EFFECTS OF INDIVIDUALIZED PRESCRIPTIVE EXERCISE PROGRAM ON SELECTED FITNESS PARAMETERS AND FATIGUE OF ACUTE LEUKEMIA PATIENTS UNDERGOING TREATMENT

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ABSTRACT

Effects of Individualized Prescriptive Exercise Program on Selected Fitness Parameters and Fatigue of Acute Leukemia Patients Undergoing Treatment

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Although standard treatment improves survival for acute leukemia patients, development of treatment side effects is of major concern. Therefore, it is important to explore the impact of adjunct therapies, such as exercise, in mitigating treatment-related side effects. The primary purpose of this study was to examine the effects of exercise on selected fitness parameters and fatigue in acute leukemia patients undergoing treatment. A secondary purpose was to examine the relationship between changes in selected fitness parameters and fatigue. Ten patients with acute leukemia participated in this study. Exercise protocol included aerobic, resistance, and flexibility performed 3 times/week for 6 weeks. Significant changes in cardiovascular endurance and overall fatigue ($p = 0.009$ for both), with no changes in overall muscular endurance ($p= 0.715$) were observed. In conclusion, the results of this study suggest that administration of exercise during the leukemia treatment promotes improvement of cardiovascular endurance, maintenance of muscular endurance and reduction in fatigue levels.

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CHAPTER I

INTRODUCTION

Leukemia is a group of blood cancers that affects bone marrow and results in uncontrolled accumulation of abnormal (malignant) blood cells. The accumulation of malignant cells interferes with the body's production of normal blood cells and can result in severe anemia, decreased ability to fight infections and a predisposition to bleeding.

In most types of leukemia, the abnormal cells are white blood cells. There are several types of leukemia that can be grouped in two ways. Firstly, depending on the type of blood cells affected, leukemia can be Myelogenous (myeloid cells) or Lymphocytic (lymphoid cells). Secondly, leukemia can be divided into acute (fast forming) or chronic (slow growing). Acute leukemia is a rapidly progressing disease that results in the accumulation of immature, functionless cells in the marrow and blood. Chronic leukemia progresses more slowly and allows greater number of more mature, functional cells to be made. Acute types of leukemia are more dangerous and account for nearly 9 percent more of the cases than chronic types of leukemia (The Leukemia and Lymphoma Society, 2006). This is one of the reasons why present study is focused on acute leukemia types.

Acute leukemia affects both physiological and psychological health. Anemia, nausea, infections and uncontrollable bleeding are common physiological side effects reported by leukemia statistics (The Leukemia and Lymphoma Society, 2006). The diagnosis of leukemia, as any other cancer, often provokes a profound emotional response in the patient.

Anxiety, depression, stress, and fear are frequently reported to be usual reactions (Servaes et al., 2002). Furthermore, pain, fatigue, and depression are the most common complains of all cancer patients undergoing chemotherapy (National Cancer Institute, 2006).

Presently, there are approximately 10.1 million people in the United States with cancer history and about 208,080 of them are living with or in remission from leukemia (The Leukemia and Lymphoma Society, 2006). National Cancer Institute reported 21,608 deaths from leukemia in United States in 2003. In 2005, an estimated 34,810 new cases of leukemia were diagnosed with approximately 22,570 cases resulting in death (National Cancer Institute, 2006). The incidence and mortality rates for all types of leukemia have not changed substantially over the last 30 years. National Cancer Institute (2006) reported average annual incidence rate of 12.9 and mortality rate of 7.9 per 100,000 men and women for the period 1975-2003, comparing to 11.9 and 7.4 for 2003.

Treatment for leukemia as for any other type of cancer is complex. Standard treatment for leukemia usually involves either chemotherapy, or radiation therapy, or combination of both. Most patients with leukemia are treated with chemotherapy. Some also may have bone marrow transplantation. Standard medical treatment has been proven to be effective in fighting most types of cancer and safe for patients (Leukemia and Lymphoma Society, 2006). Although standard treatment improves survival for individuals with all types of leukemia, the side effects can be significant (Leukemia and Lymphoma Society, 2006).

There is number of treatment strategies that are currently used to alleviate these side effects. Most of them are based on medication and prescribed by a physician. For example, Erythropoietin Alfa (Prednisone or Dexamethasone) is used to treat anemia, Methylphenidate is frequently prescribed to alleviate depression. In addition to the prescribed treatment, many patients will seek other remedies or treatments, sometimes called complementary or alternative therapies. For cancers other than leukemia such as breast, stomach and prostate cancer exercise therapy has been shown as an alternative treatment strategy to cope with cancer treatment-related side effects (Courneya et al., 2003; Dimeo, 2001; Kolden et al., 2002).

Review of exercise intervention studies in cancer patients by Galvão and Newton (2005) has shown that majority of the studies suggest physiological and psychological benefits of regular exercise. However, out of twenty-six studies only three included leukemia patients. Moreover, all three studies used different types of exercise intervention making them difficult to compare. In the study by Dimeo et al. (2003) daily walking at intensity of 70% of maximal heart rate (MHR) was the only cardiovascular component of the exercise program. Another study by Cinningham et al. (1986) focused on resistance training at unspecified intensity 3-5 times a week. Adamsen et al. (2006) performed the only study that used combination of resistance training, cycling and relaxation. In Adamsen et al. study exercise was performed 4 times a week and included 3 sets of 5-8 repetitions at 85-95% of 1-RM, cycling at 60-100% of MHR and relaxation. Out of all three studies the one by Adamsen et al. (2006) showed the greatest improvement in outcome measures: 32.5 % improvement in whole body strength, 16% improvement in maximal oxygen uptake (VO_{2max}) and maintenance of quality of life.

In present study exercise intervention program included a combination of cardiovascular, resistance, and flexibility exercises in order to provide the maximal benefits to the patients.

There are very few studies that examined the effect of exercise on combating the side effects of leukemia treatment. Moreover, to the knowledge of the author, no study has ever been conducted at the hospital while acute leukemia patients were undergoing treatment. Since exercise has demonstrated to be a promising intervention in combating cancer treatment-related side effects in different cancer patients, it is plausible to believe that exercise benefits could also be attained in the leukemia population.

Purpose of the Study

The primary purpose of this study was to examine the effects of an individualized exercise prescription on selected physical fitness parameters and overall fatigue in acute leukemia patients undergoing chemotherapy (Induction phase of the treatment). A secondary purpose was to examine a relationship between selected fitness parameters and fatigue assessed at the beginning and at the end of the exercise program.

Hypotheses

According to the purposes of the study it was hypothesized that:

H1: There will be a significant difference in cardiorespiratory endurance between the beginning and the completion of the exercise program.

H2: There will be a significant difference in overall muscular endurance between the beginning and the completion of the exercise program.

H3: There will be a significant difference in overall fatigue levels between the beginning and the completion of the exercise program.

H4: There will be a significant inverse relationship between changes in cardiorespiratory endurance and fatigue levels assessed prior to and at the end of the study.

H5: There will be a significant inverse relationship between changes in overall muscular endurance and fatigue levels assessed prior to and at the end of the study.

Definition of Terms

Acute Leukemia: A rapidly progressing blood cancer that starts in blood-forming tissue such as the bone marrow, and causes increased production of white blood cells that enter the blood stream and accumulate.

Induction phase of treatment: Portion of the treatment when patients receive chemotherapy for a period of approximately 6 days following an in-hospital recovery period of approximately 3 weeks.

Consolidation phase of treatment: After recovering at home for a period of two weeks post induction, patients return to the hospital to receive a second bout of chemotherapy (consolidation). Consolidation is the administration of chemotherapy every other day for a period of 6 days. After the 6^{th} day, patients are usually released to return home for a three weeks recovery until returning to the hospital for further evaluation or another consolidation bout of chemotherapy.

Blood cell count, also called complete blood count (CBC): A test to check the number of red blood cells, white blood cells, and platelets in a sample of blood.

Platelet count: a test to check the number of platelets in a sample of blood.

Overall muscular endurance: The summation of the results of the muscular endurance tests of the upper body (biceps curls) and lower body (squats) exercises.

Cardiorespiratory endurance: Total time of cycling recorded at the end of the test.

Heart Rate Reserve (HRR): Difference between patient's maximum heart rate and resting heart rate.

Fatigue: Usually is defined as a feeling of tiredness, weariness, or lack of energy. However, fatigue in cancer patients can be described as a complex phenomenon: as a lack of concentration and a loss of memory (mental fatigue); an inability to begin task or a tendency to avoid social contacts and activities (volitional fatigue); tiredness and easy exhaustion from activities requiring physical effort (physical fatigue) (Dimeo, 2001).

Assumptions

- All patients enrolled in the study were able to complete the exercise protocol 3 to 4 times per week during the entire study.
- The impact of different drugs used during the treatment resulted in similar side effects experienced by the patients including fatigue and depression.
- The patients only exercised during the scheduled exercise sessions followed the proposed exercise protocol.
- Subjects honestly and accurately answered the Revised Piper Fatigue Scale.

Delimitations

- Subjects were recruited from the “Leukemia” unit of Oncology/Hematology division at the UNC-Hospitals.
- Subjects participated in two exercise sessions per day, three days per week, with a minimal rest period between exercise sessions of 24 hours, for a total of approximately six weeks.
- The exercise group exercised at intensities no higher than 60% of a predicted maximal capacity (60% of HRR or RPE of 4 on the CR10 Modified Borg Scale).

Limitations

- This study was not a randomized controlled trial (Post-test design study).
- The small sample size (n = 10) significantly decreases the power of the statistical analyses.

- The patients of a large age range (18-55 years old) may vary in physiological responses to exercise program.
- Infections contracted by some of the patients during the study interrupted the exercise training protocol for more than two days.
- Low blood cell count during the study (particularly platelet count) impeded some patients to exercise following the proposed scheduled exercise protocol.

Significance of the Study

The benefits of exercise for the cancer population have been reported in the literature to be a promising complementary therapy in combating side effects usually developed during cancer treatment (Adamsen et al., 2003; Courneya et al., 2003; Dimeo, 2001; Kolden et al., 2002; Lucia et al., 2005; Winningham et al., 1989). To our knowledge, this is the first study to explore the effects of exercise in the adult acute leukemia population during the induction phase of treatment. Since leukemia patients are usually restricted to a hospital room for a period of approximately 4 weeks, during the induction phase of treatment, the association between decrease in physical activity levels and side effects commonly developed during treatment may exacerbate the decline in overall health usually observed in this population while undergoing treatment. Furthermore, the physical health and the impact of the deconditioning process that is believed to occur due to diminished physical activity level, change in nutrition, and side effects developed during treatment can be devastating and interfering with desired treatment outcomes. Therefore, present study was an attempt to examine the possible benefits of exercise in acute leukemia patients and to serve as a starting point for future research on acute leukemia population.

CHAPTER II

LITERATURE REVIEW

Detrimental Side Effects of Cancer-Related Treatment

Standard medical treatments have been proven to be safe and effective in fighting most types of cancer (Leukemia and Lymphoma Society, 2006). Although standard treatments improve survival for individuals with all types of cancer including leukemia, treatment-related side effects are commonly reported to have negative effect on recovery, physiological and psychological health of cancer patients (Servaes et al., 2002). The most prevalent side effect experienced by cancer patients is fatigue. According to several studies, fatigue affects from 48% to 96% of cancer population (Dimeo, 2001; Servaes et al., 2002; Winningham, 2001). Moreover, about 48-75 % of cancer patients undergoing treatment experience fatigue that is moderate to severe (Servaes et al., 2002). This treatment-related fatigue can persist for years after cessation of treatment imposing limitations on normal daily activities.

Other side effects, such as psychological distress and depression, are reported by 25% of cancer population (American Cancer Society, 2006) with depression often related to fatigue (Dimeo et al., 2004). In order to reduce fatigue in patients undergoing treatment, they are often advised to rest and avoid physical exertion. As a result, physical inactivity induces muscle wasting and diminished functional capacity. Several studies report skeletal muscle wasting and cachexia as common treatment-related side effects that lead to loss of whole body strength (Al-Majid and McCarthy, 2001; Hemming and Maher, 2005). Decrease in cardiopulmonary efficiency and range of motion experienced by cancer patients leads to decrease in overall physical functioning (Courneya et al., 2003). Overall de-conditioning induced by decrease in body strength and functional capacity leads to easy fatigability and, paradoxically, to a further increase in fatigue (Dimeo et al., 1999). All these side effects impose limitations on normal daily activities and in combination may undermine quality of life. Several studies done on patients of various cancers reported diminished quality of life as a common effect of cancer and cancer-related treatment (Courneya et al., 2000; Schwartz, 1999). These physiological and psychological side effects not only impact overall treatment outcome and recovery process but may also persist for years after completion of the treatment potentially leading to premature mortality. Therefore, there is a great need in understanding the preventive methods and complimentary therapies in managing cancer and cancer treatment-related side effects.

Exercise as a Complementary Therapy in Managing Cancer and Cancer Treatment-Related Side Effects

Exercise therapy has been shown by many studies to have a positive effect on the recovery and normal functioning during and after the cancer-related treatment (Battaglini et al., 2006; Galvao and Newton, 2005). In a recent review, Galvão and Newton (2005) summarizes twenty-six exercise intervention studies in various cancer populations. The majority of the studies were conducted on breast or prostate cancer patients, and only very few were conducted on hematological diseases including leukemia (three studies), on stomach (one study) and on colorectal cancer (one study). The results of the majority of these studies demonstrate physiological and psychological benefits of regular exercise and suggest that exercise therapy should be considered as an alternative treatment strategy to cope with cancer treatment-related side effects.

Several studies on exercise intervention during or after the treatment used cardiovascular training and reported no detrimental effects in cancer patients of any age (Burnham and Wilcox, 2002; Shore and Shepard, 1999; Marchese et al., 2004). For example, Burnham and Wilcox (2002) showed that a low-to-moderate intensity aerobic exercise could be both safe and effective in breast or colon cancer survivors 40-65 years old. Shore and Shepard (1999) and Marchese et al. (2004) also found that exercise was safe and beneficial for children of 4-15 years old with acute leukemia.

Aerobic exercise intervention has been shown to improve or at least maintain cardiovascular capacity (Dimeo et al. 1998) and lean body mass (Winningham et al., 1989). The latter study reported the effect of a 10- to 12-week aerobic exercise program on body composition of 24 breast cancer patients undergoing chemotherapy. Twelve patients were randomly assigned to the exercise group, and twelve to the control group. Patients in the control group received no exercise treatment but were asked to continue with their daily activities. Exercise group participated in the individualized Winningham Aerobic Interval Training (WAIT) program three times per week for 20-30 minutes with intensities set at 60%-85% of maximal heart rate. All subjects were asked to maintain their eating patterns throughout their participation. Upon completion of the WAIT program, the exercise group showed an increase in lean body mass and a decrease in percent body fat relative to the control group. This suggests that exercise had a moderating effect on gain in body fat and loss of lean muscle tissue during the cancer treatment.

In the study by Dimeo et al. (1998) five patients with various cancer types participated in a 6-week aerobic training program. The program consisted of daily walking on a treadmill with intensity corresponding to lactate concentration of 3.0 ± 0.5 mmol/L. This lactate concentration was equivalent to the heart rate of 80 ± 5% of the maximum reached during the stress test. The results of the training program demonstrated a significant improvement in maximal physical performance, measured as maximal walking speed and distance covered, as well as a reduction in heart rate and lactate concentration. At the same time, all patients experienced reduction in fatigue and could perform their normal daily activities without limitations. These results suggest that an aerobic exercise program of precisely defined intensity, frequency and duration can be prescribed as a therapy for fatigue in cancer patients.

In their later study Dimeo et al. (1999) used control-group design to examine the effect of physical activity on fatigue and psychological status of cancer patients aged 18-60 years undergoing chemotherapy. A group of twenty-seven patients with various cancers completed an exercise program consisting of daily biking on supine cycle ergometer for 30 minutes according to the interval-training pattern: each 1 minute of biking (with intensity of at least 50% of heart rate reserve) was followed by 1-minute pause. Thirty-two patients in control group did not exercise. The duration of the exercise program was not specified but was described as supervised training carried out during hospitalization period. By the time of hospital discharge, patients in the control group showed significant increase in fatigue and reduction in vigor while no changes were observed in the exercise group. Furthermore, training group showed a significant decrease in psychological distress compared to control group.

The results of several other studies (Burnham and Wilcox, 2002; Courneya et al., 2003; Schwartz et al. 1999) are also consistent with findings reported by Dimeo et al. (1998) and Dimeo et al. (1999) that aerobic exercise program can improve physical performance and decrease treatment-related fatigue. Schwartz et al. (1999) showed that home-based aerobic exercise program of low-to-moderate intensity was feasible for women with breast cancer receiving chemotherapy. Twenty-seven women, all over 18 years old, completed an unsupervised 8-week exercise program consisting of 15-30 minutes of unspecified self-paced aerobic exercises performed 3-4 times a week. Patients were asked to exercise at intensity that would not provoke or intensify their symptoms. Women who adopted the exercise program (60%) showed significant improvements in functional ability and quality of life. However, fatigue levels increased but this increase was related to the third dose of chemotherapy. These results suggest that maximum effect of exercise on quality of life may be mediated by treatment-related fatigue.

More recently, Burnham and Wilcox (2002) and Courneya et al. (2003) used control-group design to examine the effect of aerobic exercise on both physiological and psychological functions in cancer patients. Eighteen survivors of breast or colon cancer aged 40-65 years, rehabilitating from cancer treatment (at least two month post treatment) participated in the study by Burnham and Wilcox (2002). Subject were matched by relative aerobic capacity and quality of life and then randomly assigned to either a control group with no exercise (n = 7), a low-intensity (n = 7) exercise group or a moderate-intensity (n = 7) exercise group. The results showed no difference between the two exercise groups. When both exercise groups were combined, the results showed that 10 weeks of low-to-moderate intensity (25-50% heart rate reserve) aerobic exercise program significantly improved aerobic capacity, body composition, lower body flexibility, and quality of life compared to control group. Moreover, fatigue and anxiety significantly decreased in the exercise groups but not in the control group.

Courneya et al. (2003) had fifty-two postmenopausal breast cancer survivors (aged 50-69 years) randomly assigned to an exercise (n = 25) or a control (n = 28) group. The exercise group completed a 15-week supervised exercise program that consisted of biking on recumbent or upright cycle ergometer three times per week for 15 minutes during the first three weeks, gradually increasing to 35 minutes during weeks 13 through 15. The control group did not train. The exercise group showed significant improvements in peak oxygen consumption and overall quality of life when compared to the control group. Moreover, results of correlation analysis indicated that the increase in peak oxygen consumption was correlated with the increase in quality of life ($r = 0.45$; $p < 0.01$) again suggesting beneficial effect of exercise on quality of life.

However, study by Battaglini et al. (2004) found no significant relationship between reduction in fatigue and improvement in physical fitness ($r = 0.32$, $p = 0.94$). Twenty-seven cancer patients (24-78 years old) undergoing treatment participated in a supervised exercise program two times per week for 24 weeks. In this study the exercise program combined aerobic exercise, resistance training, and stretching exercises in a single exercise session. An exercise session consisted of 5-10 minutes of stretching, 10-20 minutes of aerobic exercise using treadmill or cycle ergometer with intensity set at 50-55% of maximal cardiac frequency, and resistance exercises performed at 50% of a maximal repetition (1RM) for all major muscle groups. Responses to the exercise program showed improvements in cardiovascular capacity (treadmill time) and muscular strength, and decreases in body fat and overall fatigue score. Statistical significance of the improvements was not reported. Although the relationship between reduction in fatigue and improvement in physical fitness was not significant, it was linear and positive suggesting a positive trend.

In another study conducted by Dimeo et al. (1997), the relationship between physical performance and fatigue was examined. Maximal physical performance was assessed in 78 patients with different cancers who performed treadmill test until voluntary exhaustion. Heart rate was recorded at the end of the test and VO_{2max} was estimated for each patient. Patients' psychological state was assessed by completing two questionnaires, the short version of the Profile of Mood Status (POMS) and the Symptom Check List (SCL-90-R). The results showed a strong correlation between intensity of fatigue and several indicators of psychological distress such as depression ($r = 0.68$) and anxiety ($r = 0.63$; $p < 0.001$ for both), while only a weak association between fatigue and physical performance (VO2max) was observed ($r = -0.30$; $P < 0.01$). Furthermore, patients with higher levels of physical performance had significantly lower scores for depression {$p = 0.005$) and anxiety ($p = 0.08$) than patients whose physical performance was lower.

Similar to Battaglini et al. study, other studies used resistance training alone or in combination with cardio and flexibility exercises in order to explore the effects of different types of exercise on side effects of cancer treatment (Kolden et al., 2002; Segal et al., 2003). Segal et al. (2003) conducted a 12-week whole body resistance training program in patients with prostate cancer undergoing treatment. Hundred and fifty-five males participated in the program consisted of two sets of 8-12 repetitions at 60-70% of 1 RM for all major muscle groups performed three times a week. Results showed significant improvements in both upper (42%) and lower (36%) body strength, decrease in fatigue, and improvement of quality of life with no change in body composition. These outcomes suggest that resistance training could be beneficial in attenuation of treatment-related muscle wasting and fatigue.

Kolden et al. (2002) performed a pilot study with exercise intervention that included a combination of cardiovascular, resistance and flexibility training. Forty women over the age of 45, undergoing adjuvant therapies for breast cancer, participated in a supervised structured group exercise training (GET) three times per week for 16 weeks. One-hour sessions were administered by two exercise physiologists and included 10-15 minutes warm-up, 20 minutes of different aerobic activities, 20 minutes of resistance training and a cool-down with emphasis on stretching. Initial intensity levels were prescribed on the individual basis at 40–60% of estimated maximal aerobic capacity that increased to 70% over the 16-week period. The results demonstrated that GET was feasible, safe, and well tolerated. Furthermore, significant improvements were observed in whole body strength (estimated sub-maximum leg press and bench press), cardiovascular capacity (estimated VO_{2max}) and flexibility (sit-and-reach test). Other important benefits of GET included a significant decrease in depression and improvement in the overall quality of life.

Exercise Therapy and Acute Leukemia

Side effects of traditional treatments for acute leukemia are reported to be similar to other cancers (Leukemia and Lymphoma Society, 2006). Therefore, this study focuses on examining the effect of exercise on some of the major side effects such as increase in overall fatigue, and decrease in cardiovascular and muscular capacities.

Review of existing literature on exercise and its effect on side effects of leukemia treatment showed that most of the research is focused on child leukemia as opposed to studies on adult. One of the child leukemia studies (Marchese et al., 2004) was done on twenty-eight children aged 4-15 years old with acute lymphoblastic leukemia (ALL) receiving maintenance chemotherapy. A 4-month home-based exercise program consisting of ankle dorsiflexion stretching, lower extremity strengthening and aerobic exercise resulted in improved muscle function, stamina and overall quality of life. Another study by Shore and Shephard (1999) demonstrated positive responses to a 12-week extra-hospital aerobic exercise program in six children aged 13-14 years, successfully treated for ALL and other types of neoplasm. Results revealed significant improvements in maximal oxygen uptake, body composition, and anxiety scores upon completion of aerobic training at 70-85% of maximal heart rate three times a week for 12 weeks.

The most recent study by San Juan et al. (2007) also showed that young children in the maintenance phase of treatment against ALL could safely perform both aerobic and resistance training. Seven children 4-7 years of age completed 16-week intrahospital individually supervised exercise program consisting of resistance (11 exercises for major muscle groups) and aerobic training (30 min at about 70% maximum heart rate) performed three times a week. The results revealed significant increase in peak oxygen uptake (VO_{2peak}), ventilatory threshold (VT), upper- and lower-body muscular strength, and functional mobility. Moreover, after a 20-week detraining period muscular strength was well maintained (significantly greater than before training and not significantly lower than after training). However, VO_{2peak}, VT, and functional mobility were only partially retained (not significantly different from before and after training). No significant improvements in quality of life or ankle range of motion were found.

In contrast to many child acute leukemia studies, there are very few studies focused on adults with acute leukemia, especially performed during the treatment. Moreover, these existing studies use different types of exercise intervention and report contradictory results. Two studies showed that two different exercise intervention programs had no significant effect on either muscular or cardiovascular fitness but showed trends towards preserving them (Cunningham et al., 1986; Dimeo et al., 2003). Cunningham et al. (1986) found no effect of 5-weeks resistance training program (3-5 times a week at unspecified intensity) on skinfold measures, arm circumference and nitrogen balance in 30 leukemia patients 14-44 years old. Patients were studied during recovery from bone marrow transplantation. The only significant finding observed was decreased level of creatinine excretion, which indicated muscle protein-sparing effect of exercise and diminishing muscle protein loss during the treatment.

The results of the second study by Dimeo et al. (2003) are in agreement with findings by Cunningham et al. (1986) showing no change in physical performance (walking speed) in response to a 2-week in-hospital aerobic exercise program. Sixty-six patients (20-73 years old) with hematological malignancies (including leukemia) started the exercise program while undergoing chemotherapy. All patients walked on a treadmill every day for about 33 minutes using an interval-training pattern: after 3-minute warm-up, the patients walked 3 minutes at a speed corresponding to 70% of their maximum heart rate; followed by 3-minute walk at half speed to recover. Although walking speed did not change upon completion of the study, Dimeo et al. concluded that daily aerobic exercise mitigated treatment-related loss of physical performance and showed the trend towards preserving it.

However, a third study, by Adamsen et al. (2006), showed that multidimensional exercise program significantly improved whole body strength and cardiovascular capacity in various cancer patients undergoing chemotherapy. Eighty-two cancer patients (16 with hematological malignancies) aged 18-65 years participated in a 6-week high-intensity supervised exercise program for 9 hours a week. The program consisted of cycling at 60-100% of maximal heart rate, resistance training at 85-95% of 1RM (5-8 repetitions for major muscle groups), and massage and relaxation exercises. The program resulted in a significant increase in muscular strength (32.5%) and cardiovascular capacity (16% increase in VO_{2max}). The patients also reported significant reduction in pain and fatigue. Although some measures of quality of life and well-being improved, no significant changes were found in overall quality of life.

As a summary, results of all these studies suggest that exercise program is feasible, safe, well-tolerated, and beneficial for patients with any type of cancer, including leukemia, during and after the cancer-related treatment.

CHAPTER III

METHODOLOGY

This study was designed to examine the effects of an individualized exercise prescription on selected fitness parameters and fatigue in acute leukemia patients undergoing chemotherapy (Induction phase of the treatment). A secondary purpose was to examine if a relationship exists between the selected fitness parameters and fatigue assessed during the study. This study is retrospective in nature and used archived data from "The EQUAL Project" study (Exercise and Quality of Life in Leukemia/Lymphoma Patients) conducted at UNC Chapel Hill.

Subjects

Patients were volunteers recruited from the University of North Carolina Hospitals (UNC-CH Hospitals), division of Oncology/Hematology. A group of 10 patients with acute leukemia, males and females, were recruited for this study. The inclusion criteria were as follow:

- Newly diagnosed with acute leukemia or newly relapsed and receiving re-induction therapy for acute leukemia;
- An expected hospital stay of 3-4 weeks or longer;
- Participation in the study had to be approved by the physician directly responsible for the patient's care while at UNC-CH Hospitals;
- Designated for chemotherapy treatment;

- Ages ranging from 18 to 55 years at the time of the study.

Participation in this study involved the same risks as any exercise regimen. Given the potential risks involved, patients were screened for exclusion based upon the following exclusion criteria:

- Cardiovascular disease (unless the disease would not compromise the patient's ability to participate in the exercise rehabilitation program);
- Acute or chronic respiratory disease that would compromise the patient's ability to participate in the exercise rehabilitation program;
- Acute or chronic bone, joint, or muscular abnormalities that would compromise the patient's ability to participate in the exercise rehabilitation program;
- Immune deficiency that would compromise the patient's ability to participate in the exercise rehabilitation program.

Each patient was introduced to the study protocol and informed about the risks involved with exercise regimen. Prior to participating in the study each patient signed a Consent form, approved by the University of North Carolina at Chapel Hill Biomedical Institutional Review Board.

General Procedures

<u>Recruitment of Subjects</u>

Patients were introduced to the research study by oncology physicians from the UNC-CH Hospitals during the diagnostic meeting. Oncology physicians were provided with an advertisement flier for the study containing the purpose, a brief explanation of study protocols, and research team members' information (Appendix I). When a patient expressed interest in participating, the physician passed the patient's information to the nurse coordinator of the oncology unity and member of the research team. The nurse coordinator then contacted the principal investigator or the oncology research nurse member of the research team and a visit was scheduled to the patient's room. The principal investigator or the oncology research nurse then visited the patient at the patient's hospital room and discussed more information about criteria for participation and a more detail explanation of the study protocols was given at that time. After all questions were answered regarding the study protocol and the patient agreed to participate in the study, subjects were then asked to sign an informed consent form and the HIPAA authorization form for use and disclosure of health information for research purposes. Then an initial assessment meeting was scheduled. During this visit, patients also received pre-assessment guidelines (Appendix II). The initial assessment was scheduled to take place within three days post-diagnosis/beginning of the induction (phase 1) treatment.

Each patient recruited for the study participated in an approximately 6-week exercise rehabilitation program. Following the initial assessment, all subjects enrolled in the study participated in an individualized prescriptive exercise intervention 3-4 times per week for a period of approximately 3-4 weeks or longer. After patients were released from hospital for 2 weeks of recovery they were asked to continue unsupervised exercise prescription. The final assessment was administered upon patient's coming back to the hospital for another bout of treatment (consolidation phase). Table 1 below represents summary of events according to the study protocol timeline.

Assessment Protocol

All assessments and the exercise program were administered in the patient's room in the hospital by the investigator or a Research team member. Prior to the administration of the initial assessments, subjects received further information about the study, in-depth explanation of all assessment protocols, and explanations regarding the exercise regiment. A physician from the research team reviewed the patient's medical file and determined if the patient was able to participate in physical activity. The physician also made recommendations on physical limitations that were to be taken into consideration during the assessment and the administration of exercise intervention.

Table 1. Timeline of study protocol events.

Week	**Day**	**Event**
1	1	Introduction to the study by physician
		Physician referral to nurse coordinator
		Nurse coordinator contacts research team member
	1 or 2	Research team member visit to patient's room (information about the study, secured informed consent, arrange initial assessments meeting, and information on pre-assessment guidelines)
	2 or 3	Administration of initial fitness and fatigue assessments
	4	Exercise intervention began
2, 3, 4, and or 5	3-4 times per week	Administration of intervention
5,6 or 6,7 - 2 weeks of home recovery	3-4 times per week	Home based aerobic exercise
Week 7 or 8, following home recovery	Immediately after re-admission to hospital (prior to consolidation treatment)	Administration of final fitness and fatigue assessments

The assessments included:

1. The Revised Piper Fatigue Scale.
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. Cardiorespiratory endurance test.
5. Dynamic muscular endurance tests.

For the assessment of fatigue, The Revised Piper Fatigue Scale questionnaire was used (Appendix III). The Revised Piper Fatigue Scale was administered by an oncology research nurse clinician prior to the administration of the fitness assessments.

Two fitness assessments were administered to all participants. The fitness assessments included the assessment of resting vitals (blood pressure, heart rate, and hemoglobin saturation), anthropometric measures (body weight, height, and body circumferences), cardiorespiratory endurance, and a dynamic muscular endurance test. All fitness assessments were performed by the primary investigator.

The assessment of resting vitals was performed immediately after the administration of the questionnaires. Heart rate was assessed using a heart rate monitor, blood pressure via mercury sphygmomanometer, and hemoglobin saturation via a finger pulse oximeter. Weight and height were assessed using a balance beam physician scale equipped with height rod. Body circumferences were assessed following the standardized sites for circumference measures, as recommended by the American College of Sports Medicine (ACSM, 2006). The sites that were used for the assessment of body circumferences included shoulder, chest, arms, waist, gluteus, thighs, and calves.

The cardiorespiratory assessment was performed on a recumbent cycle ergometer or treadmill. The subject was asked to cycle or walk at a target submaximal intensity of 60 % of their percentage of heart rate range (%HRR determined by using the Karvonen method) until a RPE (Rate of Perceived Exertion) of 7 was reached on the modified Borg Scale or when the subject requested termination. The Borg modified RPE scale is a scale ranging from 0 to 11 where 0 means no exertion at all and 11 equals to an exertion of absolute maximum (Appendix IV). The total time of cycling or walking was recorded immediately after the test was completed. The administration of the cycle or the treadmill test was determined according to the patient's physical limitations to perform either on a cycle ergometer or a treadmill. Patients who were not able to perform the cardiorespiratory test on the bike performed the treadmill test and patients unable to perform on the treadmill were tested using a cycle ergometer.

The assessment of dynamic muscular endurance was the last of the fitness assessments and included two tests. The first test was a leg squat exercise using the fit ball (large, ~ 65cm in diameter, soft plastic/rubber ball) performed with no external load besides the patient's own body weight. To perform squat exercise subject was required, with the assistance of the exercise specialist team member, to stand with back towards the wall, feet shoulder width apart, and the fit ball placed between wall and subject's back. The subject was asked to squat to a 75 degree knee angle with a moderate speed, pressing back against the ball at all times. This exercise was repeated until the subject achieved an RPE of 7 or required to stop. The second muscular endurance test was the bicep curl exercise. The bicep curl test was performed following a protocol developed at the Rocky Mountain Cancer Rehabilitation Institute (RMCRI), Greeley, Colorado (Appendix V). The protocol involved the administration of the biceps curls done with dumbbells. Subject was asked to perform as many repetitions as possible during an alternated biceps curl exercise using a percentage of their body weight as resistance. The percentage of body weight to be lifted was calculated according to the protocol developed at the RMCRI. The test was terminated when the subject reported an RPE of 7 or required to stop.

Exercise Protocol

The exercise program began approximately 24 hours after the completion of initial assessments. Each patient followed an individualized prescriptive exercise program 3-4 times per week with at least 36 hours of rest in between the sessions. The duration of each exercise session depended on patient's physical state on the day of exercise. Each exercise session were divided into two bouts. One bout was administered in the morning and the second one late in the afternoon. By exercising in two different periods of the day, patients did not have to exercise for longer than 30 minutes each bout. There was a period of rest of at least 36 hours between each exercise sessions (i.e. if a patient exercised on Tuesday, the next exercise session was administered on Thursday).

All patients exercised in his/her room in the hospital with all necessary equipment provided. Each exercise session included: 3-5 minutes of light stretching, 5-10 minutes of cycling on the recumbent cycle ergometer or walk on the treadmill, 5-15 minutes of resistance training (with dumbbells, resistance bands and exercise ball), and 5-10 minutes of core exercises. All exercises were performed at submaximal intensities determined using Heart Rate Reserve (HHR) for cardiorespiratory exercise and RPE for the resistance portion of the exercise bout. Intensity was constantly monitored never exceeded 5 on the CR10 modified Borg scale for any exercise performed during the session. 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. The exercises that were used to target the upper portion of the patient's body (upper body exercises) include 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 that were used for the lower body workouts will include 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 performed on a chair.

The amount of time for each component of the exercise period was adjusted according to the physical state of the patient prior and during each session. If a patient reported to be extremely tired prior or during an exercise session, the duration of the session was significantly reduced, while during days when patients felt better, the length of each exercise training session were lengthened but never longer than 30 minutes.

The exercise intervention was administered by the primary investigator or a research team member at the hospital for approximately 3-4 weeks or until the patient was released from the treatment to recover at home. During the two weeks of home recovery, induction phase of the treatment, patients were asked to continue exercising following a prescribed program composed of aerobic activities (primarily regular walks). After coming back to the hospital for consolidation treatment, the patients underwent the same battery of assessments administered at the beginning of the study protocol.

Instrumentation

Selected fitness parameters (cardiorespiratory endurance and muscular endurance) of each subject were assessed two times in the study. The first fitness assessment was 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 wore an F1 Polar heart rate monitor (Lake Success, NY) to assess both resting heart rate and heart rate during the assessments and exercise sessions. Intensity of cardiovascular exercise was monitored using an A3 Polar heart rate monitor (Lake Success, NY) and adjusted based on each subject's self-reported feelings of exertion (Borg CR 10 Rate of Perceived Exertion (RPE) Scale). Height and body weight were assessed using a Detecto Model 437 Physician Beam Scale (Webb City, MO). A body fat analysis was performed with an Omron HBF-306 Bio-Impedance Body Logic analyzer (Vernon Hills, IL) and Lange C-130 Beta Technology calipers (Cambridge, MD). Circumference measurements followed standardized sites for circumference measurements (ACSM's Guidelines, 2006) 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) were used to assess blood pressure. Cardiovascular endurance assessments were performed on a Recumbent bike model cateye EC 3500 (Dallas,TX) or Treadmill (Pro-Form model 350, Logan, UT) . Muscular endurance/strength exercises (lateral and frontal raises, military press, chest press, low rows, biceps curls, triceps extensions, leg extensions, squats, leg curls, and calf raises) were performed using deluxe vinyl dumbbells, ranging from 2 to 15 pounds, from Power Systems Sports (Knoxville, TN) and/or rubber tubing (Dyna Bands), with strengths varying from light, to medium, to heavy (Power Systems Sports; Knoxville, TN).

Statistical Analyses

All data were gathered and entered into an electronic database for analysis. Then all data were analyzed on SPSS version 14.0 for Windows, a statistical software program. Descriptive statistics are presented in the form of means and standard deviations. Each hypothesis was analyzed as follows:

Hypothesis 1 stated that there will be a significant difference in cardiorespiratory endurance between the beginning and the completion of the exercise program. It was tested using a paired samples t-test. The dependent variable, cardiorespiratory endurance was assessed within three days post-diagnosis/beginning of the induction treatment (initial assessments) and at the end of the study (final assessment, prior to consolidation treatment). The variable used to measure cardiorespiratory endurance was total time of cycling until RPE of 7 was reached or until the subject requested termination, as explained in detail above.

Hypothesis 2 stated that there will be a significant difference in overall muscular endurance between the beginning and the completion of the exercise program. It was tested using a paired samples t-test. In this case, the dependent variable used for analysis was the summation of the results (total number of repetitions) of the muscular endurance tests of the upper body (biceps curls) and lower body (squats) exercises, assessed at the beginning of the induction treatment (initial assessment) and at the end of the study (final assessment).

Hypothesis 3 stated that there will be a significant difference in overall fatigue between the beginning and the completion of the exercise program. It was tested using a paired samples t-test. The dependent variable, overall fatigue level was assessed within three days post-diagnosis/beginning of the induction treatment (initial assessments) and at the end of the study (final assessment). Initial and final total scores of the Revised Piper Fatigue Scale were recorded and used for the analysis.

Hypothesis 4 stated that there will be a significant inverse relationship between changes in cardiorespiratory endurance and fatigue levels assessed prior to and at the end of the study. It was tested using regression analysis. The variables included in the regression model were the change score for the cardiorespiratory endurance and change score for the fatigue, where:

- Independent variable, change score for cardiorespiratory endurance (Δ_{CE}) was calculated as Δ_{CE} = Total time of cycling (final assessment) – Total time of cycling (initial assessment).
- Dependent variable, change score for fatigue level (Δ_F) was calculated as Δ_F = Total score of fatigue (final assessment) – Total score of fatigue (initial assessment)

Hypothesis 5 stated that there will be a significant inverse relationship between changes in overall muscular endurance and fatigue levels assessed prior to and at the end of the study. It was tested using regression analysis. The variables included in the regression model were the change score for the overall muscular endurance and the change score for the fatigue, where:

- Independent variable, change score for muscular endurance (Δ_{OME}) was calculated as Δ_{OME} = Total number of repetitions (final assessment) – Total number of repetitions (initial assessment)
- Dependent variable, change score for fatigue level (Δ_F) was calculated as Δ_F = Total score of fatigue (final assessment) – Total score of fatigue (initial assessment)

CHAPTER IV

RESULTS

All data were gathered and entered into an electronic database for analysis. All data were analyzed using SPSS version 14.0, a statistical software program for Windows. A significance level of 0.05 was used for all statistical tests. Hypotheses 1 –3 were analyzed using paired samples t-tests, while hypotheses 4 and 5 were analyzed using simple linear regression. Descriptive statistics of all variables are presented in the form of means and standard deviations.

Subjects

Patients were volunteers recruited from the University of North Carolina Hospitals (UNC-CH Hospitals), division of Oncology/Hematology. A group of 10 patients aged from 18 to 55 diagnosed with acute leukemia were recruited for this study. Two patients were later excluded from the study due to either severe health issues or moving to another hospital to complete treatment. Only 8 patients, 6 males and 2 females aged from 24 to 48, completed the study protocol. Their characteristics are summarized in Table 2 below.

Table 2. Subjects' characteristics.

	Age (years)		**Height (cm)**		**Body Weight (kg)**		**Body Composition (% Body Fat)**	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Acute leukemia patients	35.8	8.9	172.7	8.1	99.0	32.3	25.2	9.3

n = 8

Hypothesis 1

Hypothesis 1 states that there will be a significant difference in cardiorespiratory endurance between the beginning (CREpre) and the completion (CREpost) of the exercise program. It was tested using a paired samples t-test. The variable used to measure cardiorespiratory endurance was total time of cycling in minutes until subject reached RPE of 7 or requested termination. The descriptive statistics of the analyses of Hypothesis 1 is presented in Table 3 below.

Table 3. Descriptive statistics of cardiorespiratory endurance at the beginning and the completion of exercise program.

Variable	Mean	SD
CREpre (minutes)	8.94	8.88
CREpost (minutes)	17.01	14.32

n = 8

A statistically significant difference was found in cardiorespiratory endurance at the completion of the exercise program when compared to baseline measures (p= 0.009). Table 4 below presents the results of the t-test used to analyze Hypothesis 1.

Table 4. Difference in cardiorespiratory endurance at the beginning and the completion of exercise program (t-test).

	Paired Differences			t	df	Sig. (2-tailed)
	Mean	**Std. Deviation**	**Std. Error Mean**			
CREpost - CREpre	8.07	6.41	2.26	3.561	7	0.009

n = 8

Hypothesis 2

Hypothesis 2 states that there will be a significant difference in overall muscular endurance between the beginning and the completion of the exercise program. It was also tested using a paired samples t-test. In this case, the dependent variable used for analysis was the summation of results (total number of repetitions) of the muscular endurance tests of the upper body (biceps curls) and lower body (squats) exercises, assessed at the beginning (OMEpre) and at the end of the study (OMEpost). The descriptive statistics of the analysis of Hypotheses 2 are presented in Table 5.

Table 5. Descriptive statistics of overall muscular endurance at the beginning and the completion of exercise intervention.

Variable	Mean	SD
OMEpre (repetitions)	57.50	21.35
OMEpost (repetitions)	61.25	24.01

n = 8

No statistically significant difference was found in overall muscular endurance at the completion of the exercise program when compared to baseline measures (p= 0.715). Table 6 below presents the results of the t-test used to analyze Hypothesis 2.

Table 6. Difference in overall muscular endurance at the beginning and the completion of exercise program (t-test).

	Paired Differences			t	df	Sig. (2-tailed)
	Mean	**Std. Deviation**	**Std. Error Mean**			
OMEpost -OMEpre	3.750	27.920	9.87	.380	7	0.715

n = 8

Hypothesis 3

Hypothesis 3 states that there will be a significant difference in overall fatigue levels between the beginning and the completion of the exercise program. It was tested using a paired samples t-test. The dependent variable, overall fatigue level was measured using total scores on the Revised Piper Fatigue Scale, assessed at the beginning of the induction treatment and at the end of the study. The descriptive statistics of the analysis of Hypotheses 3 are presented in Table 7 below.

Table 7. Descriptive statistics of overall fatigue levels at the beginning and the completion of exercise intervention.

Variable	Mean	SD
Fatigue (pre)	4.60	1.73
Fatigue (post)	1.80	1.67

n = 8

A statistically significant difference was found in overall fatigue levels at the beginning and the completion of the exercise program ($p = 0.009$). Table 8 below presents the results of the t-test used to analyze Hypothesis 3.

Table 8. Difference in overall muscular endurance at the beginning and the completion of exercise program (t-test).

	Paired Differences			t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean			
Fatigue(post) –Fatigue(pre)	-2.800	2.204	.779	-3.593	7	0.009

n = 8

Hypothesis 4 and 5

Hypotheses 4 and 5 were analyzed using a simple linear regression model and included the following variables: the change score for the cardiorespiratory endurance (Δ_{CRE}), the change score for the overall muscular endurance (Δ_{OME}), and the change score for overall fatigue level (Δ_F). The descriptive statistics for these three variables for a simple linear regression analyses are presented below in Table 9.

Table 9. Descriptive Statistics for Simple Regression Analysis.

Variable	**Mean**	**SD**
Δ_{CRE}	8.07	6.41
Δ_{OME}	2.75	23.95
Δ_{F}	-2.80	2.20

n = 8

Hypothesis 4

Hypothesis 4 states that there will be a significant inverse relationship between changes in cardiorespiratory endurance and overall fatigue levels assessed prior to and at the end of the study. The independent variable in the regression was the change score for the cardiorespiratory endurance (Δ_{CRE}), calculated as the difference in total time of cycling between the final and initial assessments (Δ_{CRE} = CREpost - CREpre). The dependent variable was the change score for overall fatigue level (Δ_{F}), calculated as the difference in total score of fatigue between the final and initial assessments (Δ_{F} = Fatigue(post) – Fatigue(pre). No statistically significant relationship was found between Δ_{CRE} and Δ_{F} in this test (r (7) = -0.26, p = 0.534). The non-significant results of the regression analysis of Hypotheses 4 are presented in Table 10 below.

Table 10. Relationship between changes in cardiorespiratory endurance and overall fatigue levels.

		$\mathbf{\Delta_{F}}$
$\mathbf{\Delta_{CRE}}$	R^2	.068
	Slope	-.089
	P value	.534

n = 8

Hypothesis 5

Hypothesis 5 states that there will be a significant inverse relationship between changes in overall muscular endurance and overall fatigue levels assessed prior to and at the end of the study. The independent variable in the regression was the change score for the overall muscular endurance (Δ_{OME}), calculated as the difference in total number of repetitions between the final and initial assessments (Δ_{OME} = OMEpost – OMEpre). The dependent variable was the change score for fatigue level (Δ_F), calculated as the difference in total score of fatigue between the final and initial assessments (Δ_F = Fatigue(post) – Fatigue(pre). No statistically significant relationship was found between the Δ_{OME} and Δ_F in this test (r (7) = -0.335, p = 0.417). The non-significant results of the regression analysis of Hypotheses 5 are presented in Table 11 below.

Table 11. Relationship between changes in overall muscular endurance and overall fatigue level.

		Δ_F
	R^2	.112
Δ_{OME}	Slope	-.026
	P value	.417

n = 8

CHAPTER V

DISCUSSION, CONCLUSION, AND RECOMMENDATIONS

Introduction

Although standard treatments improve survival for individuals with all types of cancer including leukemia, treatment-related side effects are commonly reported to have negative effect on recovery process, physiological and psychological health of cancer patients, and can potentially interfere with desired treatment outcomes (Servaes et al., 2002; Hemming and Maher, 2005). These physiological and psychological changes may also persist for years after completion of the treatment and can lead to functional disability and premature mortality (Battaglini et al., 2006). Therefore, there is a great need in understanding the preventive methods and complimentary therapies in managing cancer and cancer treatment-related side effects.

The benefits of exercise for the cancer population have been reported in the literature to be a promising complementary therapy in minimizing or even reverting both physiological and psychological side effects of cancer and cancer treatment (Adamsen et al., 2006; Courneya et al., 2003; Cunningham et al., 1986; Dimeo, 2001; Segal et al. 2003; Kolden et al., 2002). However, the majority of these studies were conducted on breast and prostate cancer patients using different exercise protocols making it difficult to compare their results. Segal et al. (2003) and Cunningham et al. (1986) used resistance training only, Courneya et al. (2003) and Dimeo et al. (2001) conducted aerobic training program, while studies by Adamsen et al. (2006) and Kolden et al. (2002) used a combination of aerobic, resistance and flexibility exercises. Several studies used unsupervised exercise protocol; others performed supervised in-hospital training and used different modes and intensities of exercise.

In the present study, a combination of aerobic, resistance, and flexibility exercises performed at low to moderate intensities were used as the exercise protocol. Moreover, each exercise session was supervised and individually prescribed for each patient depending on his/her health status on the day of exercise.

The current study was the first study to explore the effects of exercise on the adult acute leukemia population during the induction phase of treatment. Therefore, the primary purpose of this study was to examine the effects of an individualized exercise prescription on selected physical fitness parameters (cardiorespiratory and overall muscular endurance) and overall fatigue in acute leukemia patients undergoing chemotherapy. A secondary purpose was to examine a relationship between selected fitness parameters and fatigue assessed at the beginning and at the end of the exercise program.

Improvement in Cardiorespiratory Endurance

According to Hypothesis 1, there would be a significant difference in cardiorespiratory endurance (CRE) between the beginning and the completion of the exercise program. The results of the analyses showed a significant improvement in CRE measured as total cycling time ($p = 0.009$). These results are consistent with the results of two other studies that performed similar exercise protocol including a combination of cardiovascular, resistance and flexibility training (Adamsen et al., 2006; Kolden et al., 2002). Adamsen et al. (2006) showed that a 6-week high-intensity supervised exercise program improved cardiovascular capacity (VO_{2max}) by 16% in various cancer patients including leukemia. A pilot study performed by Kolden et al. (2002) with women undergoing adjuvant therapies for breast cancer also reported significant improvement in cardiorespiratory fitness after completion of 16-week structured supervised group exercise training.

In contrast to the results of the current study, Dimeo et al. (2003) reported no change in CRE (walking speed) in response to an in-hospital aerobic exercise program administered to patients with various different types of blood cancer. The intervention used in Dimeo et al. study lasted 2 weeks and included aerobic training only, compared to a 6-week combined training protocol of the current study. Significant physiological adaptations to an exercise program usually occur within first 3-8 weeks (ACSM's guidelines, 2006), therefore 2 weeks was probably not enough to elicit any significant change, especially in the cancer population. Although walking speed did not change in Dimeo et al. study, daily aerobic exercise reduced treatment-related loss of physical performance and showed the trend towards preserving it. This is a very important observation to note because once chemotherapy begins, patient's blood cell count drops drastically, resulting in severely compromised immune and cardiovascular systems, increase in overall tiredness and fatigue, leading to decrease in physical activity, followed by overall deconditioning, and decline in overall patients' health (Battaglini et al., 2006).

The results of the current study showed that improvement in the CRE can be achieved in acute leukemia patients undergoing treatment. The possible explanation could be that the intensity, frequency and duration of the exercise prescription adopted for each patient individually allowed for improvements in CRE. The exercise sessions were conducted twice a day at light to moderate intensity just long enough to elicit RPE of 4 on the Borg Modified Scale, which seemed to be well tolerated by all patients. Therefore, the exercise protocol used in the current study seemed to be an appropriate protocol to use in acute leukemia population. In addition, the fact that benefits of the exercise were explained to each patient and every exercise session was supervised and encouraged, could have potentially given patients hope and psychological support while combating the disease. These psychosocial factors may have contributed to motivation to perform exercise that was observed throughout the program.

There have been many other studies involving the use of aerobic exercise in other types of cancer besides patients with blood cancers. The majority of the studies have reported significant improvements in CRE (Burnham and Wilcox, 2002; Courneya et al., 2003; Marchese et al., 2004; Schwartz et al. 1999). The current study suggests that similar positive response of CRE to aerobic exercise may also be attained in the acute leukemia population.

Effect of Exercise on Overall Muscular Endurance

According to Hypothesis 2, there would be a significant difference in overall muscular endurance (OME) between the beginning and the completion of the exercise program. The results of the analyses showed no significant changes in OME ($p = 0.715$). Cunningham et al. (1986) reported similar findings where 5-week resistance training program had no effect on arm circumference and skinfold measurements among 30 leukemia patients recovering from bone marrow transplantation. It is important to note that no change in muscular fitness parameters found in both Cunningham et al. and this studies suggest that resistance training may be used to preserve muscle mass and to combat the muscle wasting effect, which is often observed in cancer patients undergoing chemotherapy (Al-Majid and McCarthy, 2001).

Two other studies that used a similar multidimensional exercise program to the current study, found significant improvements in both upper and lower body strength of patients of various types of cancer (Adamsen et al., 2006; Kolden et al., 2002). However, a higher frequency of the exercise sessions in Adamsen et al. study (9 hours a week), much longer duration of the exercise intervention in Kolden et al. study (16 weeks), and differences in cancer populations, may all explain the difference in the results between these studies and the current one. Moreover, different tests were used to assess upper and lower body strength. Also, multiple types of resistance exercises were performed in both of the abovementioned studies targeting all major muscles of the body. This was different from the protocol used in the current study, which was limited to only a small number of exercises. The OME measure in the current study only included two muscle groups (biceps and quadriceps), and may not have reflected well the patient's actual overall muscular endurance.

In addition, some patients in the current study were unable to perform upper body resistance training in the amount and frequency expected under the proposed exercise protocol, due to a port or IV inserted in either side of the chest or arms. Therefore, some patients ended up decreasing upper body muscular endurance, which affected OME, since OME combined the results of the endurance tests administered for upper and lower body. This could have compromised the overall results of the analyses.

Moreover, Kolden et al. (2002) created a protocol with intensity progression based on functional capacity and health status of the subjects. No progression in the exercise intensity was attempted in the current study, as it was maintained at low levels to avoid possible injuries or complications, and varied significantly from day to day according to the physical state of each patient prior to each exercise session.

There are several other possible explanations for the absence of significant changes in OME in the current study. Individual differences in age, gender and fitness level resulted in a large variability of the sample, and may have compromised the significance of the results.

The psychological impact of the disease sometimes did not allow for consistency in the administration of the exercise protocol, imposing another challenge to the study. For example, one of the patients was experiencing a high level of depression during the study and was not willing to exercise even after encouragement from physicians, nurses, and research team personnel. His OME decreased by the end of the study creating an outlier and increasing the variability of the responses.

Furthermore, some patients experienced nausea during the treatment and could not maintain an adequate diet. All patients were consuming hospital food during 4 weeks of the induction phase of treatment, and hospital diet might have been insufficient to provide adequate caloric and nutritional intake. All these factors in addition to the small sample size may have compromised the outcome of the study.

Therefore, if the current study had more control over individual differences and nutritional aspects of the program different, perhaps more significant, results could have been attained. Nevertheless, no change in OME suggests that the combined exercise program used in this study preserves muscle mass and helps combat muscle wasting effect in acute leukemia patients. Therefore, the maintenance of OME should be seen as a positive outcome in the acute leukemia population during treatment.

Decrease in Overall Fatigue

Another important finding of this study was significant reduction in overall fatigue level ($p = 0.009$), from moderate (4.6) at the beginning of the study to very mild (1.8) upon completion of the exercise program, measured by the Revised Piper Fatigue Scale. These results were consistent with the results of many other studies that also reported significant decrease in fatigue in response to exercise programs of various designs, modes, intensities, duration, and different types of cancer patients (Adamsen et al., 2003; Battaglini et al., 2006; Dimeo et al., 2004; Segal et al., 2003). Therefore, the results of the current study also suggest and agree with previous studies that exercise does assist in reducing fatigue in acute leukemia patients undergoing treatment.

This finding is very important because increase in fatigue has been reported as the most prevalent side effect experienced by the cancer patients undergoing chemotherapy (Servaes et al., 2002). It indirectly impacts many physiological systems, and, most important of all, contributes to a significant reduction in overall quality of life (Dimeo et al., 1999). If not treated, fatigue can become a chronic condition that is complex and very different from fatigue experienced by healthy population. Fatigue experienced by cancer patients should be considered as a multidimensional phenomenon that affects physical, psychological, and even social domains of patients' health (Battaglini et al., 2006; Dimeo, 2001). Especially in the acute leukemia population, the psychological impact of the disease diagnosis and the nature of the treatment (high doses of chemotherapy associated with an in-hospital recovery protocol) seem to affect them more than other cancer patients recovering outside of the hospital. Leukemia patients are usually restricted to a hospital room for approximately 4 weeks during the induction phase of treatment, which results in a decrease in physical activity. Such physical inactivity combined with the treatment-related side effects, especially increase in fatigue, lead to a severe deconditioning, which negatively impacts many physiological and psychological parameters (Battaglini et al., 2006). This decline in physical conditioning can further the fatigue and create a debilitating fatigue cycle, which if not treated, could result in further decrease in overall functionality putting limitations on normal daily activities and thus decreasing overall quality of life (Battaglini et al., 2006).

Thus, significant decrease in overall fatigue observed in this study suggests that exercise intervention promotes positive physiological and psychological changes by breaking the debilitating fatigue cycle. Therefore, this result has a significant clinical relevance for acute leukemia population undergoing treatment.

Relationship between Changes in Cardiorespiratory Endurance and Fatigue

According to Hypothesis 4, there would be a significant inverse relationship between changes in cardiorespiratory endurance and fatigue from pre-to-post assessments. Significant improvements in both, cardiorespiratory endurance and fatigue were observed during the study ($p = 0.009$ for both). However, no significant relationship was found between the change scores of these two variables ($r (7) = -0.26, p = 0.534$). The results of regression analysis were also non-significant ($p = 0.708$) and showed that CRE explained only 2.5% of the variance in fatigue (Table 9).

The results of this study are consistent with the results reported by Battaglini et al. (2004). After examining a group of 27 patients of different cancer types, Battaglini et al. found no significant relationship between reduction in fatigue and improvement in cardiorespiratory fitness measured as total treadmill time ($r = 0.001, p = 1.00$). The exercise protocol used by Battaglini et al. was similar to the protocol used in present study and also included supervised aerobic, resistance, and stretching exercises in a single exercise session. In Battaglini et al. study, other physiological parameters were included in a regression model such as specific fitness components (total time on a treadmill as measure of cardiorespiratory endurance, modified sit-and-reach flexibility test, and % body fat) as well as results of specific strength exercises tested during the study (number of repetitions on the chest press, leg press, and abdominal exercises). Battaglini et al. found that when all these fitness parameters were included in a regression model, even though the model presented a not significant result ($p = 0.351$), the researchers found a positive, linear relationship, suggesting a possible trend. The authors suggested that the non-significant findings were due to the small sample size and the variability of the sample, composed of patients with different types of cancer. They also suggested that fatigue is multifactorial in cancer patients, and therefore not only one physiological parameter, but a combination of many factors impact fatigue in cancer patients, suggesting that fatigue should not be treated unidimentionally.

The trend towards decrease in fatigue with improvement in aerobic fitness was observed in other studies (Dimeo et al., 1998; Adamsen et al., 2006). Dimeo et al. (1998) conducted aerobic exercise program with only five cancer patients and reported significant improvement in maximal physical performance, measured as maximal walking speed and distance covered. At the same time, all patients experienced reduction in fatigue and could perform their normal daily activities without limitations. A larger study by Adamsen et al. (2006) showed that multidimensional exercise program significantly improved cardiovascular capacity (VO_{2max}) of eighty-two patients with various cancers, who at the same time reported significant reduction in fatigue. However, no correlation analysis was performed in either study to look at the relationship between the changes in these two variables.

In a study conducted by Schwartz (1999), a significant positive relationship was found between an increase in fatigue with improvement in cardiorespiratory fitness, measured by distance covered in 12-minute walk ($r^2 = 0.353$, $p = 0.02$). However, the major limitation in Schwartz's study was that the intervention was unsupervised home-based exercise program. Patients were instructed to exercise at their own pace of preference and were free to choose the type of aerobic activity. This protocol limits the ability to generalize the results of the study and therefore should be viewed with caution.

The contradictory results of the studies described above may be explained by many factors, including differences in exercise protocols (intensity, duration, type of exercise, supervised vs. unsupervised, in-hospital vs. home-based, different measures and tests used to assess cardiorespiratory fitness, different cancer populations) and conditions in which these patients were studied (during the treatment or during the recovery).

Nevertheless, the majority of the studies have shown significant decreases in fatigue, which confirms the positive impact of exercise in assisting cancer patients to battle side effects developed during the treatment. The results of the current study are in agreement with Dimeo et al. (1999), where the authors suggested that fatigue should be seen as a multifactorial process in the cancer population, and therefore examinations of physiological parameters performed independently should be revised. Even though significant changes in cardiorespiratory endurance were observed in the current study, the impact of aerobic, resistance and flexibility training on fatigue should be analyzed in combination and not in an isolated manner. Furthermore, psychological support and encouragement from physicians, nurses, and exercise trainers during exercise sessions could be considered as an important social support component of the therapy, which could have affected the reduction in fatigue but not changes in cardiorespiratory endurance observed in the study.

Therefore, future studies should perform multidimensional analyses, where multiple parameters, including some psychosocial ones, are included into a model, so better conclusions can be made on the impact of exercise on fatigue reductions. Since the variability within cancer patients is quite large, this approach may also be explored on a case by case basis, where specific conclusions can be made to each patients individually. Baseline measures of all these parameters may be used to define more specific treatment plans.

Relationship between Changes in Overall Muscular Endurance and Fatigue

Similar to Hypothesis 4, Hypothesis 5 stated that there would be a significant reverse relationship between changes in overall muscular endurance (OME) and fatigue from pre-to-post assessments. Results of correlation analysis again showed no significant relationship between change scores of OME and fatigue ($r(7) = -0.335$, $p = 0.417$) with OME explaining only 1.3% of the variance in fatigue, according to non-significant results of regression analysis ($p = 0.79$). Despite the lack of statistical significance, the results of the current study are again consistent with those reported by Battaglini et al. (2004).

In the contrast, two other studies showed significant reduction in fatigue with improvements in overall muscular strength (Adamsen et al., 2006; Segal et al., 2003). The study by Adamsen et al. (2006) showed that, along with improvements in cardiorespiratory fitness, multidimensional exercise program significantly improved overall muscular strength and resulted in a significant reduction in fatigue. Segal et al. (2003) conducted 12-week whole body resistance training and showed significant improvement in overall body strength with significant decrease in fatigue. However, the sample size in both studies was large ($n = 82$, $n = 155$) suggesting higher statistical power. Again, no correlation analysis of the relationship between the changes in the two variables was performed in either study.

The results of the analyses of hypothesis 5 of the current study suggest again using the multidimensional approach when measuring fatigue. Therefore, overall muscular endurance should not be used in regression analysis separately from other physiological and psychological parameters.

Other Factors that Could Have Impacted the Study Results

The non-significant results of correlation between changes in physical fitness parameters and fatigue could possibly be attributed to the following additional factors.

First, the study was a one-group pre-to-post design, not a randomized controlled study, in which the results are compared to the control group, thus improving the power of the analyses. For example, using a control-group design and aerobic exercise program Dimeo et al. (1999) found no change in fatigue in the exercise group, while patients in the control group showed significant increase in fatigue and reduction in vigor.

Second, as already mentioned above, the small sample size (n = 8) may have resulted in low statistical power of regression analyses, which was one of the major limitations of the current study. Other potential factors, including inability to control for differences in age, gender and fitness levels that together contributed to the large variability of the sample, are discussed below.

The presence of two outliers (a very fit person and a very unfit person) out of 8 subjects greatly increased variability of the sample and affected the power of the statistical analyses (large standard deviations in both cardiorespiratory and muscular endurance). In healthy populations, individuals with low initial levels of fitness generally demonstrate the greatest increase in cardiorespiratory capacity (ACSM's Guidelines, 2006). In contrast, more modest increases occur in healthy individuals with high initial fitness levels. Similarly, a great variability in subjects' fitness level resulted in a large variability in the responses (change scores) to the exercise program. For example, on average leukemia patients showed about 8 minutes improvement in total time of cycling (the mean for the change score of cardiorespiratory endurance was 8.07 minutes and SD was 6.42 minutes) while the individual improvements varied from 0 to 17 minutes.

In addition, the gender differences (2 females and 6 males) and a wide range of patients' age in this study (24 to 48 years old) might have also increased the variability in the responses to the exercise program. According to ACSM's guidelines (2006) women generally have lower physiological responses to a same exercise program than men, especially when resistance exercise is included into a program. Similarly, older adults (for example, over 40 years old in this study) are usually shown to have lower responses when compared to younger adults (24-28 years in the current study). Unfortunately, due to a small sample size in this study it was not possible to control for either age or gender. Thus, all of the above factors could have affected the statistical power compromising the regression analysis.

At last, as mentioned previously in the document, fatigue is believed to be multidimensional phenomena that have physical as well as psychological and even social components in it (Battaglini et al., 2006; Dimeo, 2001). When fatigue is measured, using Revised Piper Fatigue Scale (Piper et al., 1998), the physical domain is not addressed to the same extend of the psychological and social domains (behavioral, emotional, sensory, and cognitive) where only 6 out of 27 questions of the instrument are related to physical fatigue. This study utilized Revised Piper Fatigue Scale and examined the relationship between overall fatigue and physiological parameters, and not psychological or social ones. In a related study, Dimeo et al. (1997) found a strong correlation between intensity of fatigue and several indicators of psychological distress such as depression ($r = 0.68$) and anxiety ($r = 0.63$; $p < 0.001$ for both), while only a weak association between fatigue and physical performance (estimated VO_{2max}) was observed ($r = -0.30$; $P < 0.01$). Thus, a non-significant relationship between changes in physical fitness parameters and fatigue found in the current study may also be explained by the multidimensional nature of treatment-related fatigue and by limitations of the instrument used to measure fatigue.

Conclusion

Exercise has been shown to be a promising adjunct therapy to cancer treatment. Many studies have reported numerous benefits of exercise to cancer patients, including positive changes in physiological parameters such as cardiorespiratory endurance, muscular endurance, flexibility, overall functionality, as well as psychological parameters such as reductions in depression, fatigue, and anxiety and improvement in overall quality of life (Galvao and Newton, 2005).

Up to now, most of the studies in area of cancer and exercise have focused on breast and prostate types of cancer. Present study was the first to explore the effect of individually prescribed exercise program in adult acute leukemia population undergoing chemotherapy. The results of the current study are in agreement with the majority of the studies where improvements in many physiological and psychological parameters were observed.

In conclusion, the results of the current study suggest that the administration of exercise for acute leukemia patients undergoing chemotherapy (induction phase of treatment) is feasible, well tolerated by patients, promoting increase in cardiorespiratory endurance, maintenance of overall muscular endurance, while reducing the level of fatigue.

Even though there were limitations believed to have impacted some of the study analyses, the overall outcomes of the exercise intervention used in the current study are very promising and should encourage physicians and researchers to continue to explore the impact of exercise in the acute leukemia population. Although adjustment in the methodology of the current study should be considered for future experiments, the current study should be used as a starting point for future research in this area.

Recommendations

Based on the results of this study and limitations observed, the following are recommendations for future research in the area of cancer and exercise, specifically related to acute leukemia population:

1. A further randomized controlled study with a larger sample size is needed to increase statistical power of the analysis and credibility of the results;
2. Control for individual differences in age, gender and fitness level may be valuable to examine if any of these factors affect the outcomes of the exercise program during leukemia treatment. A larger sample size in this case will be necessary.
3. When creating an overall muscular endurance protocol there is also a need to improve the upper body resistance training while patient has a chemotherapy port inserted;
4. Achieve a better control over unsupervised portion of the exercise program (during 2-week recovery phase);
5. Explore the possibility of creating a better measurement of fatigue that takes into consideration some physiological parameters;
6. Include assessment of psychological parameters such as anxiety, depression and motivation in future studies to better understand the psychological mechanisms affecting patients' health status and outcomes of an exercise intervention;

7. The implementation of recreation therapy and nutritional counseling in addition to combined exercise protocol, as a mean of improving both the physiological and psychological aspects of the patients' health during treatment;
8. Provide education for leukemia patients to prepare them to deal with side effects and different issues of the treatment and disease itself, as well as education on exercise benefits for leukemia population;
9. If possible to extend the duration of the program including the consolidation portion of the treatment plan to promote further benefits of exercise for acute leukemia population;
10. Follow up studies should be done in the future to examine the long-term impact of the exercise intervention on leukemia re-occurrence and survivorship rates.

APPENDIX I:

Study Advertisement Flyer

EQUAL Project #1:

Title of Study: In-Hospital Individualized Prescriptive Exercise Intervention for Acute Leukemia Patients Undergoing Chemotherapy

Purpose of the study: The purpose of this pilot study is to examine the effects of an individualized prescriptive exercise intervention, administered in-hospital during the treatment-recovery of acute leukemia patients, on selected fitness and blood parameters, fatigue levels and quality, of life.

Criteria for Participation:

- Newly diagnosed with acute leukemia or newly relapsed and receiving re-induction therapy for acute leukemia;
- An expected hospital stay of 3-4 weeks or longer;
- Participation in the study must be approved by the physician directly responsible for the patient's care while at UNC-Hospitals;
- Designated for chemotherapy treatment;
- Ages ranging from 18 to 60 years at the time of the study.

For further information, please contact any of the following:

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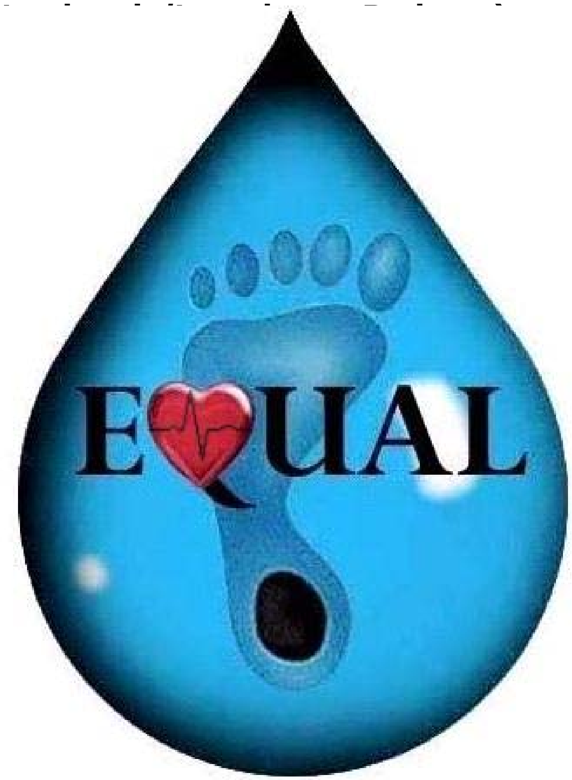
The EQUAL Project
(Exercise and Quality of Life in



Project Sponsored By:

UNC N.C. CANCER HOSPITAL LINEBERGER COMPREHENSIVE CANCER CENTER

EXSS Exercise and Sport Science

About the EQUAL Project:

The EQUAL Project is a series of research projects that have the intent of assisting leukemia/lymphoma patients in battling the side effects produced by cancer treatment. The main intent of the project is to improve the overall quality of life for leukemia patients during and possibly post-treatment throughout the administration of exercise.

The EQUAL Project utilizes an individualized prescriptive exercise intervention approach as the main tool in an attempt to alleviate the symptoms developed during treatment.

Each patient enrolled in the EQUAL Project is assigned to an exercise specialist that will design and conduct an individualized exercise routine during treatment.

For more information about the project, please contact:

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Background Information: Very few studies have been conducted that detail how exercise may affect other types of cancer, such as lung cancer and leukemia. Leukemia is a malignant disease that affects bone marrow and the blood, and is characterized by an uncontrolled accumulation of blood cells.

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 week chemotherapy regimen that requires the patient to remain in his or her private room within a hospital recovering from the chemotherapy treatment for approximately 4 weeks (induction treatment). Following these four weeks, the patient is allowed to return home or to a nearby hotel for two more weeks of recovery, only to return to the hospital for another bout of chemotherapy after these two weeks have elapsed (consolidation treatment).

Since leukemia patients are generally confined to their room during a period of low blood counts and immune suppression during induction and consolidation phases of treatment, their opportunities to engage in physical activity are markedly reduced. 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 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 (ACS, 2005), and it is believed that these benefits can be also observed in the acute leukemia population as well.

Study Design:

- Pilot study with a pre-test post-test methodology that includes 1 group of 10 leukemia patients.
- The study protocol involves the recruitment and participation of 10 total male and female subjects recently diagnosed with acute leukemia.
- The study will take place at the University of North Carolina Hospitals (UNC-CH hospitals), division of Oncology/ Hematology.
- All subjects will participate in the following assessments:

1. Quality of life, fatigue, and depression questionnaires
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
5. Cardiorespiratory fitness
6. Dynamic muscular endurance and handgrip dynamometry

- Patients enrolled in the study will participate in a 4-week exercise program in hospital while receiving treatment, and 2-weeks of self-administered prescribed exercise.

APPENDIX II:

The EQUAL Project
Pre-Assessment Guidelines

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

Pre-Assessment Guidelines

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- 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.

ACSM's Guidelines for Exercise Testing and Prescription, 7th Edition, 2006, p. 53-54.

APPENDIX III:

Revised Piper Fatigue Scale

Name: ______________________________ Date: ______________

Revised Piper Fatigue Scale

Directions: For each of the following questions, circle the number that best describes the fatigue you are experiencing now. Please make every effort to answer each question to the best of your ability. Thank you very much.

1. How long have you been feeling fatigued? (*check one response only*)
   - a. Minutes_____
   - b. Hours______
   - c. Days_____
   - d. Weeks_____
   - e. Months_____
   - f. Other (*please describe*):______________________________

2. To what degree is the fatigue you are feeling now causing you distress?

   No distress **A great deal of distress**

   0 1 2 3 4 5 6 7 8 9 10

3. To what degree is the fatigue you are feeling now interfering with your ability to complete work or school activities?

   None **A great deal**

   0 1 2 3 4 5 6 7 8 9 10

4. To what degree is the fatigue you are feeling now interfering with your ability to visit or socialize with your friends?

   None **A great deal**

   0 1 2 3 4 5 6 7 8 9 10

5. To what degree is the fatigue you are feeling now interfering with your ability to engage in sexual activity?

   None **A great deal**

   0 1 2 3 4 5 6 7 8 9 10

6. Overall how much is the fatigue, which you are experiencing now, interfering with your ability to engage in the kind of activities you enjoy doing?

   None **A great deal**

   0 1 2 3 4 5 6 7 8 9 10

7. How would you describe the degree of intensity or severity of the fatigue which you are experiencing now?

   Mild **Severe**

   0 1 2 3 4 5 6 7 8 9 10

To what degree would you describe the fatigue which you are experiencing now as being:

8. **Pleasant** **Unpleasant**

0 1 2 3 4 5 6 7 8 9 10

9. **Agreeable** **Disagreeable**

0 1 2 3 4 5 6 7 8 9 10

10. **Protective** **Destructive**

0 1 2 3 4 5 6 7 8 9 10

11. **Positive** **Negative**

0 1 2 3 4 5 6 7 8 9 10

12. **Normal** **Abnormal**

0 1 2 3 4 5 6 7 8 9 10

13. To what degree are you now feeling:

Strong **Weak**

0 1 2 3 4 5 6 7 8 9 10

14. To what degree are you now feeling:

Awake **Sleepy**

0 1 2 3 4 5 6 7 8 9 10

15. To what degree are you now feeling:

Lively **Listless**

0 1 2 3 4 5 6 7 8 9 10

16. To what degree are you now feeling:

Refreshed **Tired**

0 1 2 3 4 5 6 7 8 9 10

17. To what degree are you now feeling:

Energetic **Unenergetic**

0 1 2 3 4 5 6 7 8 9 10

18. To what degree are you now feeling:

Patient **Impatient**

0 1 2 3 4 5 6 7 8 9 10

19. To what degree are you now feeling:

Relaxed **Tense**

0 1 2 3 4 5 6 7 8 9 10

20. To what degree are you now feeling:

Exhilarated **Depressed**

0 1 2 3 4 5 6 7 8 9 10

21. To what degree are you now feeling:

Able to concentrate **Unable to concentrate**

0 1 2 3 4 5 6 7 8 9 10

22. To what degree are you now feeling:

Able to remember **Unable to remember**

0 1 2 3 4 5 6 7 8 9 10

23. To what degree are you now feeling:

Able to think clearly **Unable to think clearly**

0 1 2 3 4 5 6 7 8 9 10

24. Overall, what do you believe is most directly contributing to or causing your fatigue?

____

____

25. Overall, the best thing you have found to relieve your fatigue is:______________

____

26. Is there anything else you would like to add that would describe your fatigue better to us?____

____

27. Are you experiencing any other symptoms right now?

No

Yes Please describe:____

____

Revised Piper Fatigue Scale Calculations

Calculate each section separately. The answer should be between 0 and 10.
Add each of the total numbers and divide by 22 to get overall score of 0 to 10.

Missing Data

Follow this procedure if patient answered at least 75%-80% of the questions in each section.

1. add the values of the questions answered in that section
2. divide by the number of questions answered in that section
3. substitute that number for the missing number
4. calculate total score for that section by using the substituted number

Example:

#5 is commonly not answered

Behavioral/Severity	Score
#2 - distress-----------	6
#3 - work/school------	5
#4 - socialize---------	7
#5 - sex---------------	____
#6 - activities---------	8
#7 - severity---------	5
Total	____ ÷ 6 = _____

Add 6+5+7+8+5 = 31 ÷ 5 = 6.2   Substitute 6.2 for #5

Behavioral/Severity	Score
#2 - distress-----------	6
#3 - work/school------	5
#4 - socialize---------	7
#5 - sex---------------	6.2
#6 - activities---------	8
#7 - severity---------	5
Total	37.2 ÷ 6 = 6.2

Patient Name: ______________________

Revised Piper Fatigue Scale Calculations

Date:______	**Date:**______	**Date:**______
Behavioral/Severity Score	Behavioral/Severity Score	Behavioral/Severity Score
#2 - distress----------- ____	#2 - distress----------- ____	#2 - distress----------- ____
#3 - work/school------ ____	#3 - work/school------ ____	#3 - work/school------ ____
#4 - socialize---------- ____	#4 - socialize---------- ____	#4 - socialize---------- ____
#5 - sex--------------- ____	#5 - sex--------------- ____	#5 - sex--------------- ____
#6 - activities--------- ____	#6 - activities--------- ____	#6 - activities--------- ____
#7 - severity---------- ____	#7 - severity---------- ____	#7 - severity---------- ____
Total ____ ÷ 6 = _____	Total ____ ÷ 6 = _____	Total ____ ÷ 6 = _____
Affective Score	Affective Score	Affective Score
#8 - pleasant/un ____	#8 - pleasant/un ____	#8 - pleasant/un ____
#9 - agreeable/dis ____	#9 - agreeable/dis ____	#9 - agreeable/dis ____
#10 - protect/destr ____	#10 - protect/destr ____	#10 - protect/destr ____
#11 - positive/neg ____	#11 - positive/neg ____	#11 - positive/neg ____
#12 - normal/abn ____	#12 - normal/abn ____	#12 - normal/abn ____
Total ____ ÷ 5 = _____	Total ____ ÷ 5 = _____	Total ____ ÷ 5 = _____
Sensory Score	Sensory Score	Sensory Score
#13 - strong/weak ____	#13 - strong/weak ____	#13 - strong/weak ____
#14 - awake/sleepy ____	#14 - awake/sleepy ____	#14 - awake/sleepy ____
#15 - lively/listless ____	#15 - lively/listless ____	#15 - lively/listless ____
#16 - fresh/tired ____	#16 - fresh/tired ____	#16 - fresh/tired ____
#17 - energy/un ____	#17 - energy/un ____	#17 - energy/un ____
Total ____ ÷ 5 = _____	Total ____ ÷ 5 = _____	Total ____ ÷ 5 = _____
Cognitive/Mood Score	Cognitive/Mood Score	Cognitive/Mood Score
#18 - patient/imp ____	#18 - patient/imp ____	#18 - patient/imp ____
#19 - relax/tense ____	#19 - relax/tense ____	#19 - relax/tense ____
#20 - exhil/depr ____	#20 - exhil/depr ____	#20 - exhil/depr ____
#21 - concentr/not ____	#21 - concentr/not ____	#21 - concentr/not ____
#22 - memory/not ____	#22 - memory/not ____	#22 - memory/not ____
#23 - think/not ____	#23 - think/not ____	#23 - think/not ____
Total ____ ÷ 6 = _____	Total ____ ÷ 6 = _____	Total ____ ÷ 6 = _____
Total Score ______ ÷ 22 = ______	**Total Score** ______ ÷ 22 = ______	**Total Score** ______ ÷ 22 = ______

APPENDIX IV:

BORG CR10 Rate of Perceived Exertion (RPE) Scale

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 max exertion	Highest Possible

APPENDIX V:

Dynamic Muscular Endurance Test

Dynamic Muscular Endurance Test

(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. See Below

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)	Women (Right and Left Arm)
.085	.065

Age: 45 - 60

Men (Right and Left Arm)	Women (Right and Left Arm)
.080	.061

Exercise Load = "weight to be lifted"

Example: 45 years old male, 150lbs.
Bicep Curl (right arm) = 150 x .080 = 12lbs ("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).

Rocky Mountain Cancer Rehabilitation Institute
Ben Nighthorse Campbell Center 19th St. at 10th Ave.
Greeley, Colorado 80639
Phone 970-351-1876

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