

IN-HOSPITAL INDIVIDUALIZED PRESCRIPTIVE EXERCISE INTERVENTION
FOR ACUTE LEUKEMIA PATIENTS UNDERGOING CHEMOTHERAPY

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ABSTRACT

**BRAD GREGORY: In-Hospital Individualized Prescriptive Exercise Intervention for
Acute Leukemia Patients Undergoing Chemotherapy
(Under the direction of Dr. Claudio Battaglini)**

Exercise intervention studies among leukemia patients have previously been very limited. Therefore, the purpose of the study was to examine the effects of an individualized prescriptive exercise intervention, administered in-hospital during the treatment-recovery of leukemia patients, on fitness parameters and quality of life. Five patient volunteers were recruited for the study, and four successfully completed the six-week training protocol, which consisted of aerobic activity between 40-60% of heart rate reserve, endurance-based resistance training, and flexibility training. Physiological and psychological parameters were assessed within three days of the induction phase of chemotherapy, and again at the end of the fourth week of recovery. Non-significant differences were observed for every variable, leading researchers to believe all parameters were maintained throughout the six-week exercise training protocol. The results of this study demonstrate that an exercise program, consisting of aerobic training, resistance training, and flexibility training, enables acute leukemia patients to maintain physiology and quality of life while undergoing chemotherapy.

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Chapter 1

INTRODUCTION

A rapidly growing concern for millions of people throughout the world is the widespread threat of cancer. It is estimated that during 2005, over 1.3 million new cases will be diagnosed in the United States (American Cancer Society, 2005). Breast and prostate cancer are the most common forms of cancer affecting women and men respectively, being the third and sixth most common forms from across the globe. By 2020, it is estimated that 15 million new cases will be reported, with a total of 10 million new deaths, all due to this single disease (American Cancer Society, 2005).

Current treatments available for cancer patients have become quite successful in the reduction of mortality rates, and include such options as surgery, chemotherapy, radiotherapy, and immunotherapy. However, these treatments carry with them debilitating side effects, which can lead to decreased functionality compromising the quality of life of patients (Courneya & Friedenreich, 1999). Various side effects include nausea, vomiting, decreased physical performance, and decreased sense of independence. These treatment effects can lead many patients to experience a constant feeling of fatigue, which in turn leads to decreased physical activity levels, thereby leading to greater fatigue and, in some cases, a decreased functionality.

Only a few treatment strategies are currently used by oncology physicians to combat the side effects that are commonly developed during cancer treatments. Some of these treatments include Erythropoietin-Alpha (Prednisone or Dexamethasone) for the

treatment of anemia, selective serotonin re-uptake inhibitors (SSRI) to alleviate nausea, which is commonly observed during the administration of chemotherapy, and Methylphenidate to combat depression. Aside from these treatments cited above, other forms of adjunct therapies have started to receive more attention for the treatment or management of the side effects produced by cancer treatment. Some of these adjunct therapies include nutritional counseling, cancer support groups, psychotherapy, yoga, and exercise.

Empirical evidence has shown that exercise can be safely used as an intervention to cope with cancer treatment side effects (Galvao & Newton, 2005). It was shown by Winningham and colleagues in 1989 that twelve weeks of moderate-intensity cycling, performed three times each week, produced various health benefits to breast cancer patients, including decreased nausea, body fat, and increased lean tissue mass. Less than a decade later, Dimeo and his research team found that daily cycling for two weeks decreased hospitalization time in breast cancer patients (Dimeo et al, 1997).

It has also been reported in prostate cancer patients that resistance training, with 2 sets of 12 repetitions at 60-70% of 1-repetition-maximum for 3 weeks resulted in an increase in both upper and lower body lean tissue, a decrease in fatigue, and an increase in quality of life (Segal et al., 2003). This supports the idea that exercise of both aerobic and anaerobic natures can produce health benefits among patients diagnosed with various types of cancer.

Although it is believed regular exercise may benefit patients with different types of cancer, much of the current literature examining the effects of exercise on cancer has

focused on breast, stomach, and prostate cancer. Few studies have been conducted that detail how exercise may affect other types of cancer, such as lung cancer and leukemia. In the United States in 2004, over 33,000 new cases of leukemia were diagnosed, resulting in over 23,000 deaths from the disease (The Leukemia & Lymphoma Society, 2005). This was a 17% survival rate decrease from the 1995-2000 survival rate.

Leukemia is a malignant disease that affects bone marrow and the blood, and is characterized by an uncontrolled accumulation of blood cells. The disease is divided into two subcategories, myelogenous or lymphocytic, as well as acute or chronic, resulting in four separate categories. “Myelogenous” and “lymphocytic” are terms denoting the type of cell involved. Acute leukemia is marked by a sudden onset and sharp rise, whereas chronic leukemia has a long duration or a frequent occurrence. Acute leukemia leads to anemia in virtually all leukemia patients, and immune function becomes severely compromised due to a decreased production of white blood cells. Low platelet production is also an issue, which leads to easy bruising and uncontrollable bleeding.

Treatment for acute leukemia patients commonly consists of a four-week chemotherapy regimen that requires the patient to remain in his or her private room within a hospital (infusion treatment). Following these four weeks, the patient is allowed to return home or to a nearby hotel for two-weeks of recovery, only to return to the hospital for four more weeks of chemotherapy after these two weeks have elapsed (consolidation treatment). Since leukemia patients are not allowed to leave their room, their opportunities to engage in physical activity have all but been eliminated. This decreased level of activity can lead to constant tiredness, exhaustion, and overall fatigue.

This follows the same symptom patterns exhibited by individuals affected with various other types of cancer.

It is believed that an exercise intervention among these acute leukemia patients can help decrease disease symptoms, increase their sense of independence and, ultimately, their overall quality of life. Exercise has been shown to alleviate both physiological and psychological distresses associated with cancer (American Cancer Society, 2005), and it is believed that these benefits can be also observed in the acute leukemia population as well.

Statement of the Purpose

The purpose of this pilot study was to examine the effects of an individualized prescriptive exercise intervention, administered in-hospital during the treatment-recovery of leukemia patients, on fitness parameters and quality of life.

Hypotheses

HO₁: It was hypothesized that there will be no significant difference pre-to-post in functionality on the TGUG (Timed Get Up & Go Test).

HA₁: It was hypothesized that there will be no significant difference pre-to-post in functionality on the TGUG (Timed Get Up & Go Test). Hypothesis 1 was analyzed by using a dependent samples *t*-test. The dependent variable, TGUG score, was assessed within three days of diagnosis/beginning of treatment and also at the end of the study on week 6.

HO₂: It was hypothesized that there will be no significant differences pre-to-post in handgrip dynamometry strength.

HA₂: It was hypothesized that there will be no significant differences pre-to-post in handgrip dynamometry strength, with the post-test values showing improvement over pre-test values. Hypothesis 2 was analyzed by using a dependent samples *t*-test. The dependent variable, hand-grip dynamometry strength, was assessed within three days of diagnosis/beginning of treatment and also at the end of the study on week 6.

HO₃: It was hypothesized that there will be no significant differences pre-to-post on total exercise time on the recumbent bicycle.

HA₃: It was hypothesized that there will no be significant differences pre-to-post on total exercise time on the recumbent bicycle. Hypothesis 3 was analyzed by using a dependent samples *t*-test. The dependent variable, recumbent cycling endurance in minutes, was assessed within three days of diagnosis/beginning of treatment and also at the end of the study on week 6.

HO₄: It was hypothesized that there will be no difference pre- to-post on the score of the quality of life questionnaire.

HA₄: It was hypothesized that there will be no difference pre- to-post on the score of the quality of life questionnaire. Hypothesis 4 was analyzed by using a dependent-samples *t*-test. The dependent variable, quality of life scores, was assessed within three days of diagnosis/beginning of treatment, and at the end of the study on week 6.

Definition of terms

1. Cancer – a malignant tumor of potentially unlimited growth that expands locally by invasion and systemically by metastasis
2. Leukemia – an acute or chronic disease in humans and other warm-blooded animals characterized by an abnormal increase in the number of white blood cells in the tissues and often in the blood (Merriam-Webster, October 30, 2005)
3. Acute – having a sudden onset, sharp rise, and short course (Merriam-Webster, October 30, 2005)
4. Chronic – marked by long duration or frequent recurrence. (Merriam-Webster, October 30, 2005)
5. Myelogenous – (cells) of, relating to, originating in, or produced by the bone marrow
6. Lymphocytic – any of the colorless weakly motile cells originating from stem cells and differentiating in lymphoid tissue (as of the thymus or bone marrow) that are the typical cellular elements of lymph, including the cellular mediators of immunity, and constitute 20 to 30 percent of the white blood cells of normal human blood.

Limitations

- Small sample size ($N = 4$).
- The final two weeks of exercise intervention were self-administered, in subject's home or hotel, during recovery.

Delimitations

- Subjects were recruited from the UNC Hospital “Leukemia” unit.
- Subjects in the exercise treatment group were exposed to two exercise sessions per day, three days per week, for a total of six weeks.
- The subjects enrolled in the study exercised at intensities from 40–60% of a predicted maximal aerobic capacity, depending on subjects' subjective feelings of capacity each day.

Assumptions

- It was assumed that all subjects honestly and accurately reported their opinions and physical sensations on all subjective questionnaires.
- It was assumed that all subjects regularly engaged in their exercise prescription program during their two weeks away from the hospital.

Significance of the study

Since many leukemia patients experience a marked loss of physical activity during their in-hospital induction treatment, they can experience a loss of physical functioning as well. This study aimed to determine if exposing newly diagnosed acute leukemia patients to highly structured, individualized exercise prescriptions of moderate intensity would allow them to maintain a functionality similar to that which they had experienced prior to treatment. If a relationship exists in which functionality is improved, or even simply maintained, then these patients can continue to rely on themselves to perform routine, daily tasks which, without exercise, may become intolerable or impossible.

Chapter 2

REVIEW OF THE LITERATURE

Cancer is currently the second leading cause of death in the United States (Cancer, 2005). Over one million new cases are diagnosed in the United States alone every year. Close to half of all men and about one third of all women will contract a form of cancer sometime during their lives. Today, there are millions of people living well who have previously been diagnosed with cancer. Although it is a very serious condition that requires proper medical treatment, chances of survival are increased if the cancer is detected early, and if a healthy diet and exercise plan are followed as part of the individual's daily life (Cancer Facts, 2005).

For the purpose of organization, this literature review is divided into the following sections: 1) Cancer, 2) Leukemia, 3) Cancer Treatment, 4) Cancer Treatment-Related Symptoms, 5) Adjunct Cancer Therapies, 6) Cancer and Exercise, and 7) Cancer and Exercise in Leukemia.

Cancer

Cancer, in the most basic sense, is a rapid, uncontrolled growth of abnormal cells within the body. Although there are many different types of cancer, all of them originate as this type of uncontrolled production of cells. This abnormality in cell growth is often an indicator of a cancerous condition (Cancer Source, 2005). Normal cells follow fairly regular life patterns when it comes to growing, dividing, and ultimately, dying. During the early years of life, normal cells may divide more rapidly until an individual becomes

an adult. Once adulthood is reached, cells in most parts of the body will divide only to replace worn-out, injured, or dying cells. Because cancer cells display abnormal behavior, they do not cease growing when normal cells do. Cancer cells outlive normal cells and continue to grow and divide. This results in a proliferation of abnormal cells (Cancer Source, 2005).

Cancer cells originally develop as a result of damaged DNA. DNA, which is found in every cell within the body, is usually repairable if it becomes damaged. In cancer cells, the DNA damage is irreparable. Damaged DNA can be inherited, which explains for inherited cancers. Other DNA damage can occur through environmental exposures, such as benzene and smoking (Cancer Source, 2005). Often, once cancerous cells begin dividing rapidly in one part of the body, the cancer will move to another part of the body and begin to divide there as well. This process is known as metastasis. However, even though cancer may spread to many different parts of the body, it is always called by where it originated. For instance, if the cancer first formed in the lungs, but spread to the liver, it would still be called lung cancer (Cancer Source, 2005). Often times, the uncontrolled division of cancerous cells will result in a tumor. In some cancers, like leukemia, tumors do not form. Instead, this type of cancer involves the blood and some organs that assist in the formation of blood. The cancer is thereby able to circulate to other tissues where the cancerous cells may grow (Cancer Source, 2005).

Leukemia

There are four major types of leukemia: acute myelogenous leukemia, chronic myelogenous leukemia, acute lymphocytic leukemia, and chronic lymphocytic leukemia. Acute leukemia is a disease that progresses rapidly and affects mostly immature or

undifferentiated cells. Because these cells are not yet fully functional, they cannot carry out their normal duties. Chronic leukemia progresses more slowly and allows for the growth of more mature cells. These cells can, for the most part, carry out their normal duties (Leukemia & Lymphoma Society, 2005).

Acute Myelogenous Leukemia (AML) is the most commonly diagnosed form of leukemia. Almost 12,000 new cases of AML are diagnosed each year in the United States. Chronic Lymphocytic Leukemia (CLL) is the second most commonly diagnosed form of leukemia. Each year, nearly 9,730 people in the United States are diagnosed with CLL. The occurrences of Acute Lymphocytic Leukemia (ALL) and Chronic Myelogenous Leukemia (CML) are far below that of AML and CLL. Even so, about 4,600 new cases of CML are diagnosed, with ALL being responsible for about 3,830 new cases each year (Leukemia & Lymphoma Society, 2005).

Cancer Treatments

Currently, there are many varied treatments for leukemia, ranging from radiation therapy, chemotherapy, and immunotherapy, to bone marrow transplantation. Radiation therapy, also called radiotherapy, is used to alter the size of body tissues affected by cancer by giving the patient X-rays or gamma rays in specific areas. Radiotherapy can be beneficial in controlling symptoms associated with cancerous growths. In particular, if a tumor is pressing against a bone or nerve, radiotherapy can be used to shrink the tumor and alleviate pressure. Although a specific amount of radiation is introduced into the cancerous tissue, some portion of the treatment is introduced into the normal, healthy tissue as well. In some cases, as in leukemia, where much of the body is treated with

radiotherapy prior to a stem cell transplant, radiation administered to non-affected tissue can result in cachexia, which is a wasting of viable, healthy tissue (Cancer Source, 2005). Chemotherapy is another treatment available for leukemia patients. Chemotherapy involves the use of chemicals or drugs, many times in various combinations, to destroy or damage cancerous cells. Depending on which drug is used for treatment, the cancer cell DNA may be completely destroyed, or damaged to the point of irreparability. The goal is to completely destroy all cancer cells, so that there is no longer any sign of the disease (remission), or to damage the cancer cells to the point where progress of the disease itself is reduced. However, there is a risk of damaging normal cells in the process as the cancerous cells are being killed (Cancer Source, 2005).

Immunotherapy is the most recent development in therapy for patients with leukemia. Immunotherapy is based on the concept that the body's immune cells or their products, antibodies, can be specially engineered to recognize and destroy cancer cells. Because immunotherapy utilizes the body's own natural immune system, it is often called biological therapy. Therefore, it is believed that this type of therapy may ultimately be safer than radiotherapy and chemotherapy for leukemia patients, since the therapy is more "natural" than these alternatives (Cancer Source, 2005).

Bone marrow transplantation is a procedure performed that replaces diseased marrow with normal, healthy bone marrow. Transplants can be autologous, which uses the patient's own marrow, or can be allogenic, in which the bone marrow from a normal (non-leukemic) donor is used. Autologous transplants are performed when the patient is in remission, when evidence of the disease is very low or not present at all. The goal of both types of transplants is to replace the patient's bone marrow with non-diseased

marrow. Because all blood cell types originate in the bone marrow, it is believed that new, healthy blood cells will be produced following a transplant procedure (Cancer Source, 2005).

Cancer Treatment-Related Symptoms

Although tremendous advancements have been made in the area of cancer treatments, these newer forms of therapy do not come without consequence. Radiation therapy, while it is effective in shrinking cancerous growths, also places healthy tissue at risk as well. Although chemotherapy targets cancerous cell DNA, it also damages the DNA of some healthy cells as well, leading to a destruction of viable muscle tissue (Cancer Source, 2005). A decrease in muscle mass leads to a decrease in oxygen consumption capacity, which subsequently leads to a decreased time to reach fatigue in an individual who has been treated with radiotherapy. With a decreased muscle mass, metabolism may slow down, providing an increased risk of unhealthy weight gain due to diminished energy expenditure. Ultimately, an individual may tire much more rapidly while performing routine, everyday activities that previously presented no threat of physical exhaustion. This wasting of muscle tissue, known as cachexia, can be due to malnutrition or the side effects of radiotherapy and chemotherapy. Because metabolism has decreased, there can be a decreased appetite, resulting in lower food consumption. This lack of energy consumption feeds back into a feeling of constant tiredness, which subsequently results in a further reduction in appetite. The end result is a chronic debilitating fatigue that many cancer patients experience, and can result in a dramatically reduced quality of life (Galvao & Newton, 2005).

Among leukemia patients in particular, anemia can also be a very real threat. Damage to blood cells sustained by chemotherapy and bone marrow transplants can lead to decreased levels of hemoglobin via a reduction in red blood cells. An overall loss of blood volume can also trigger anemic conditions as well (Cancer Source, 2005). Anemia can cause a forced decrease in physical activity, simply because the individual is unable to transport enough oxygen to the skeletal muscles. Much like what is seen among other types of cancers, leukemia patients may be required to depend on others to perform duties and responsibilities that they are no longer capable of handling on their own. This decreased independence can directly impact quality of life (Galvao & Newton, 2005). Pain is also a side effect that many cancer patients experience, and it can be a tremendous deterrent to performing everyday activities. Due to damage sustained by healthy as well as damaged cells, pain can develop during radiotherapy treatment. Other side effects that contribute to pain are dry skin, difficulty swallowing, and sores on the skin. In leukemia patients, pain can develop as leukemic cells form masses near nerves, in the joints, or near the spinal cord. As a result, swelling may form at these areas, placing pressure on the joints or nerves themselves (Leukemia & Lymphoma Society, 2005).

Perhaps the most common symptom that affects cancer patients is fatigue. “Normal” fatigue can be likened to a general malaise that can affect both the mind and the body, but the fatigue experienced by many cancer patients is a debilitating chronic condition that leads to an inability to perform routine, daily tasks. One cancer survivor recounts her experiences during treatment by claiming that once she had figured out what she wanted to do, she was already too tired to do it (Cancer Source, 2005). The physical as well as psychological drain experienced during treatment makes it difficult for patients

to continue performing the same tasks they are accustomed to performing. Not only can treatment lead to fatigue, but it has been observed that fatigue itself can lead to a compromised posture, leading to increased pain, which feeds back into greater fatigue (Cancer Source, 2005). Higher levels of fatigue can cause an even further inability to function, thereby worsening posture and decreasing body mechanics, resulting in even more pain and fatigue. This “debilitating fatigue cycle” plays a major role in decreasing the quality of life experienced by many cancer patients (Battaglini et al, 2004).

Adjunct Cancer Therapies

In an attempt to combat some of the debilitating side effects of traditional cancer treatments, many alternative therapies have emerged. Vitamins, herbal remedies, massage, and acupuncture have been particularly useful among leukemia patients, as they help combat some of the stressors of radiation and chemotherapy (Cancer Source, 2005). Acupuncture involves inserting thin, flexible needles of varying lengths into certain areas, known as acupoints, to relieve stress and other conditions. Although it is not believed to be effective in preventing or treating cancer, it has been shown to help alleviate feelings of nausea associated with chemotherapy and surgical anesthesia (Cancer Source, 2005).

Hydrotherapy can include the use of warm, moist compresses, which are placed on the skin, to dilate blood vessels. This can temporarily help increase circulation, allow muscles to relax, and alleviate pain. Hydrotherapy can also comprise the use of ice packs to reduce circulation to particular areas of the body via constriction of the blood vessels. This can be beneficial as it allows for a decrease in swelling and inflammation (Cancer Source, 2005).

Hyperbaric Oxygen Therapy, or HBOT, has become an accepted form of alternative therapy for cancer patients. This type of therapy requires a hyperbaric chamber, pressurized at 1.5 to 3 times normal atmospheric conditions, in which the individual breathes pure oxygen. Conditions such as osteoradionecrosis, in which there is a delayed onset of bone damage caused by radiotherapy, and soft tissue damage can be improved through the use of HBOT. Because the oxygen-carrying system of the body can become compromised during traditional cancer treatments, HBOT delivers a concentrated amount of oxygen to the tissues that do not normally receive adequate amounts (Cancer Source, 2005).

Music therapy is another form of treatment for cancer patients. There is evidence that, when combined with traditional treatments, music therapy can alleviate pain and decrease feeling of chemotherapy-induced nausea. In addition, music therapy has been shown to lower heart rate, blood pressure, and breathing frequency, producing an elevated state of relaxation in cancer patients. It can also reduce depression and aid in sleeplessness. Music therapists instruct patients on writing music, provide various types of music for them to listen to, and discuss lyrics. Because music therapy can be done in a hospital room, a patient's home, cancer centers, and hospices, patients are almost always in a place where they can benefit through this form of therapy, which can be calming or stimulating depending on each individual's needs (Cancer Source, 2005).

Cancer and Exercise

In an attempt to increase the quality of life among cancer patients, research studies done by Dimeo (1999) as well as Mock (1997) have attempted to increase patient functionality, to allow him or her to maintain the same level of independence when

engaging in regular, everyday tasks. Dimeo noted that psychological distress decreased among breast, lung carcinoma, seminoma, and Hodgkin's lymphoma patients who engaged in 30 minutes of daily cycling at 50% of heart rate reserve (1999). Mock and colleagues employed a self-paced walking protocol among breast cancer patients, and noted decreased fatigue with just 30 minutes of walking, four to five days a week, over the course of six weeks (1997, 2001). Schwartz et al (2001) observed a similar decrease in fatigue among breast cancer patients. This protocol included self-paced walking for twelve minutes, three to four times a week, for eight weeks. These data are promising because they show that exercise does not have to be particularly intense to see measurable benefits. Such relatively low intensities could be helpful in promoting adherence to exercise programs in cancer patients who may already doubt their ability to perform.

Due to the promising results of physical activity in recent studies, exercise has become another important therapy that can greatly enhance quality of life in cancer patients via its benefits on the body as well as and mind. Exercise has been shown to increase oxygen uptake (VO_2) and lean muscle mass, which can counter tissue loss due to radiotherapy. Exercise encourages movement of joints throughout their entire range of motion, which can aid in increasing flexibility. It also improves strength, allowing for an increased sense of independence because one is able to continue engaging in normal, routine tasks (Galvao & Newton, 2005).

In 1997, Dimeo reported that walking 30 minutes a day 5 days a week increased maximal performance by 32% as well as hemoglobin by 30%. In 1999, Durak and his research team discovered that resistance training increased whole-body strength by 45%

in just two weeks. His research team also observed that cardiovascular resistance training, coupled to flexibility training, produced a 43% increase in whole-body strength, a 41% increase in maximal performance, and an overall increase in quality of life.

Exercise has also been shown to have health benefits that counter the side effects produced by cancer treatments. Nausea, a common side effect of chemotherapy, was decreased after 12 weeks in a study by Winningham's research team (1988). In this study, subjects performed cardiovascular cycling for 20-30 minutes at 60-85% of maximal heart rate for just three days a week over the 3-month exercise intervention. Dimeo et al (1997) observed that cycling at 50% of heart rate reserve resulted in a decrease in thrombopenia (a decreased level of platelets in the blood) and neutropenia (a decreased level of neutrophils in the blood), as well as a decrease in duration of hospitalization. In addition, Segal and colleagues (2003) observed that cardiovascular walking at 50-60% of $VO_{2\text{ max}}$ 5 times a week for 26 weeks increased physical functioning, which allowed for a greater sense of independence.

In addition to promoting physical well-being in cancer patients, exercise has been shown to increase psychological well-being as well. Porock et al (2000) reported that cardiovascular resistance training for 4 weeks decreased depression and anxiety. Just two years prior, Segal's research team found that cardiovascular walking, for 30-40 minutes at 60% of maximal heart rate also decreased depression and anxiety. In 1999, Dimeo and colleagues reported that daily cardiovascular cycling, for 30 minutes at 50% of maximal heart rate, decreased psychological distress. Kolden's research team, in 2002, observed that a combination of cardiovascular walking, cycling, stepping, resistance training, and flexibility increased flexibility, maximal oxygen uptake, whole-body lean tissue mass,

and quality of life, as well as decreased resting systolic blood pressure, when the exercises were performed three days a week over the course of four months. These findings present compelling evidence that exercise, both aerobic and anaerobic in nature, can increase various physiological and psychological parameters that can ultimately lead to an increased quality of life for cancer patients who regularly engage in activities of this nature (Galvao & Newton, 2005).

Cancer and Exercise in Leukemia

One of the most promising benefits of exercise for leukemia patients in particular is the production of new red blood cells (erythropoiesis) independent of bone marrow transplants. Exercise encourages this new red blood cell formation, which can counter the effects of anemia and total blood volume loss. With more red blood cells, there is an increased oxygen-carrying capacity. This means that energy levels can stay elevated longer, and can delay the onset of fatigue and exhaustion. Aerobic training also increases plasma blood volume, which aids in the maintenance of blood pressure and allows for a lower resting heart rate (Brooks, Fahey, and White 2000).

In regard to exercise training in adult leukemia patients, relatively little previous research has been done. However, existing literature has examined the effects of exercise in pediatrics and has shown promising results. Marchese and colleagues (2004) observed increased flexibility and lower body strength in children ages 4-18 who engaged in four months of aerobic activity at home. An increase in lower extremity strength is important among these patients because it can aid in their ability to safely walk up and down stairs. In 2005, Lucia et al implemented an in-hospital training program, consisting of resistance and aerobic training, for children under the age of ten who had been diagnosed with acute

lymphoblastic leukemia (ALL) in hopes to counter the debilitating fatigue and deconditioning that is so commonly observed among adults with this disease. Upon publication of Lucia's commentary, seven children had begun the program, and more were expected to enroll within the near future.

The existing data among adults with cancer are promising when it comes to offsetting some of the debilitating side effects of traditional cancer therapies. In 2003, Adamsen and colleagues observed that a combination of resistance training, cycling, and relaxation therapy resulted in a 32.5% increase in whole-body strength and a 16% increase in maximal oxygen uptake ($VO_{2\text{ max}}$). In 1998, Dimeo and colleagues found that progressive walking up to 80% of maximal heart rate for 30-35 minutes decreased heart rate by 18% at a given intensity and increased distance walked and maximal performance in patients with Hodgkin's as well as Non-Hodgkin's lymphoma.

These forms of alternative cancer therapy, in addition to many others, are vital players in the holistic treatment of cancer. While some of them treat only physical symptoms, many address psychological symptoms such as depression and anxiety. Through combinations of traditional and alternative therapies, the mind, body, and spirit can all be treated, allowing for objective as well as subjective improvements in all three (Cancer Source, 2005).

Chapter 3

METHODOLOGY

Subjects

Ten subjects, ages 18-60, will be recruited for this pilot study. The subjects will be newly diagnosed with acute leukemia, or will be newly relapsed with acute leukemia and currently undergoing re-introduction therapy. All subjects will be designated for chemotherapy treatment at the University of North Carolina Hospitals (UNC-CH Hospitals), Division of Oncology/Hematology.

Participation in this study will involve the same risks as any exercise regimen. Given the potential risks involved, patients will be screened for exclusion based upon the following criteria: cardiovascular disease, unless the disease will not compromise the patient's ability to participate in the exercise rehabilitation program; acute or chronic respiratory disease; acute or chronic bone, joint, or muscular abnormalities; immune deficiency.

A research team physician will review the medical history of each subject and determine if any of the aforementioned criteria are met for exclusion. If any of the exclusion criteria are observed, the patient volunteers will be informed and excluded from participating in the study.

Procedures

Recruitment of subjects

The recruitment process will involve making newly diagnosed and relapsed acute leukemia patients aware of the opportunity to participate in the study via an advertisement by oncology physicians at the University of North Carolina at Chapel Hill Hospitals (UNC-CH Hospitals). Patients will be introduced to the research study by oncology physicians from the UNC-CH Hospitals during the diagnostic meeting. Oncology physicians will be provided with an advertisement flier for the study containing the purpose, a brief explanation of study protocols, and research team members' information. Patients will be asked for permission by the physician to be contacted by a research team member via phone to receive more information about criteria for participation and a brief explanation of the study protocols. If a patient expresses interest in participating in the study, the physician will make a note in the patient's file so that a nurse member of the research team can contact one of the research team members responsible for the screening and scheduling of the first assessment. A research team member will then contact the potential subject via phone call and screen the subject to ensure that the criteria for participation in the study are met. If the criteria are met and the patient agrees to participate in the study, an assessment meeting will be scheduled. During the phone call, subjects eligible and interested in participating in the study will receive instructions regarding pre-assessment guidelines (Attachment A). The initial assessments will be scheduled to occur within three days post-diagnosis/beginning of the induction (Phase 1) treatment.

Assessment Protocols

All assessment protocols will be administered in the hospital in the subject's room. Prior to the administration of the initial assessments, subjects will receive further information about the study, in-depth explanation of all assessment protocols, and explanations regarding the exercise regimen. A physician from the research team will review the patient's medical file and determine if the patient is able to participate in physical activity as well as point out any physical limitations that must be taken into consideration during the assessment and the administration of exercise intervention. After all questions are answered regarding the study protocol and the subject agrees to participate in the study, subjects will then be asked to sign an informed consent form and the HIPAA authorization for use and disclosure of health information for research purposes form (Attachment B) prior to the beginning of the administration of the assessments.

The assessments will be administered in the following order:

1. Quality of life questionnaires (FACT-G)
2. Resting heart rate (RHR), blood pressure (BP), and pulse oximetry for the determination of hemoglobin saturation
3. Body weight, height, body circumferences (anthropometry), and body composition
4. Functional mobility skill test (TGUG)
5. Cardiorespiratory fitness
6. Dynamic muscular endurance and handgrip dynamometry

The Functional Assessment of Cancer Therapy-General (FACT-G) will be administered to assess the quality of life (QOL) of the subjects enrolled in the study (Attachment C). The QOL questionnaire to be used in this pilot study will be administered by an oncology research nurse clinician four times during the study. The first assessment will be administered prior to the beginning of the administration of the exercise intervention, and the other ones will occur at the end of 2nd, 3rd, and 6th week of the study, which is prior to the beginning of the consolidation treatment of Phase 2.

Two fitness assessments will be administered to all subjects. The first assessment will be scheduled on week 1 of the study, within three days post-diagnosis/beginning induction (Phase I) treatment and the second one at the end of the study on week 6 (prior to the beginning of the second phase of treatment - consolidation). The fitness assessments will include the assessment of resting vital values, anthropometry (body weight, height, and body circumferences), body composition, a functional mobility skill test (Timed Get-Up & Go test – TGUG), analysis of cardiorespiratory fitness, a dynamic muscular endurance test, and handgrip dynamometry for the assessment of overall muscular strength. All fitness assessments will be performed by the primary investigator, trained medical personnel, or a trained graduate student from the University of North Carolina, Department of Exercise and Sport Science.

The assessment of resting vitals will be performed immediately after the administration of the questionnaires. Heart rate will be assessed using a heart rate monitor, blood pressure via mercury sphygmomanometer, and hemoglobin saturation via a finger pulse oximeter. Weight and height will be assessed using a balance beam physician scale equipped with height rod. Body circumferences will be assessed

following the standardized sites for circumference measures from the American College of Sports Medicine (ACSM), 2005. The sites used for the assessment of body circumferences will include shoulder, chest, arms, waist, gluteus, thighs, and calves.

Body composition and body circumference measurements (anthropometry) are the only assessments to be performed multiple times during the study to monitor possible changes in the body composition and swelling of the subjects. Body composition and anthropometry will be assessed prior to the beginning of the exercise protocol, and at the end of weeks 2, 3, 4, 5, and 6. Body composition analyses will be performed via skin fold measurements following generalized three-site skinfold equations for male and females recommended by the ACSM, 2005 (Attachment D) and via the utilization of a bioelectrical impedance body fat analyzer device.

The functional mobility of the subjects who participate in the study will be assessed through the Timed Get-up and Go (TGUG) test. The administration of the TGUG will include measuring a distance of 3 meters from the legs of a straight-backed armchair with a seat height of approximately 46 centimeters. The subject will be asked to sit with the back against the chair with the arms on the arm rests. When instructed to begin the test (on the command “Go”), the subject will stand upright then walk at a normal walking pace toward the 3-meter mark placed on the ground, turned around, return to the chair, and sit down. The stopwatch will be started on the word “Go” and stopped when the subject returns to the starting position.

The cardiorespiratory assessment will be performed on a recumbent ergometer bike. Subjects will be asked to cycle at a target submaximal intensity of 60 % of their percentage of heart rate range (Karvonen %HRR) until a Rate of Perceived Exertion (RPE) of 7 is reached on the modified Borg Scale or when the subject asks to have the test terminated at any time before an RPE of 7 is reached. The Borg modified RPE scale is a scale that ranges from 0 to 11 where 0 means no exertion at all and 11 equals to an exertion of absolute maximum (Attachment E). The total time cycling on the bike and heart rate (HR) at the end of the test are to be recorded immediately after the test is completed.

The assessments of dynamic muscular endurance and handgrip strength will be the last assessments to be tested during the battery of fitness assessments. The dynamic muscular endurance assessment will include the administration of the fit ball squat exercise with no load (other than the subject's own body weight) and a biceps curl exercise. The squat exercise will require the subject, with the assistance of the exercise specialist, to stand with back toward the wall, feet shoulder-width apart, and the fit ball placed in the small of the subject's back. Subjects will be asked to squat to a 75-degree knee angle with moderate speed, pressing back against the ball at all times, for as many repetitions as required for the subject to report an RPE of 7 or wishes to stop before that. The biceps curls exercise test will follow a protocol developed at the Rocky Mountain Cancer Rehabilitation Institute (RMCRI), Greeley, Colorado. The protocol will involve the administration of the exercise biceps curls, to be done with dumbbells. Subjects will be asked to perform as many repetitions as possible during an alternated biceps curl exercise with a pre-determined weight to be lifted calculated according to the protocol

developed at the RMCRI (Attachment F). The test will be terminated when the subject reports an RPE of 7 or wishes to stop before that. Handgrip strength will be tested using a handgrip dynamometer. Subjects will be asked to stand and hold the handgrip dynamometer in one hand in line with the forearm that will be placed beside the body. Maximum grip strength will then be determined without swinging the arm and by squeezing the handgrip dynamometer as hard as possible using one brief maximal contraction with no extraneous body movement. The test will be administered three times for each hand with a one-minute rest in between trials. The best score among the three trials for each arm will be used for analysis.

All patients will be asked permission to allow research team members to have access to their treatment records so values on white blood cell and red blood cell count as well as hemoglobin and hematocrit levels during treatment can be retrieved for research analyses. All blood parameters to be included in the study design will be obtained from patients' records during treatment with the exception for the analyses of cytokines. Data on blood parameters cited above will be retrieved from patient's file twice a week (at the beginning and at the end of the week). During the study, four samples of blood in the amount of 5ml will be requested for the analyses of cytokines. To minimize stress on the patient, an oncology nurse member of the research team will make sure to collect the sample at the same time blood samples are being collected as part of the regular treatment regiment. Blood samples for the analyses of cytokines will be collected at the beginning of weeks 1, 3, 4, and 6.

Instrumentation

Fitness Assessments and Exercise Training

The fitness level of each subject will be assessed two times in the study. The first fitness assessment will be administered within three days of diagnosis and the second one at the end of the study, after two weeks of the in-home self-administered exercise program. Each patient will wear an F1 Polar heart rate monitor (Lake Success, NY) to assess both resting heart rate and exercise heart rate. Intensity of cardiovascular exercise will be determined via heart rate analysis and will be adjusted based on each subject's self-reported feelings of capacity. Height and body weight will be assessed using a Detecto Model 437 Physician Beam Scale (Webb City, MO). Body fat analyses will be performed with an Omron HBF-306 Bio-Impedance Body Logic analyzer (Vernon Hills, IL) and C-130 Beta Technology calipers (Cambridge, MD). Circumference measurements will be made using anthropometric measuring tape by Creative Health Products (Ann Arbor, MI). An ADC 922 Series aneroid sphygmomanometer (Hauppauge, NY) and a Littmann Stethoscope (St. Paul, MN) will be used to assess blood pressure. Cardiovascular endurance assessments will be performed on a recumbent bike model Cateye EC 3500 (Dallas, TX). Muscular strength assessments will incorporate the following exercises: lateral and frontal raises, military press, chest press, low rows, biceps curls, triceps extensions, leg extensions, squats, leg curls, and calf raises. Hand weights will be deluxe vinyl dumbbells, ranging from 2 to 15 pounds, from Power Systems Sports (Knoxville, TN). Rubber tubing will consist of DynaBands, with strengths varying from light, to medium, to heavy (Power Systems Sports; Knoxville, TN). Hand grip dynamometry will be measured using a J-20 Jamar hydraulic

dynamometer (Bolingbrook, IL). Blood oxygen content will be measured using a SportStat SS-100 pulse oximeter (Plymouth, MN).

Quality of life (QOL) was measured using the Functional Assessment of Cancer Treatment: General Version (FACT-G) by Dr. David Cella. It comprises 27 questions that assess four primary dimensions of QOL: physical (PWB; 7 items), social and family (SFWB; 7 items), emotional (EWB; 6 items), and functional well-being (FWB; 7 items). It uses 5-point response categories, Likert style, ranging from 0 (“Not at all”) to 4 (“Very much”). The FACT-G total score is the summation of the 4 subscale scores and ranges from 0 to possible 108 points. In studies of patients with general tumors, the Cronbach’s Alpha reliability coefficient ranged from 0.78 to 0.91 (Cella et. al, 1993).

Exercise Protocol

All subjects participated in an individualized prescriptive exercise intervention 3 to 4 times per week, depending on the physical status of each subject during each week, for a period of 6 weeks. The exercise intervention began on week 1 of the study, the day after the first battery of initial assessments was concluded. Each exercise session was divided into two bouts. One bout was administered in the morning and the second one late in the afternoon. This way subjects did not need to exercise for more than 30 minutes each bout, had a rest period to recover before the next exercise bout, and were able to experience a complete exercise session. There was a period of rest of at least 36 hours between each exercise sessions (i.e. if a patient exercised on Monday, the next exercise session was administered on Wednesday). All exercise sessions were administered in the subject’s room. Each room was equipped with exercise equipment. A recumbent cycle ergometer, dumbbells, fit ball, and rubber exercise bands were available in each subject’s

room. Every exercise session followed the same structure; however, the morning exercise period focused on exercises for the upper body while the afternoon session focused on exercises for the lower body during the resistance portion of the exercise training. Each exercise session had the following structure: 3 to 5 minutes of light stretching (stretching component), 5 to 10 minutes of cycling on the recumbent bicycle (cardiorespiratory component), 5 to 15 minutes of resistance training (resistance training component) with hand dumbbells, exercise tubing, rubber bands, and fit balls, and 5-10 minutes of abdominal exercises (core muscles component). The amount of time for each component of the exercise period was adjusted according to the physical state of the subject prior and during each session. If a subject reported to be extremely tired prior or during an exercise session, the duration of the session was significantly reduced, while on days when subjects felt better, the length of each exercise training session was lengthened but never made longer than 30 minutes. The exercises used to target the upper portion of the subject's body (upper body exercises) included lateral, frontal, or military press for shoulders, chest press with dumbbells or rubber bands for chest, low rows with rubber bands for back, and arm curls and arm extension with dumbbells or rubber bands for arms. The exercises used for the lower body workouts included leg extension and leg curls with rubber bands, squats using the fit ball, and calf raises. Abdominal exercises were administered during every exercise bout. The exercises that targeted the abdominal region included regular crunches (curl-ups), and oblique abdominals. All exercises were performed at submaximal intensities that varied between 40% and 60% of the subject's predicted maximal capabilities for each exercise component included in the exercise bout. The intensities of each of the exercises included in the exercise program varied according

to the physical state of the subjects prior to and during the exercise bout. The intensity of the cardiorespiratory workout on the recumbent bike varied between 40% and 60% of the subject's predicted maximal heart rate that was obtained via their percentage of heart rate range calculated using the Karvonen %HRR method (Attachment G). During the resistance portion of the exercise session, each exercise was administered 1 to 3 times, with the number of repetitions per exercise varying from 8 to 15, depending on the physical state of the subject during the exercise bout. Intensity of the exercises was monitored using RPE via the modified Borg Scale. No subjects exercised with intensities higher than a 5 on the Borg scale.

The in-hospital exercise training program lasted for approximately four weeks. After subjects were released from the hospital, they were sent home or to a nearby hotel for two weeks of recovery. During this period, subjects received an exercise prescription containing primarily cardiovascular workouts and were asked to continue exercising on a regular basis until they returned to the hospital for their second phase of treatment. Upon return to the hospital, they were assessed again for fitness and psychological measures using the same procedures as before.

Statistical Analyses

All data were gathered and entered into an electronic database for analysis. Descriptive statistics are presented in the form of means and standard deviations. All data were analyzed on SPSS version 12.0 for Windows, a statistical software program. Each hypothesis was analyzed as follows:

Hypotheses

HO1: It was hypothesized that there would be no significant difference pre-to-post in functionality on the TGUG (Timed Get Up & Go Test).

HA1: It was hypothesized that there would be no significant difference pre-to-post in functionality on the TGUG (Timed Get Up & Go Test). Hypothesis 1 was analyzed by using a dependent samples *t*-test. The dependent variable, TGUG scores, was assessed within three days of diagnosis/beginning of treatment and also at the end of the study on week 6.

HO2: It was hypothesized that there would be no significant differences pre-to-post in handgrip dynamometry strength.

HA2: It was hypothesized that there would be significant differences pre-to-post in handgrip dynamometry strength, with the post-test values showing improvement over pre-test values. Hypothesis 2 was analyzed by using a dependent samples *t*-test. The dependent variable, hand-grip dynamometry strength, was assessed within three days of diagnosis/beginning of treatment and also at the end of the study on week 6.

HO3: It was hypothesized that there would be no significant differences pre-to-post on total exercise time on the recumbent bicycle.

HA3: It was hypothesized that there would be no significant differences pre-to-post on total exercise time on the recumbent bicycle. Hypothesis 3 was analyzed by using a dependent samples *t*-test. The dependent variable, recumbent cycling endurance in

minutes, was assessed within three days of diagnosis/beginning of treatment and also at the end of the study on week 6.

HO4: It was hypothesized that there would be no difference across time on the score of the quality of life questionnaire.

HA4: It was hypothesized that there would be no difference pre- to post on the score of the FACT-G quality of life questionnaire. Hypothesis 4 was analyzed using a dependent-samples *t*-test. The dependent variable, quality of life scores, was assessed within three days of diagnosis/beginning of treatment, and at the end of week 5.

Chapter 4

RESULTS

The purpose of this pilot study was to examine the effects of an individualized prescriptive exercise intervention, administered in-hospital during the treatment-recovery of leukemia patients, on fitness parameters and quality of life. All reported variables were measured for analyses prior to the beginning of chemotherapy, induction phase of treatment, (Pre-assessment) and at the end of the study, prior to beginning of the consolidation phase of treatment for Acute Leukemia Patients (Post-assessment). An alpha level of 0.05 was employed for all statistical analysis procedures to determine significance.

Subjects

Subjects consisted of four male subjects and one female subject, ranging in age from 28 to 50, who were recently diagnosed with acute leukemia and were scheduled to begin chemotherapy treatment. Subjects were recruited from the UNC Hospitals between February and June, 2006. Characteristics are presented in Table 1 below. Due to treatment complications, one male subject was unable to complete the study protocol, and therefore all statistical analyses were performed on only four subjects.

Table 1.

<i>Subject Characteristics</i>							
Age		Body weight		Height		Body composition	
(years)		(kilograms)		(centimeters)		(% body fat)	
Mean	<i>SD</i>	Mean	<i>SD</i>	Mean	<i>SD</i>	Mean	<i>SD</i>
38.4	11	90.2	6.4	173.6	2.9	20.6	5.4

Hypothesis One

There will be no significant difference pre-to-post on the TGUG (Timed Get Up & Go Test) functionality test. This hypothesis was tested using a dependent-samples *t*-test, with the dependent variable being time, in seconds, to complete the standing and walking TGUG functionality test. The descriptive statistics for the analysis of the variable “completion time” are presented in Table 2.

Table 2.

Descriptive Data for TGUG Completion Time

	Mean (seconds)	<i>SD</i>
Prior to Induction (Pre-Assessment)	8.18	0.48
Prior to Consolidation (Post-Assessment)	8.04	0.64

n= 4

No significant change in completion time during the TGUG functionality test was observed from the beginning to the end of the study, with $p = 0.658$ ($\alpha = 0.05$).

Hypothesis Two

There will not be significant differences pre-to-post on grip strength as determined through handgrip dynamometry. This was tested using a dependent-samples *t*-test, with the dependent variable, grip strength, measured in kilograms. Descriptive statistics for the four subjects are presented in Table 3 below.

Table 3.

Descriptive Statistics for Handgrip Dynamometry Strength

	Mean (kilograms)		SD	
	Right	Left		
Prior to induction (pre- assessment)	22.0	20.5	8.60	4.20
Prior to consolidation (post-assessment)	16.5	15.5	6.76	5.20

No significant differences were found through the study for either the right hand ($p = 0.566$, $\alpha = 0.05$) or the left hand ($p = 0.851$, $\alpha = 0.05$).

Hypothesis Three

Hypothesis three stated that there would be no significant differences pre- to-post on total exercise time on the recumbent bicycle. The dependent variable, time, was measured in minutes. Descriptive statistics for endurance cycling time are presented below in Table 4.

Table 4.

Descriptive Statistics for Endurance Cycling Time on the Recumbent Bicycle

	Time (minutes)	<i>SD</i>
Prior to induction (pre-assessment)	9.63	12.02
Prior to consolidation (post-assessment)	17.66	18.87

No significant difference in total exercise time on the recumbent bike was observed from pre- to post assessments ($p = 0.15$, $\alpha = 0.05$).

Hypothesis Four

It was hypothesized that there would be no difference pre-to-post on the total score of the Fact-G, Quality of Life Questionnaire. Hypothesis four was analyzed using a dependent-samples *t*-test. The dependent variable analyzed in hypothesis four was the total score obtained from the summation of the 4 subscales contained within the FACT-G questionnaire, assessed prior to induction phase of treatment (Pre-assessment) and at the end of study, prior to the beginning of consolidation treatment (Post- assessment). Descriptive statistics for the FACT-G, Quality of Life Questionnaire are presented below in Table 5.

Table 5.

Total score of the Fact-G, Quality of Life Questionnaire

	Mean (raw score)	<i>SD</i>
Prior to Induction (Pre-Assessment)	236.00	31.54
Prior to Consolidation (Post-Assessment)	204.00	40.55

No significant difference in the total score of the FACT-G, Quality of Life Questionnaire ($p = 0.376$, $\alpha = 0.05$) was observed from prior to induction (Pre-assessment) to prior to consolidation (Post-Assessment).

Chapter 5

DISCUSSION

The purpose of this pilot study was to examine the effects of an individualized prescriptive exercise intervention, administered in-hospital during the treatment-recovery of leukemia patients, on fitness parameters and quality of life. Standard care for newly-diagnosed acute leukemia patients involves the administration of chemotherapy on week one of treatment called induction phase and a recovery period in-hospital in a private room that usually lasts approximately four weeks. Depending on the recovery process and treatment efficiency, the patient's stay at the hospital may be longer during the induction phase. After the induction phase is completed, multiple bouts of six days of chemotherapy called consolidation treatments will occur once a month. The goal of consolidation treatment is to keep the patient in remission of the disease or until a bone marrow transplant is scheduled in cases where the transplant becomes medically necessary and is viewed as being the only chance for a cure. After the induction phase is completed, the patient then recovers for three weeks in his or her private hospital room, waiting for the blood cell count to return to normal levels before the patient can be released to go home for a two-week period prior to returning to the hospital for a consolidation bout of treatment. During the hospital stay after induction, patients are confined to their private rooms in order to minimize the risk of developing an infection, while waiting for blood cell counts to return to normal levels and, therefore, opportunity

to engage in physical activity becomes very scarce. Once physical activity is diminished, many patients become very weak, which reduces tolerability of any activity, including simple daily tasks such as getting out of the bed to use the bathroom on their own. The decline in overall functionality is believed to be a factor involved in the development of a debilitating fatigue experienced by patients that undergo chemotherapy (Battaglini, et al, 2006, in press). This fatigue allows for an even more diminished capacity to engage in or tolerate activity, which further adds to fatigue. This debilitating fatigue cycle can have a tremendous impact on functionality, independence, and overall quality of life of any cancer patients including leukemia patients (Battaglini, et al, 2006, in press).

In 1997, Mock et al showed that fatigue significantly decreased among breast cancer patients, aged 35-64, when twenty to thirty minutes of self-paced cardiovascular walking was employed four to five times a week (Mock et al, 1997). Four years later, Schwartz et al found a decrease in fatigue among breast cancer patients, aged 27-69, when twelve minutes of self-paced cardiovascular walking was employed three to four times a week (Schwartz et al, 2001). Then in 2003, Segal et al showed that resistance training, performed three times a week at 60-70% of maximal resistance, decreased fatigue among prostate cancer patients who had a mean age of 68 years.

In this pilot study, both aerobic and anaerobic activities, as well as flexibility training, were used in the training protocol. Dimeo et al found that a cardiovascular training protocol significantly increased hemoglobin concentration over controls following high-dose chemotherapy (Dimeo et al, 1997). Increased hemoglobin concentrations would result in an increased availability of oxygen throughout the body, both during exercise and at rest. Resistance training, performed three to five times a

week, was shown to have no effect on arm circumference and skinfold measurements among leukemia patients (Cunningham et al, 1986). This is important to note because it demonstrated that resistance training combats the wasting effect, cachexia, often seen among leukemia patients undergoing chemotherapy. Additionally, a combined cardiovascular, resistance, and flexibility training program of 16 weeks was demonstrated to improve quality of life among breast cancer patients undergoing chemotherapy (Kolden et al, 2002). Although research studies identical in nature have never been attempted before, it is believed that the exercise assessment and prescription, based on related previous research, seemed to be appropriate for the leukemia group that participated in this present study. It seems that the frequency, duration, and intensity of the exercise protocol adopted in this study allowed for maintenance of physiological as well as psychological parameters. Improvements of clinical relevance were also observed and will be discussed in the following paragraphs.

Previous research among cancer patients has focused largely on breast and prostate patients, with very little research having been done on leukemia patients. In this study, the exercise sessions were tolerable for all subjects who had been recently diagnosed, allowing researchers to infer that similar training protocols among other newly-diagnosed leukemia patients would be feasible as well. Difficulties arise when working with this population, and these would need to be taken into consideration when planning future research studies. Once chemotherapy begins, blood cell count is drastically reduced, leaving the patient with a severely compromised immune system and compromised oxygen transport system. Due to these physiological changes that occur with the administration of chemotherapy, it is important and fundamental for the success of any

exercise program administered to leukemia patients, that the exercise prescription should be individually prescribed and constantly modified according to the patient's physical status prior to each session. This includes changes in the duration, intensity, modes of exercise, and even frequency. Fever, low platelet count, abnormal resting blood pressure and heart rate values, recent bone marrow biopsies, as well as a consultation with a nurse prior to each exercise session may dictate the exercise plan for that particular day. All of these issues must be seriously considered prior to every single bout of exercise. To minimize even further any treatment complications, anyone who enters the patient's room poses a potential health threat to the patient, and entering individuals would ideally wear at least a face mask and gloves in order to minimize risk of transmitting illness to the patient. Furthermore, all neutropenic procedures should be strictly followed by exercise trainers and researchers, which also include the weekly cleaning of exercise equipment that remains in the room throughout the entire recovery process.

Also, due to the fact that chemotherapy destroys red blood cell counts, it may have previously been thought that leukemia patients would be unable to tolerate exercise due to decreased blood-oxygen availability. Therefore, if exercise is begun early during treatment, it was shown during this study that patients seemed to experience fewer side effects and were able to tolerate the treatment with fewer complications.

In an attempt to enable patients to maintain functionality, this pilot study involved administering in-hospital exercise sessions beginning during the induction/recovery phase of the treatment. In doing so, it was hoped that leukemia patients would also experience the physiological and psychological benefits of exercise as other types of cancer patients have reported in previous research (Adamsen et al, 2003; Dimeo et al, 2003), increasing

chances for better treatment outcomes, as recently has been demonstrated in other types of cancer populations (Demark-Wahnefried, 2006; Meyerhardt et al, 2006). Therefore this present study, in the knowledge of the authors, becomes the first one to explore the possible benefits of exercise in leukemia patients.

Although five subjects were initially enrolled in the pilot study, only four were successfully able to complete the training protocol. Subject two, unlike the other four subjects, was a newly relapsed leukemia patient, and after enrollment was only able to complete the initial fitness and psychological assessments, in addition to just two exercise training sessions. Due to his severely compromised physiology, he was excluded from this study.

Doxorubicin, a drug used extensively in chemotherapy, has been shown to induce chronic cardiac dysfunction and reduced coronary bloodflow. However, aerobic exercise training was shown to attenuate doxorubicin-induced cardiac dysfunction in animal models. Chicco, Schneider, and Hayward (2006), assessed the effects of exercise on doxorubicin-induced cardiac dysfunction in mice. The results of the study demonstrated that chronic exercise training prior to doxorubicin treatment guards against cardiac dysfunction once treatment ends. This study is one of the first that demonstrates the possible mechanism in which aerobic exercise may prevent against doxorubicin-induced cardiac dysfunction. However, few questions are raised regarding the subject who was unable to complete the training protocol. Had the subject exercised regularly during and after the first induction treatment, could doxorubicin-induced cardiac dysfunction have been avoided? Could the debilitating decrease in functionality due to the devastating deconditioning suffered during the first induction have been avoided with exercise?

These are questions that remain unanswered, and studies involving human subjects in the issue of exercise as a preventative intervention against doxorubicin-induced cardiac dysfunction should be explored.

The next section of this discussion will focus on the results found in this study. For hypothesis one, it was expected that there would be no significant difference pre-to-post in functionality on the TGUG (Timed Get Up & Go Test) in patients that participated in this pilot study. A non-significant difference was found between the initial TGUG values and the final TGUG values. However, failing to reject this null allows inferences to be made such that the exercise training, over the course of chemotherapy treatment, allowed subjects to maintain their functionality, rather than experience a decline in functionality, normally observed in patients that just receive standard care for the treatment of acute leukemia. Segal et al found that physical functioning increased among breast cancer patients over the course of 26 weeks when cardiovascular walking at 50-60% of VO_{2max} 5 times a week was utilized (Segal et al, 2001). The protocol in this leukemia project involved a similar approach. Even with intensities lower than those used by Segal in his experiment, the functionality could be maintained in our leukemia population. This pilot study would have benefited from a larger sample size so that statistical power could have been reached, with similar results found in the breast cancer population studied by Segal in 2001. It is also important to note that the amount of time, approximately four weeks, was much less than the 26 weeks used in the study by Segal et al, 2001.

The results from this study may imply that patients who exercise regularly during induction therapy could begin consolidation treatment without compromised functionality. It may also be that these patients could tolerate the second bout of

chemotherapy with fewer detrimental side effects, and come away from the treatment with compromised physiology of a lesser degree than those who do not exercise throughout the treatment. More research is needed to confirm or refute this supposition.

Hypothesis two assumed that there would be significant differences pre-to-post on handgrip dynamometry strength. The null failed to be rejected, as shown by non-significant differences between initial and final values on handgrip strength for the right as well as left hands. However, measuring handgrip strength using dynamometry among cancer patients may not be the most effective way to determine relationships with overall body strength. This may be due to the damage to nerves in the periphery known as chemotherapy-induced peripheral neuromyopathy (CIPN) which can develop as one undergoes current chemotherapy agents (Davis et al, 2005).

Fortunately, in this pilot study, subjects maintained handgrip strength. This may suggest point to the overall efficacy of the exercise training program. The use of rubber tubing and hand dumbbells may have resulted in the successful maintenance of handgrip strength. Even though gains in strength were not seen, maintenance of strength suggests that future leukemia patients may potentially benefit from exercise as subjects become more conditioned and are able to better tolerate daily tasks without becoming compromised. This could have a positive impact on their overall quality of life, as shown in Kolden's study from 2002. In it, quality of life increased among breast cancer patients who underwent a combined cardiovascular, resistance, and flexibility training program 3 times a week for 16 weeks (Kolden et al, 2002). Research from Segal also demonstrated an increase in quality of life among prostate cancer patients who participated in a resistance training program 3 times a week for 12 weeks (Segal et al, 2003). The results

of the present study may be in agreement with Kolden and Segal's studies where overall body strength was found to assist patients in increasing quality of life while receiving treatment. Even though handgrip dynamometry may not truly represent the changes in overall body strength, the known decrease in grip strength observed in this study is quite promising and should be further examined.

According to hypothesis three, it was assumed that there would be no significant differences pre-to-post on cardiovascular endurance time on the recumbent cycle ergometer. In this study, due to the small sample size the null failed to be rejected, suggesting that subjects were successfully able to maintain aerobic endurance throughout the course of chemotherapy treatment. While results showed no statistically significant improvement, there may be clinical significance to this finding. As one becomes better aerobically trained, there is an increased availability of oxygen throughout the body. As oxygen transport increases, or remains constant, the risk of ischemic fatigue decreases, and the body is more able to tolerate even routine, daily tasks (Brooks and Fahey, 2000).

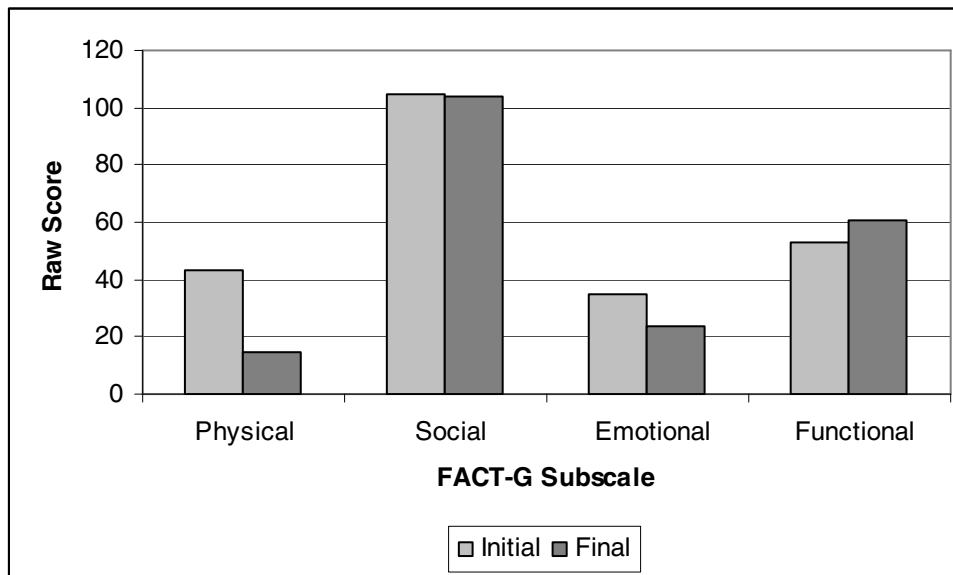
Although sample size was too small for statistical significance to be reached, all subjects in the present study maintained or improved endurance time on the recumbent bicycle. One subject completed over 27 minutes of cycling during the initial assessment, and completed 45 minutes in the final assessment. Another subject completed just over 2 minutes during his initial assessment, and successfully rode for 15 minutes during the final fitness assessment. These improvements, while not statistically significant, hold tremendous clinical significance. Such improvements strongly suggest that the cardiovascular system of leukemia patients could potentially be improved during chemotherapy treatment.

It was believed that, according to hypothesis four, there would be no difference between initial and final values on the FACT-G quality of life questionnaire. Quality of life remained unchanged in various research studies done previously, and results from this study are in agreement. Courneya et al, 2003 found that quality of life remained unchanged following 16 weeks of cardiovascular walking and flexibility training, performed 3-5 times a week at 65-75% of maximal heart rate among colorectal cancer patients (Courneya et al, 2003). Adamsen and colleagues found that heavy resistance training, combined with moderate-intensity cardiovascular cycling and relaxation techniques, failed to improve quality of life among leukemia patients and those with other forms of cancer, when performed 4 times a week for 6 weeks.

While there was no significant difference overall based on summation of all four subscales, there were surprising exploratory findings on some of the subscales that comprise the FACT-G that may have contributed to the maintenance of quality of life among the patients enrolled in this study. As exploratory variables, each subscale was studied separately in order to have a better understanding of the overall quality of life maintained during the present study. Dependent samples *t*-tests were used to analyze each subscale.

Figure 1 below graphically displays results observed from the initial to the final quality of life assessment.

Figure 1. FACT-G Subscale Values During the Initial ($n = 4$) and Final ($n = 4$) Fitness Assessments.



As can be noted from Figure 1, an improvement was observed in functionality. Due to small sample size, this difference was not statistically significant ($p = 0.130$, $\alpha = 0.05$). Measures of functionality assessed by this subscale include ability to perform routine tasks, ability to maintain control of one's body, and ability to sleep well at night. Though statistically non-significant, on a day-to-day basis this increased functionality may well be clinically significant in the lives of leukemia patients who are able to maintain functionality and, thereby, independence when performing routine, everyday tasks. This increased sense of independence could directly relate to increased quality of life, simply because patients are not required to depend on others to help them perform tasks which, until chemotherapy treatment, were able to be managed by the patients alone.

Conclusion

Even with the limitations and unforeseen setbacks experienced with this pilot study, the overall feasibility of such a training program is certainly worth examining again in future studies. Although statistically significant improvements in functionality, handgrip strength, and aerobic endurance were not shown, maintenance of these physiological parameters was shown, and producing similar results in subsequent clinical trials is unquestionably possible. It is believed that similar training protocols could greatly benefit patients in leukemia units in hospitals throughout the world. Future trials are necessary to confirm and to further explore the results of the current experiment so that it can be proven that patients should not decrease their physical activity levels too much during treatment to maintain functionality, aerobic endurance, strength, and, as a result, quality of life overall.

In conclusion, the primary purpose of this pilot study was to examine the effects of an individualized prescriptive exercise intervention, administered in-hospital during the treatment-recovery of leukemia patients, on fitness parameters and quality of life. The researchers have concluded that the exercise protocol administered in this study was appropriate for newly-diagnosed acute leukemia patients scheduled to undergo chemotherapy. Previous research conducted on this population has been very limited until now; however, the results from this study support the idea that exercise training protocols of this nature are not only appropriate for the leukemia population, but are highly recommended for them as well. It was shown that individuals in this population are physically capable of participating in exercise training programs of this nature, and promising benefits, both physiological as well as psychological, were readily observed.

When initiated prior to the induction phase of chemotherapy treatment, an exercise program consisting of submaximal aerobic activity, submaximal resistance training, and flexibility training can increase physiology and psychological status, and enable leukemia patients to better withstand the debilitating side effects of stand care for this population.

Recommendations for Future Research

When replicating this training protocol in the future, it is believed that patient education would be of vital importance. In this study, all but one subject was newly-diagnosed with leukemia. Upon receiving a diagnosis of such magnitude, patients may succumb to a learned helplessness that they have witnessed among cancer patients in general, regardless of type. Cancer has, up until now, been shown to have a very high mortality rate, and this may negatively affect the desire of cancer patients to try to overcome their disease, simply because they believe in their minds that it cannot be done. Educating participants in similar research studies about the benefits of regular exercise may serve to offer a new hope that previously has not been available to cancer patients.

Based on the limitations and findings observed in this pilot study, the following suggestions for future research are recommended:

- A larger randomized controlled clinical trial with a control and experimental group.
- A multi-site research program so that greater statistical power can be attained and so that generalizations can be made to the leukemia population.

- The inclusion of other exploratory variables such as number of transfusions received during treatment, duration of hospital stay, number of infections contracted during treatment, and blood count recovery time.
- The use of inflammatory proteins as an attempt to understand the development of fatigue during treatment.
- The use of other exercise protocols varying exercise frequency, duration, and intensity.
- Include an extension of the exercise protocol to encompass the period in which the first consolidation bout was administered. Also, the development of an exercise brochure to give to patients to take home in order to allow a continuation of exercise training throughout the entire treatment process.
- A possibility to combine exercise with other therapeutic interventions in order to further minimize the side effects commonly developed during treatment.
- A more precise monitoring of the heart and the possible physiological changes that can occur with chemotherapy-induced cardio toxicity and the protective effects of aerobic training on the heart.
- The use of similar protocol in other types of blood cancer patients.
- A follow-up study with leukemia patients enrolled in this exercise study to assess participation in physical activities following initial treatment and survivorship rates.

According to the results seen in this pilot study, similar projects could greatly enhance the quality of life among patients with different forms of blood cancers. Exercise may be the missing link in achieving decreased mortality rates among those

diagnosed with this disease. However, more research is needed to understand the mechanisms that underlie such an apparently obvious link.

APPENDIX A:

The EQUAL Project (Exercise and Quality of Life in Leukemia/ Lymphoma Patients)

Pre-Assessment Guidelines

- Wear comfortable clothing, socks, and athletic shoes if available.
 - Women: Wear a loose-fitting, short-sleeved blouse that buttons down the front. Also, avoid restrictive undergarments.
- Drink plenty of fluids (water or sports drink) during the 24-hour period before the test.
- Refrain from eating, smoking, and drinking alcohol or caffeine for 3 hours prior to the test.
- Do not engage in any physical activity the day of the test.
- Get adequate sleep (6 or more hours) the night before the test.
- Continue taking any medications on their usual schedule so that the exercise responses will be consistent with responses during exercise training.

APPENDIX B:

HIPAA Authorization for Use and Disclosure of Health Information for Research Purposes

University of North Carolina-Chapel Hill

IRB Study # 05-EXSS-885-ORC

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9. Anthony Hackney, Ph.D.
10. Diane G. Groff, Ed.D.
11. Bradley Gregory, B.A.
12. Christopher J. Clark.

This is a permission called a “HIPAA authorization.” It is required by “The Health Insurance Portability and Accountability Act of 1996” (known as “HIPAA”) for us to get information from your medical records or health insurance records to use in this research study.

1. If you sign this HIPAA authorization form you are giving your permission for the following people or groups to give the researchers certain health information about you: Any health care providers or health care professionals or health plans that have provided health services, treatment, or payment for you such as physicians, clinics, hospitals, home health agencies, diagnostics centers, laboratories, treatment or surgical centers, including but not limited to the UNC Health Care System, health insurance plans, and government health agencies.

2. If you sign this HIPAA authorization form, this is the health information about you that the people or groups listed in #1 may give to the researchers to use in this research study:

All patients will be asked permission to allow research team members to have access to their treatment records so values on white blood cell and red blood cell count as well as hemoglobin and hematocrit levels and number of transfusions performed during treatment can be retrieved for research analyses. Data on blood parameters cited above will be retrieved from patient's file twice a week (at the beginning and at the end of the week) for the duration of the study.

3. The people or groups listed in #1 may give this health information to the researcher listed at the top of this form (UNC-Chapel Hill Principal Investigator) or to another researcher working on this research study.

4. The health information you allow the researchers to get may be seen or used by people who do not have to follow HIPAA rules. You can ask the researchers any questions you have about how they will protect your personal information in this research study.

5. If you do not sign this HIPAA authorization form you cannot be in this research study, but if you do not sign this HIPAA authorization form the people or groups listed in #1 will not change your right to treatment, payment, enrollment or eligibility for anything that is not part of this research study just because you did not sign this HIPAA authorization form.

6. This HIPAA authorization will stop on December 1, 2006.

7. You have the right to stop this HIPAA authorization at any time. HIPAA rules are that you must stop this HIPAA authorization in writing. You may give your written stop of this HIPAA authorization directly to the people or groups listed in #1 or you may give it to the researcher and tell the researcher to send it to any person or group the researcher has given a copy of this HIPAA authorization. Stopping this HIPAA authorization will not stop information sharing that has already happened.

8. You will be given a copy of this signed HIPAA authorization.

Signature of Research Subject

Date

Print Name of Research Subject

For Personal Representative of the Research Participant (if applicable)

Print Name of Personal Representative: _____

Please explain your authority to act on behalf of this Research Subject:

I am giving this permission by signing this HIPAA Authorization on behalf of the Research Participant.

Signature of Personal Representative

Date

APPENDIX C:

FACT-G (Version 4)

Below is a list of statements that other people with your illness have said are important. By **circling one (1) number per line, please indicate how true each statement has been for you during the past 7 days.**

<u>PHYSICAL WELL-BEING</u>		Not at all	A little bit	Some- what	Quite a bit	Very much
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

<u>SOCIAL/FAMILY WELL-BEING</u>		Not at all	A little bit	Some- what	Quite a bit	Very much
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with family communication about my illness	0	1	2	3	4

GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4
	I am satisfied with my sex life	0	1	2	3	4

By circling one (1) number per line, please indicate how true each statement has been for you during the past 7 days.

EMOTIONAL WELL-BEING

		Not at all	A little bit	Some- what	Quite a bit	Very much
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness	0	1	2	3	4
GE3	I am losing hope in the fight against my illness	0	1	2	3	4
GE4	I feel nervous	0	1	2	3	4
GE5	I worry about dying	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

FUNCTIONAL WELL-BEING

		Not at all	A little bit	Some- what	Quite a bit	Very much
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4

GF4	I have accepted my illness	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4

APPENDIX D:

Skinfold Measurements Guideline (ACSM)

Skinfold Method:

1. Obtain subject's age and present weight.
2. Measure the skinfolds at the gender-specific sights on the right side of the body.
3. Make all measurements in triplicate to the nearest 0.5 mm and average the two closest readings.
4. Be sure the skin is dry and lotion free.
5. Do not measure immediately after exercise.

Sites: A) **Abdomen:** vertical fold taken 3 cm lateral and 1 cm inferior to center of the umbilicus

B) **Chest:** diagonal fold taken between axilla and nipple as high as possible on anterior axillary fold with measurements taken 1 cm below fingers

C) **Suprailiac:** horizontal fold grasped posteriorly to midaxillary line and superiorly to iliac crest along natural cleavage of skin with caliper applied 1 cm below fingers

D) **Thigh:** vertical fold on the front of the thigh, midway between inguinal crease and proximal border of patella. Body weight is shifted to left foot and caliper is applied 1 cm below fingers

E) **Triceps:** vertical fold over triceps, halfway between the shoulder and elbow

F) **Subscapular:** Fold is along natural cleavage line of skin just inferior to inferior angle of scapula, with caliper applied 1 cm below fingers

Regression Equations to Predict Body Density from Skinfold Measurements

MALES

18 – 61 years

$$D_b = 1.1093800 - 0.0008267 (\text{sum of 3}) + 0.0000016 (\text{sum of 3})^2 - 0.000257 (\text{age})$$

Where (sum of 3) = chest, abdomen, and thigh

FEMALES

18-55 years

$$D_b = 1.0994921 - 0.0009929 (\text{sum of 3}) + 0.0000023 (\text{sum of 3})^2 - 0.001392 (\text{age})$$

Where (sum of 3) = triceps, suprailiac, and thigh

Non-Specific

$$D_b = 1.0982 - 0.000815 (\text{sum of 3}) + 0.00000084^2 (\text{sum of 3})^2$$

Where (sum of 3) = triceps, subscapular, and abdominal

(Body Density) D_b = _____

Percentage Body Fat Calculation

Age 20-80, Male $[(4.95 / D_b) - 4.50] \times 100 = \underline{\hspace{2cm}}$

Female $[(5.01 / D_b) - 4.57] \times 100 = \underline{\hspace{2cm}}$

Jackson AS, Pollock ML. Practical Assessment of Body Composition. *Phys Sport Med* 1985; 13(3):
Reprinted in ACSM's Guidelines for Exercise Testing and Prescription, 7th Edition, 2006.

APPENDIX E:

BORG CR10 Rate of Perceived Exertion (RPE) Scale

0	Nothing at all	No Intensity
0.3		
0.5	Extremely weak	Just noticeable
0.7		
1	Very weak	
1.5		
2	Weak	Light
2.5		
3	Moderate	
4		
5	Strong	Heavy
6		
7	Very strong	
8		
9		
10	Extremely strong	Strongest intensity
11	Absolute maximal exertion	Highest Possible

APPENDIX F:

Dynamic Muscular Endurance Test

(Squat and Biceps exercise)

(Rocky Mountain Cancer Rehabilitation Institute Protocol)

Patients will execute repetitions until RPE of 7 is reached during the bicep curl exercise using a predetermined % of their body weight calculated according to their age and sex. The squat exercise uses no external load.

Formula to determine “weight to be lifted”:

BW x Protocol Percentage (constant for the exercise) = Exercise Load

Where:

BW = Patient Body Weight

Protocol Percentage = (% body weight to be lifted)

Age: < 45

Men (Right and Left Arm)
.085

Women (Right and Left Arm)
.065

Age: 45 - 60

Men (Right and Left Arm)
.080

Women (Right and Left Arm)
.061

Exercise Load = “weight to be lifted”

Example: 45 years old male, 150lbs.

Bicep Curl (right arm) = $150 \times .080 = 12\text{lbs}$ (“weight to be lifted”)

Important considerations:

- 1) Ensure that subjects are properly "warmed-up" before initiation of the test protocol.
- 2) Patients should perform as many complete repetitions as possible, until an RPE of 7 is reached.
- 3) Compute "weight to be lifted" according to the age, sex, and body weight specifications outlined.
- 4) Assist the client with the 1st repetition and then continue to "spot" throughout the test.
- 5) Repetitions should be performed at a controlled cadence ("1, 2, 3" - Up, "1, 2, 3" - Down).

Squat Exercise: Using the fit ball (large (~42" in diameter, soft plastic/rubber ball) and no external load. The squat exercise will require the subject, with the assistance of the exercise specialist, to stand with back toward the wall, feet shoulder width apart, and the fit ball placed in the small of the subject's back. Subjects will be asked to squat to a 75-degree knee angle with moderate speed, pressing back against the ball at all times. This is repeated as many repetitions as it takes for the subject to report an RPE of 7 or wishes to stop.

Handgrip strength: Tested using a handgrip dynamometer. Subjects will be asked to stand and hold the handgrip dynamometer in one hand lined with the forearm that will be placed beside the body. Maximum grip strength is then determined without swinging the arm and by squeezing the handgrip dynamometer as hard as possible using one brief maximal contraction with no extraneous body movement. The test will be administered three times for each hand with a one-minute rest in between trials. The best score within the three trials for each arm will be the one that will be used for analysis.

Biceps Curl Test

Weight _____ Repetitions _____

Squat Test using body weight (no external load)

Repetitions _____

Handgrip Dynamometry

Trial 1 _____ Trial 2 _____ Trial 3 _____

APPENDIX G:

HR (Heart Rate) Reserve Method
(Karvonen)

Formula to determine target heart rate for the cardiorespiratory assessment and cardiovascular workout heart rate range:

$$\text{Target Heart Rate} = (HR_{\text{max}} - HR_{\text{rest}}) \times \text{percent intensity} + HR_{\text{rest}}$$

Where:

HR_{max} = 220 – age of the patient

HR_{rest} = Resting heart rate

Percent Intensity = Prescribed exercise intensity

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