voluntary and your care does not depend on whether or not you take part.

"WHY IS THIS STUDY BEING DONE?"

To date, very few studies have looked at the effects of exercise for rectal cancer patients receiving neoadjuvant combined radiation and chemotherapy. Prior to examining the possible relationship between exercise and outcomes such as health-related physical fitness, fatigue, depression, anxiety and quality of life we must determine if it is feasible for this patient group to exercise.

"WHAT DO WE HOPE TO LEARN?"

The primary objective of this study is to determine if rectal cancer patients are able and willing to exercise during neoadjuvant combined radiation and chemotherapy and during the recovery period prior to their scheduled surgery date. We will also be collecting some preliminary data on the following outcomes: health-related physical fitness and other outcomes such as fatigue, depression and anxiety and quality of life.

We hope to learn that it is feasible for rectal cancer patients receiving neoadjuvant combined radiation and chemotherapy to exercise while on treatment (and during the recovery phase prior to surgery).

"WHAT IS INVOLVED IN THIS STUDY?"

Study participants will be given a 12-week individualized aerobic (walking, biking, etc.) exercise program and will be asked to exercise for 3 days/week for the duration of the exercise intervention. While you are undergoing treatments (5-6 weeks), you will be asked to exercise at the Behavioral Medicine Fitness Centre on the University of Alberta campus (within a 2 minute walk from the Cross Cancer Institute). Once you have completed your treatments, you will have the option of continuing to exercise at our fitness center, exercising on your own or a combination of both for the remaining duration prior to your scheduled surgery. You will also be asked to undergo fitness and quality of life assessments at three time points: prior to starting your cancer treatments, within one week of completing your cancer treatments and approximately one week prior to your scheduled surgery.

"HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?"

Overall we hope to recruit 15-20 people for this study from the Cross Cancer Institute.

"WHAT WILL MY PARTICIPATION INVOLVE?"

If you take part in this study, you will be asked to do the following:

- Complete three assessments, one before you start your chemoradiotherapy, one right after completing your treatments, and one about one week prior to your surgery. Each assessment will take about 2 hours and include the following:
    - Walking on a treadmill with a gradual increase in speed and elevation. Your heart rate, blood pressure and how hard you feel you are working will be watched by the physical activity specialist throughout the test. You can request to stop this test at any time. The treadmill test should take no more than 45 minutes to complete.
    - A physical function assessment consisting of chair stands, arm curls, sit and reach and back scratch flexibility tests, walking around an 8-foot course, and walking for 6 minutes. The physical function assessment should take no longer than 45 minutes to complete.
    - Your body composition will be estimated by measurements of height, weight, and circumferences. Height and weight will be obtained using a balance beam scale and stadiometer. Waist and hip circumference will be measured using a nonstretching tape measure. This assessment will take approximately 5 minutes to complete.
    - Complete self-administered questionnaires that talk about your current health status, physical activity, perceived fatigue, stress and sleeping patterns. In total, these questionnaires should take between 30-45 minutes to complete.
    - Attend supervised exercise sessions 3 days/week for the duration of your treatments (about 5-6 weeks). Continue to exercise 3 days/week following the completion of your treatment, until your scheduled surgery (about 5-6 weeks). These exercise session do not have to be supervised. The total length of the exercise intervention is 12 weeks.
    - The duration and intensity of your exercise prescription will increase slowly over the 12 week program and will be adjusted according to any immediate or persistent negative effects of the treatment that you may be experiencing at any given time.

- The supervised exercise sessions will take place at the Behavioral Medicine Fitness Centre (University of Alberta). Exercise sessions will be available any time between 7 am and 5 pm, however, for your convenience, we suggest you come exercise immediately following your radiation treatment.

Type of Assessment	Baseline	Post Treatment	Pre-Surgical
Cardiorespiratory Fitness	X	X	X
Physical Functioning	X	X	X
Anthropometrics	X	X	X
Questionnaires	X	X	X

"HOW LONG WILL I BE INVOLVED IN THE STUDY?"

The exercise intervention is 12 weeks. Keep in mind that we will be doing one baseline test sometime before you start your cancer treatments, one after you have completed these treatments and again once you have completed the 12 week exercise intervention and prior to your scheduled surgery date. As such, the time frame may vary from person to person but should be about 14 weeks in total.

"WHAT ARE THE SIDE EFFECTS?"

There are a few risks associated with participating in this research. It is possible that some people will experience muscle soreness and fatigue following the fitness testing. This type of response is usual, and generally poses no threat to health. Do not take any over the counter medications without speaking to your doctor first. If the soreness persists more than five days, or might be associated with a muscle or joint injury, participants should see a physician. Some of the side effects of chemoradiotherapy could be made worse with exercise (e.g., fatigue, diarrhea, cardiac problems), but no research has shown this to be the case. These risks will be reduced as much as possible by the attention and careful instruction of research staff and by the fact that your exercise testing will be conducted by certified fitness appraisers.

There is some risk associated with the aerobic fitness tests. During and immediately after the tests, it is possible to experience symptoms such as abnormal blood pressure, fainting, light-headedness, muscle cramps or strain, nausea, and in very rare cases (1 per 20,000 in testing facilities) heart rhythm disturbances or heart attack. While serious risk to healthy participants is highly unlikely, such risks must be acknowledged, and participants must willingly assume the risks associated with exercise.
If you have any side effects, either those on the list or others, or if you want more information you should call your doctor, or the Principal Investigator or Trial Coordinator in charge of the study. Their telephone numbers are on page 6 of this form.

Unique Side Effects/Special Precaution

The exercise specialist will adjust your exercise program according to how you are feeling. We understand that patients may respond differently to the cancer treatments. Diarrhea is one of the most commonly reported side effects from the cancer treatment you will be receiving. As such, special attention will be paid to diarrhea: bathroom facilities will be readily available to participants. The exercise specialist will also monitor you closely for any other symptoms you may be feeling (fatigue, pain, nausea) and adjust accordingly.

"**WHAT ARE MY RESPONSIBILITIES?"**

You must be willing to attend all scheduled study visits and undergo all of the procedures described above. It is very important that you inform the study doctor, Principal Investigator or Trial Coordinator of any side effects or health problems that you may be experiencing as well as any medications that you are taking while on this study. Additionally, you must be willing to fill out the questionnaires that are part of the study protocol.

"WHAT ARE MY ALTERNATIVES?"

You may choose not to participate in this study and obtain advice about exercise from your doctor or a private fitness center.

"ARE THERE ANY BENEFITS TO PARTICIPATING IN THIS STUDY?"

Participation in this study may or may not be of personal benefit to you. However, based on the results of this study, we hope to learn whether rectal cancer patients are able to exercise while on treatment and what, if any, benefits they may experience. As part of participating in this study, you will receive a 12 week exercise program including a personal fitness trainer and access to a well-equipped fitness facility at no cost.

"CAN I WITHDRAW FROM THIS STUDY?"

Taking part in this study is voluntary; you may withdraw from the study at any time if you wish to do so. If you decide to stop participating in the study, we encourage you to talk to your doctor, Principal Investigator or Trial Coordinator first.

Should you decide to withdraw from the study at any time, information collected on you up until that point would still be utilized in this study unless you request to remove the information. The information collected in this study will be used for research and teaching purposes, and to help develop guidelines for helping improve the quality of life and health for people with cancer.

"ARE THERE COSTS TO ME FOR TAKING PART IN THIS STUDY?"

You will not have to pay for any component of this research study. The costs of attending the fitness testing and supervised exercise sessions and parking will be paid for by the study.

"WHAT ARE MY RIGHTS AS A PARTICIPANT?"

In the event that you suffer an injury as a result of participating in this research, you will receive all medical treatments necessary. No compensation will be provided for you by the Alberta Health Services, the University of Alberta or by the research team. You still have all your legal rights. Nothing said here about treatment of compensation in any way alters your right to recover damages (e.g. legal action).

If new information becomes available that may affect your health or willingness to continue the study, you will be told in a timely manner.

"WILL MY PERSONAL INFORMATION BE KEPT CONFIDENTIAL?"

Identifiable health information will be collected from you. This information may be used by the researchers who are carrying out this study, and may be disclosed to others as described below. Any research proposal to use information that identifies you for a purpose other than this study must be approved in advance by the Health Research Ethics Board of Alberta-Cancer Committee.

Direct access to your identifiable health information collected for this study will be restricted to the researchers who are directly involved in this study except in the following circumstances:

Your identifiable health information may need to be inspected or copied from time to time for quality assurance (to make sure the information being used in the study is accurate) and for data analysis (to do statistical analysis that will not identify you). The following organizations may do this inspection:

- Health Canada, the Canadian regulatory body
- The Health Research Ethics Board of Alberta (HREBA)- Cancer Committee, the institution at this centre
- Member of the Regulatory/Audit team at the Cross Cancer Institute for quality assurance purposes
- University of Alberta and HREBA

Any disclosure of your identifiable health information will be in accordance with the Alberta Health Information Act. As well, any person from the organizations listed above looking at your records on-site at the Cross Cancer Institute and University of Alberta will follow the relevant Alberta Health Services and the relevant Alberta Innovates –Health Solutions-Health Research Ethics Board of Alberta- Cancer Committee policies and procedures that control these actions. Any disclosure of your identifiable health information to another individual or organization not listed here will need the approval of the Health Research Ethics Board of Alberta- Cancer Committee.

Your identifiable health information collected as part of this study which includes records of your assessments and your responses to the questionnaires will be kept confidential in a secure Alberta Health Service facility.

The researchers who are directly involved in your study may share information about you with other researchers, but you will not be identified in that shared information except by a number. The key that indicates what number you have been assigned will be kept secure by the researchers directly involved with your study and will not be released.

Although absolute confidentiality can never be guaranteed, Alberta Health Services will make every effort to keep your identifiable health information confidential, and to follow the ethical and legal rules about collecting, using and disclosing this information in accordance with the Alberta Health Information Act and other regulatory requirements.

The information collected during this study will be used in analyses and will be published and/or presented to the scientific community at meetings and in journals, but your identity will remain confidential. It is expected that the study results will be published as soon as possible after completion. Your study doctor will be informed of the results of the study once they are known.

"WHO DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?"

For information about the study, or to answer any questions you have about this study, you may contact the Principal Investigator: Dr. Kerry Courneya at (780) 492-1031 or the Research coordinator Andria Morielli at 780-492-2829.

If you feel, at any time, that you have not been informed to your satisfaction about the risks, benefits, or alternatives of this study, or that you have been encouraged to continue in this study after you wanted to withdraw, you can call the Alberta Health Services Patient Concerns Department at:

Edmonton 780-342-8080 or toll free at 1-877-753-2170.

UNDERSTANDING OF PARTICIPANTS

I can refuse to take part or withdraw from this study at any time without jeopardizing my health care. If I continue to take part in the study, I will be kept informed of any important new developments and information learned after the time I gave my original consent.

I also give consent for the Principal Investigator and Alberta Health Services (the Custodian) to disclose identifiable health information, as per the Alberta Health Information Act, to the organizations mentioned on the previous pages.

I have read and understood all of the information in this consent form. I have asked questions, and received answers concerning areas I did not understand. I have had the opportunity to take this consent form home for review and discussion. My consent has not been forced or influenced in any way. I consent to participate in this research study. Upon signing this form I will receive a signed copy of the consent.

(PRINT NAMES CLEARLY)

_____	_____	_____
Name of Patient	Signature of Patient	Date
_____	_____	_____
Name of Person Obtaining Consent	Signature of Person Obtaining Consent	Date

Patient Study Number or Hospital Number: _____

Was the patient assisted during the consent process in one of the ways listed below?
□ Yes □ No

If yes, please check the relevant box and complete the signature space below:

□ The consent form was read to the patient, and the person signing below attests that the study was accurately explained to, and apparently understood by the patient.

□ The person signing below acted as a translator for the patient during the consent process.

_____	_____
Signature of person assisting In the consent discussion	Date

Please note: More information regarding the assistance provided during the consent process should be noted in the medical record for the patient if applicable.