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# The Effects of an Exercise Program in Leukemia Patients

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*Purpose.* To examine the feasibility of administering an in-hospital exercise program to acute leukemia patients undergoing chemotherapy. A secondary purpose explored the impact of exercise on selected physiological, psychological, and inflammatory markers. *Methods.* Ten patients, aged 18 to 50 years, diagnosed with acute leukemia or newly relapsed were assessed for body weight, height, body composition (skinfolds), cardiorespiratory endurance (total minutes on bicycle ergometer at 60% heart rate reserve), dynamic muscular endurance (Rocky Mountain Cancer Rehabilitation Institute protocol), fatigue (Revised Piper Fatigue Scale), depression (Center for Epidemiologic Studies Depression scale, National Institute of Mental Health questionnaire), and quality of life (Functional Assessment of Cancer Therapy–General) at baseline (within 3 days of diagnosis) and at the end of induction phase of treatment. Blood draws were taken at baseline, midpoint, and at the end of induction for analyses of inflammatory markers (Linco Luminex assay). Combined aerobic and strength training exercises were administered 3 times per week, twice daily, for 30 minutes. Paired-samples *t*-tests were used for the analyses of physiological and psychological parameters. One-way repeated measures analysis of variance was used for the analyses of inflammatory markers. *Results.* Significant improvements in cardiorespiratory endurance ($P$ = .009, baseline 8.9 ± 8.8 minutes, postexercise intervention 17 ± 14.3 minutes) with significant reductions in total fatigue scores ($P$ = .009, baseline 4.6 ± 1.7, postexercise intervention 1.8 ± 1.6) and depression scores ($P$ = .023, baseline 19 ± 11.5, postexercise intervention 12 ± 8.2) were observed. Marginally significant decrease in interleukin-6 (IL-6; $P$ = .059) with no significant changes in IL-10 ($P$ = .223) or interferon-γ ($P$ = .882) were observed. *Conclusion.* Administration of exercise to acute leukemia patients undergoing treatment is feasible. The exercise protocol used increased cardiovascular endurance, reduced fatigue and depression scores, and maintained quality of life. Although no significant change in inflammation was observed, a trend demonstrating a reduction in IL-6 and an increase in IL-10 warrants further investigation.

**Keywords:** cytokines; aerobic training; strength training; induction; myelogenous; neutropenia

Leukemia is a cancer of the bone marrow and blood cells. The impact of leukemia in the bone marrow results in uncontrolled development of abnormal (malignant) blood cells. This uncontrollable development and accumulation of malignant cells compromises the body's ability to produce normal blood cells, which can result in the development of profound anemia, inability to combat infections, and a reduction in platelet production leading to possible bleeding complications. Even though there are some potential risk factors associated with the development of leukemia, such as previous chemotherapy and radiation treatment used to treat other types of cancer, chronic exposure to benzene above federal approved safety limits, and tobacco smoking,[1] the cause of leukemia remains a mystery.

In the United States today, approximately 10.5 million people live with a cancer history[2] with approximately 895 000 living with or in remission from leukemia.[1] It was estimated that in 2008, 138 530 people will be diagnosed with leukemia, lymphoma, or myeloma, which represents a 9.6% of the approximately 1 450 000 new cancer cases.[3] Based on the total of expected cancer-related deaths of approximately 566 000 in 2008, 9.4% or an estimated 53 000 deaths will be attributed to blood cancers with leukemia contributing to approximately 22 000 deaths.[3] Of extreme concern is the fact that incidence and death rates of people diagnosed with all types of leukemia have not changed substantially over the past 30 years.

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The treatment for leukemia as for any other type of cancer is quite complex. Its standard procedure involves the utilization of chemotherapy followed by a bone marrow transplant in the majority of cases. As for any type of cancer treated with chemotherapy, a constellation of side effects compromise the ability of the patient to function at precancer levels. In many cases, the decline in overall physiological and psychological functioning can compromise further administration of treatment, which can lead to poor treatment outcomes. Debilitating fatigue, nausea, loss of body mass (development of cancer cachexia), anemia, and depression are among very common side effects usually observed in leukemia patients undergoing chemotherapy.[4-6] A few strategies are used by physicians to alleviate some of the side effects cited above with the hope to keep patients on a planned course of treatment. Some examples of strategies used to mitigate side effects of chemotherapy include the use erythropoietin (Procrit) to treat anemia; dexamethasone to treat nausea/vomiting; methylphenidate, frequently prescribed to alleviate depression; and serotonin receptor antagonists to alleviate nausea.[7] Although necessary, most of these pharmaceutical treatments provide only temporary relief of symptoms. Therefore, the need for the exploration of other symptom management strategies to alleviate side effects of treatment in the adult leukemia population, including exercise, is paramount.

Recent reviews in the area of cancer and exercise have shown that when administered during or posttreatment, exercise can alleviate many of the side effects of treatment, improve overall health, and even reduce death rates.[8,9] However, very few studies have examined the impact of exercise in the adult acute leukemia population.[10,11] Because of the nature of the disease and disease treatment, leukemia patients are not allowed to leave their hospital room and therefore, their opportunities to engage in physical activity have all but been eliminated. The decreased level of physical activity during treatment can lead to constant tiredness, exhaustion, fatigue, depression, and decrease in overall quality of life (QOL). This follows the same symptom patterns experienced by individuals undergoing chemotherapy for the treatment of various other types of cancers.[12] Although regular exercise has benefited patients with different types of cancer, much of the current literature on this topic has focused on breast, prostate, and colorectal cancers.[7-9,13-21] It is postulated, however, that an exercise intervention may also mitigate treatment symptoms, increase physiological and psychological function and, ultimately, improve overall QOL in adult acute leukemia patients undergoing treatment. Therefore, the purpose of this study was to examine the feasibility of administering in-hospital exercise to acute leukemia patients undergoing chemotherapy. A secondary purpose explored the impact of exercise on selected physiological, psychological, and inflammatory markers.

## Methods

### Patients' Information

A total of 10 patients, 7 men and 3 women with acute myelogenous leukemia were volunteers recruited from the University of North Carolina Hospitals (UNC-CH Hospitals), Division of Oncology/Hematology. Patients were introduced to the study by oncology physicians from the UNC-CH Hospitals during the diagnostic meeting. Patients were included in the study if the following inclusion criteria were met: newly diagnosed with acute leukemia or newly relapsed and receiving reinduction therapy for acute leukemia; an expected hospital stay of 3 to 5 weeks; approval for participation by the physician directly responsible for the patient's care while at UNC-CH Hospitals; designated for chemotherapy treatment; and ages ranging from 18 to 55 years at the time of the study. Given the potential risks involved when participating in exercise programs, patients were screened for exclusion based on the following criteria: cardiovascular disease, acute or chronic respiratory disease, acute or chronic bone, joint, or muscular abnormalities, and immune deficiency (unless any of the factors above would not compromise the patient's ability to participate in the exercise intervention). The aforementioned criteria were determined by the patient's medical history and physical examination recommendations from each patient's oncologist. After the approval from the patient's oncologist, each patient was introduced to the study protocol by the oncology research nurse and informed about the possible risks and benefits of participating in the study. Prior to starting in the study, each patient signed a consent form, approved by the University of North Carolina at Chapel Hill Biomedical Institutional Review Board, and the HIPAA authorization for use and disclosure of health information for research purposes form. The initial assessments were scheduled to occur within 3 days postdiagnosis (beginning of the induction [phase 1] treatment [baseline assessment]).

### General Procedures

Prior to the implementation of the study, each patient's hospital room was equipped with exercise equipment. All equipment was sterilized using neutropenic procedures following the hospital guidelines. The equipment remained in the room until the completion of the study and was sanitized daily. These procedures were followed to minimize the possibility of infection. All members of the research team were advised to wash their hands, use gloves, masks, and sterilized hospital gowns every time they entered the patients' room. In the event a member had cold symptoms or was sick they were not allowed to interact with patients and another research team member completed the exercise routine for that session. Following the

baseline assessment, patients participated in an in-hospital individualized prescriptive exercise intervention 3 to 4 times per week for a period of approximately 3 to 5 weeks, followed by a 2-week period recovering from treatment at home. An aerobic-based exercise prescription was given to each patient prior to leaving the hospital to use at home during recovery. The final assessment was administered on patient's return to the hospital, prior to the next bout of treatment (consolidation phase) at the end of the study.

### Assessments

A battery of psychological and physiological assessments were administered twice during the study; at the beginning of the study (3 days postdiagnosis/beginning of the induction [phase 1] of treatment – baseline), and again at the end of the study (immediately after readmission to hospital, prior to the beginning of consolidation treatment). Blood samples were collected 3 times during the study (beginning of the study [3 days postdiagnosis/beginning of the induction-baseline], midpoint [between weeks 3 and 4 of treatment], and postexercise intervention [immediately after re-admission to hospital]) for the analyses of select inflammatory markers (Interleukin-6 [IL-6], IL-10, and interferon-γ [IFN-γ]).

Immediately after the assessment of psychosocial parameters, administered by the oncology research nurse, the primary investigator conducted the battery of physiological assessments. All the procedures were followed exactly the same way in both assessment periods and the oncology research nurse and the primary investigator were the only research team members to administer the tests. This was done to increase the reliability of the data collected and to minimize errors between testing sessions.

The psychological parameters examined in this study included fatigue, depression, and quality of life. Fatigue was assessed through the Revised Piper Fatigue Scale.[22] The Center for Epidemiologic Studies Depression Scale (CES-D) National Institute of Mental Health (NIMH)[23] was used for the assessment of depression, and the Functional Assessment of Cancer Therapy-General (FACT-G) for the quantification of QOL in cancer patients.[24]

The physiological parameters assessed included resting vitals (resting heart rate, blood pressure, and hemoglobin saturation), anthropometry (body weight and height), body composition (skinfold thickness), a cardiorespiratory test, and a dynamic muscular endurance test. First, resting heart rate was assessed using a F1 Polar heart rate monitor (Lake Success, NY), followed by blood pressure via ADC 922 Series aneroid sphygmomanometer (Hauppauge, NY) and a Littmann Stethoscope (St. Paul, MN), and then hemoglobin saturation via a finger pulse oximeter, Respironics RES-950 (Murrysville, PA). After the assessment of resting vitals, weight and height were assessed using a balance beam physician scale equipped with height rod Detecto Model 437 Physician Beam Scale (Webb City, MO). Body composition analyses were then performed via skinfold thickness using a Lange C-130 Beta Technology calipers (Cambridge, MD) using the generalized 3-site skinfold equations for male and females as recommended by the American College of Sports Medicine.[25] Given that no validated procedures exist to assess cardiorespiratory and muscular endurance in hospitalized acute leukemia patients, the following protocols were chosen to minimize the risk of an adverse effect and to create a legitimate measurement of the assessed parameters. The cardiorespiratory assessment followed the skinfold assessments and was performed on a recumbent cycle ergometer, model Cateye EC 3500 (Dallas, TX). Subjects were asked to cycle at a target submaximal intensity of 60% of their heart rate reserve (HRR) until a RPE (rate of perceived exertion) of 7 (very hard) was reached on the CR10 modified Borg Scale[26] or when the patient requested termination of the test. The total time cycling and heart rate (HR) at the end of the test was recorded immediately after the test was completed. The assessment of dynamic muscular endurance was the last of the physiological assessments administered. The dynamic muscular endurance assessment included 2 tests. The first was a squat exercise using the fit ball (42 inches in diameter, soft plastic/rubber ball) Power Systems Sports (Knoxville, TN) and no external load. The squat exercise required the patient to stand with back toward the wall, feet shoulder width apart, and the fit ball placed in the small of the patient's back. Patients were asked to squat to a 75° knee angle with moderate speed, pressing back against the ball at all times. This was repeated as many repetitions as it took for the patient to report an RPE of 7 or wished to stop. The second test was the biceps curl exercise. The biceps curls exercise test followed a protocol developed at the Rocky Mountain Cancer Rehabilitation Institute (RMCRI), Greeley, Colorado.[27] The protocol involves the administration of the exercise biceps curls, done with dumbbells, Power Systems Sports. Patients were 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 lifted was calculated according to the protocol developed at the RMCRI.[27] The test was terminated when the subject reported an RPE of 7 or wished to stop.

During the study, three 5-mL samples of blood were obtained for the analyses of cytokines. To control for possible circadian variations as well as to minimize stress on the patient, an oncology nurse member of the research team collected the sample at the same time blood samples were being collected as part of the regular treatment regimen, at the same time of the day at 3 AM, for all 3 measurements. Blood samples were then put on ice and transported to the laboratory where the samples were centrifuged for 10 minutes at 3000 × *g* in a refrigerated

centrifuge at a temperature of 4°C. After centrifugation, samples were stored at −80°C until assayed. For the analyses of IL-6, IL-10, and IFN-γ, the Luminex[100] systems (Luminex Corporation, Austin, TX) was used. The system uses xMAP microsphere technology with the capability to analyze multiple analytes per sample well. Procedural details for the Luminex assays are reported on catalog # HCYTO-60K-PMX, Human Cytokine Lincoplex Premixeg (LINCO Research, Missouri, MO). The cytokine analysis was limited to IL-6, IL-10, and IFN-γ due to their association with cancer cachexia and anorexia.

### Exercise Intervention

The exercise program began approximately 24 hours after the completion of baseline assessments. Each patient followed an individualized prescriptive exercise program 3 to 4 times per week with at least 36 hours of rest between the sessions. An exercise session was only cancelled if a patient was experiencing a fever or platelet count below 20 000/mm$^3$ (microliter) of blood ($150 \times 10^9$ to $400 \times 10^9$/L). Each exercise session was divided into 2 bouts. One bout was administered in the morning and the second one late in the afternoon. By exercising in 2 different periods of the day, patients did not have to exercise for more than 30 minutes each bout. However, the duration of each exercise session depended on patient's physical state on the day of each exercise session. All patients exercised in his or her room in the hospital with all necessary equipment provided. Each exercise session included (*a*) 3 to 5 minutes of light stretching, (*b*) 5 to 10 minutes of cycling on the recumbent cycle ergometer or walk on the treadmill, (*c*) 5 to 15 minutes of resistance training (with dumbbells, resistance bands, and exercise ball), and (*d*) 5 to 10 minutes of core exercises. All exercises were performed at submaximal intensities determined by using HRR (40% to 50% of HRR) and RPE for cardiorespiratory endurance exercise and RPE for the resistance portion of the exercise bout. Intensity was constantly monitored and intensity never exceeded 5 on the CR10 modified Borg Scale for any exercise performed during the session. Every exercise session followed the same structure. The morning exercise period focused on exercises for the upper body whereas 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) included lateral, frontal, or military press for shoulders, chest press with dumbbells or rubber bands for chest, low rows with rubber bands for back, and arm curls and arm extension with dumbbells or rubber bands for arms. The exercises that were used for the lower body workouts included leg extension and leg curls with rubber bands, squats using the fit ball, and calf raises. Abdominal exercises were administered during every exercise bout.

**Table 1.** Patients' Characteristics at Baseline and Postexercise Intervention

| Characteristics | Mean ± SD | |
|---|---|---|
| | Baseline | Postexercise Intervention |
| Age | 35.7 ± 8.9 | NA |
| BM (kg)[a] | 98.9 ± 32.2 | 94.7 ± 29.4 |
| BMI (kg/m$^2$)[a] | 32.5 ± 7.8 | 31.2 ± 7.1 |
| LBM (kg)[a] | 71.9 ± 15.2 | 70.4 ± 14.5 |
| FM (kg) | 27.0 ± 18.9 | 24.2 ±16.7 |

Abbreviations: SD, standard deviation; NA, not applicable; BM, body mass; BMI, body mass index; LBM, lean body mass; FM, fat mass.
[a] Significant difference ($P < .05$) from measurements taken at baseline and postexercise intervention.

The exercises that targeted the abdominal region included regular crunches (curl-ups) and oblique abdominals performed on a chair. During the 2 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) to be performed at least 3 times per week for a minimum of 10 minutes and a maximum of 30 minutes. A member of the research team made phone calls to patients while recovering at home to check on the patients exercise program and to continue to motivate the patients to be engaged in the exercise program.

### Statistical Analyses

Paired-samples *t*-tests were used for the analyses of physiological and psychological parameters assessed at the beginning of the induction phase of treatment (baseline) and at the end of the study. One-way repeated measures analysis of variance (ANOVA) was used for the analyses of cytokines assessed 3 times during the study at the beginning of induction (baseline), between weeks 3 and 4 (midpoint), and at the end of the study.

## Results

The mean and standard deviation of the physical characteristics of the patients are presented in Table 1. Because of disease complication and transferring to another hospital for more complete insurance coverage, 2 patients were excluded from the study and therefore all the analyses were performed on 8 patients (6 men and 2 women).

Significant reductions were observed in total fatigue and depression scores ($P = .009$ and $P = .023$, respectively) from baseline to postexercise intervention with no significant changes in QOL ($P = .292$). Means and standard deviations of the analyses on total fatigue, depression, and QOL are presented in Figure 1.

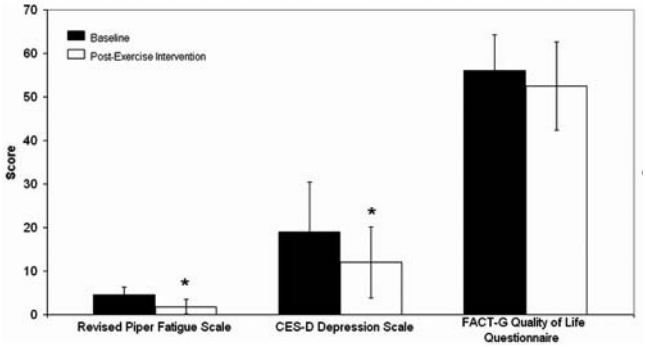


**Figure 1.** The Revised Piper Fatigue Scale total score, Center for Epidemiologic Studies Depression Scale (CES-D) score, and Functional Assessment of Cancer Therapy–General (FACT-G) quality of life overall score (mean ± standard deviation).
*$P < .05$ versus baseline.

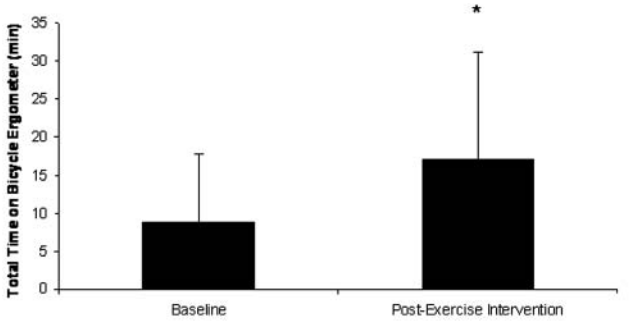


**Figure 2.** Cardiorespiratory endurance assessment (mean ± standard deviation).
*$P < .05$ versus baseline.

The impact of the exercise intervention on cardiorespiratory and muscular endurance were robust; taking into consideration the very harsh cancer treatment protocol for the treatment of leukemia and the common side effects that accompany it. Cardiorespiratory endurance was significantly improved ($P = .009$) throughout the course of induction while maintenance of muscular endurance was achieved. Figures 2 and 3 are graphic representations of the results of cardiorespiratory and muscular endurance analyses.

A marginally significant decrease in IL-6 ($P = .059$) with no difference in IL-10 or IFN-γ were observed ($P = .223$ and $P = .882$, respectively). Figure 4 presents the means and standard deviations of the cytokines analyses.

## Discussion

The standard medical protocol to treat acute leukemia patients is harsh but necessary. Further complicating the treatment process is the onset of treatment-related side effects, which, if not managed, can disrupt the course of treatment and result in diminished treatment outcomes.

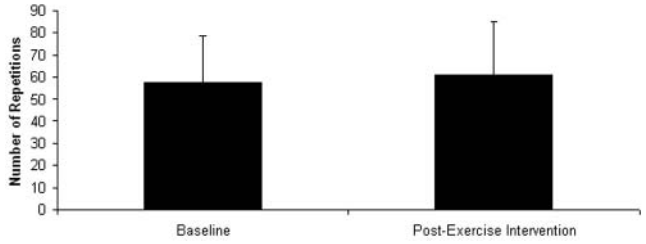


**Figure 3.** Muscular endurance (mean ± standard deviation).

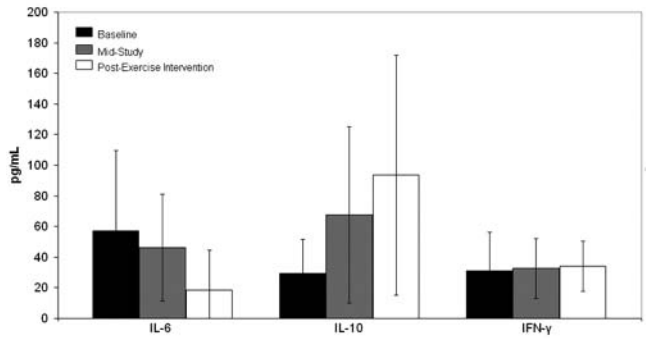


**Figure 4.** One-way analysis of variance results for the analyses of cytokines (mean ± standard deviation).

Recently, the medical community has adopted different strategies to manage treatment-related side effects. Numerous scientific reports demonstrate that exercise can be used safely as an efficacious intervention for the management of various treatment-related side effects for cancer patients. However, most studies conducted in this area focus on breast, prostate, and colorectal cancers.[7,13-21,28-30] The majority of studies investigating the impact of exercise in patients with hematological diseases involve pediatric patients.[30-32] Few studies explore the use of structured exercise programs for adult leukemia patients. Fewer address the topic for adult leukemia patients undergoing treatment.[10,11] The complexity and difficulty of implementing such programs in-hospital while maintaining safety and the course of treatment may contribute to the scarcity of such studies in the current literature.

Confinement to a hospital room for approximately 4 to 5 weeks, primarily to avoid risk of infection, is, in most cases, a recipe for decline in physical and psychological functioning, thereby making it difficult to attain favorable treatment outcomes. Our study is one of the first studies to demonstrate that it is not only clinically feasible to administer exercise to adult acute leukemia patients undergoing chemotherapy, but also that an exercise intervention, composed of a combination of aerobic and resistance training, positively affects selected physical and psychological parameters of patients in treatment.

Improved cardiorespiratory endurance, maintained muscular endurance, decreased fatigue and depression, and a healthy QOL, have all been observed in this feasibility study. These promising results concur with previous studies involving other types of cancer,[11,16-18,20,29] thereby demonstrating that exercise may also favorably affect in-hospital and in-treatment acute leukemia patients. In a study conducted by Courneya et al,[17] the response to exercise in a group of 242 women with breast cancer patients initiating adjuvant chemotherapy yielded similar results when analyzed for changes in cardiorespiratory endurance and QOL. Significant improvement in cardiorespiratory endurance in patients assigned to an exercise regimen was observed during the 17 weeks of exercise training, but no change in QOL was observed. Courneya et al attribute the stagnant QOL to the wide variability on the scores of the QOL measurement and noncontrollable factors while patients received chemotherapy. The authors also mention that the broad nature of the QOL measurement may not have had the sensitivity to detect specific changes promoted by exercise that may influence overall QOL during the treatment. Our study presents a trend, though not statistically significant, toward positive improvements in QOL.

In another study, Monga et al[20] examined the effects of an aerobic exercise regimen administered 3 times per week for 8 weeks on QOL and fatigue, for 21 prostate cancer patients undergoing treatment. Monga et al used the same instrument for the assessment of fatigue (the Revised Piper Fatigue Scale) and the specific FACT-P for the assessment of QOL. As in our study, fatigue was significantly reduced in the group of patients participating in the exercise intervention while undergoing treatment. However, a significant improvement in QOL was also observed in the group of prostate cancer patients, which could not be observed in our study. The sample size, the nature of the in-hospital treatment regimen, and a generalized version of the measurement used to assess QOL (FACT-G) for the leukemia patients in our study may have contributed to the nonsignificant finding for QOL.

In one of the very few trials involving the administration of an in-hospital exercise intervention to adult leukemia patients, Chang et al[10] found similar responses for cardiorespiratory endurance, fatigue, and depression. In Chang et al's trial, a 12-minute, 5 days per week walking protocol, at an intensity of resting heart rate plus 30 beats was used as the exercise intervention. A total of 22 patients were assigned to either an exercise intervention group or to standard care. Significant improvements in cardiorespiratory endurance and reductions in both fatigue and depression were observed in the intervention group when compared with the standard care group. As suggested by Chang's research team, it is not only feasible to administer aerobic exercise in-hospital to acute myelogenous leukemia patients, but such a program can also improve cardiorespiratory endurance and reduce fatigue and depressive status. Our study also measured significant improvements in cardiorespiratory endurance, and reductions in fatigue and depression in our patients. Because our patients were considered to be in stable clinical condition throughout the study, the results of the fatigue and depression assessments are all the more promising.

For our study, an aerobic exercise regimen was performed on a recumbent bicycle ergometer at similar intensities (40% to 50% of HRR), duration (10 to 20 minutes), and frequency (3 to 4 times per week) as those used in Chang et al's study. However, the addition of resistant training exercises, following the aerobic exercise component of the training session, differed from Chang et al's study protocol. Even though it is very difficult to compare the results of Chang et al and our trial due to differences in the exercise protocol, both trials suggest that the administration of a light exercise program is feasible, and can improve selected physical and psychological parameters in adult leukemia patients.

The goal of adding resistance training as part of the exercise protocol is to attenuate the loss of muscle mass typically observed in patients with prolonged bed rest, such as the case of leukemia patients undergoing treatment. Resistance training develops the cross-sectional area of the muscle (increase in lean body mass), which is associated with improvements in overall muscular endurance/strength. Not only healthy individuals experience the benefits of resistance training, but research shows improvements in individuals suffering from possible muscle wasting.[33] Despite the fact that muscular endurance was not significantly improved in this study, some specifics of the cancer treatment, as well as the method used to assess muscular endurance, may have hindered the possibility of detecting overall improvement. Due to the presence of a chest or arm port for the administration of chemotherapy, the upper body portion of the resistance exercise plan often had to be reduced and executed with lighter loads so that patients were able to perform prescribed exercises. Often, the ports caused discomfort and therefore some exercises had to be modified or even avoided. Because the muscular endurance variable score was created by summing the number of repetitions of the arm curl exercise and the squat exercise, the decrease in upper body endurance (observed in a few patients), may have overshadowed the overall improvement in muscular endurance. By not being able to demonstrate improvements in upper body endurance, the improvements in lower body endurance (observed in all patients) did not allow for statistical significance to be reached. Therefore, future investigations should attempt to investigate muscular endurance/strength using a protocol that is shorter in duration (less number of repetitions) such as 6RM, similar to a protocol used in a study conducted in children with leukemia by San Juan et al.[31] This would allow for a less stressful assessment due to the lower number of

repetitions. However, it is important to keep in mind that the logistics for using a different protocol may be unrealistic because of the space (size) of hospital rooms and equipment availability, thus the reason for our group's use of biceps curl and squat exercises in this study. While significant changes in body mass (decrease) and body composition were observed during the study, the development of cachexia, usually observed in 50% of cancer patients receiving treatment,[21] was mitigated with the exercise intervention in this group of leukemia patients. Through anecdotal information provided by physician and nurse members of our research team, leukemia patients undergoing chemotherapy usually lose approximately 5 to 10 kg during the induction phase of treatment. After completing induction and the participation in the exercise program, patients enrolled in our study ended up losing an average of 4.3 kg, with only a 2% reduction in lean body mass (−1.5 kg). This is a significant finding, because extreme loss in body weight with decrements in lean body mass is a strong predictor of poor treatment outcomes.[34]

Common decreases in caloric intake and gastrointestinal discomfort as a result of chemotherapy can lead to negative nitrogen balance and muscle wasting, that is, cachexia. In addition, the decline in physical activity during treatment can hasten the loss of muscle tissue.[35] The idea of exploring the response of inflammatory markers in our study was based on the premise that the interaction between cancer and immune function stimulates the increase in cytokine release, which has also been associated with muscular wasting.[34] Physical exercise is a principal means by which an enhanced anti-inflammatory cytokine response can be provoked.[36] Both acute and chronic exercise exposure in proper amounts are known to elevate activity of anti-inflammatory cytokines while facilitating a reduction in pro-inflammatory cytokines.[37] Although no significant changes in cytokines were observed in our study, the results of the ANOVA analyses show a promising trend. Through the course of the study, a near significant reduction in IL-6 with an increase in IL-10 was observed. These results suggest a decreased pro-inflammatory (↓ IL-6) and increased anti-inflammatory (↑ IL-10) response during induction chemotherapy, which may be due to the influence of exercise training.

A few limitations should be considered when interpreting these findings. A small sample size, and the method used for the analyses of IL-6, IL-10, and IFN-γ may be among possible confounding factors of our analyses. It is therefore recommended that an increase in sample size, as well as a comparison between Luminex systems and an enzyme-linked immunosorbent assay should be performed in future experiments. Nevertheless, the results of this study should be a good starting point for the field of exercise in leukemia patients. Future examinations must be performed to confirm or refute these findings.

Our study's results have important clinical relevance. Improvements in cardiovascular endurance, maintenance in muscular endurance, reduction in fatigue and depression, the possibility of changes in inflammatory response, and maintenance in QOL may follow the same exercise response observed in patients with other types of cancer. Considering the severity of the disease—harsh treatment protocols, confinement to a hospital room for weeks, post diagnosis side effects that worsen throughout treatment—the results of our study are consequential and promising. However, when designing future studies to examine the impact of exercise on acute leukemia patients undergoing treatment, it is necessary to take into consideration the limitations and confounder factors presented by the current study. Some limitations that future studies must address include (*a*) use of a larger sample size and a control group to allow for testing the efficacy of the exercise intervention, (*b*) continuing with an exercise protocol that includes resistance training, and (*c*) a meticulous attention to neutropenic procedures to ensure the safety of the patients at all times.

## Implications for Future Studies

Some confounders should also be considered when analyzing the data in future experiments. In our study, a few patients had to refrain from the exercise sessions. The sessions were cancelled as a result of fever or low platelet count only. These patients usually resumed exercise within a day or two following the fever, and just a few hours after a platelet transfusion. During days where patients were fatigued and resistant to exercise, a lighter exercise routine composed of cardio and light stretches was implemented and administered less frequently, once in some cases, that particular day. Some patients in the study underwent Neulasta (Pegfilgrastim) shots to minimize the risks for infection. These patients (2 in the current study) tolerated the treatment with fewer complications and completed almost all planned exercise sessions. For a future study, one may consider recruiting only patients that receive Neulasta shots during treatment or avoid such patients altogether. Meeting this criterion will not always be possible, primarily due to the nature of treatment and patient response to treatment.

In our study, we did not exercise our patients when platelet counts were lower than 20 000/mm$^3$ (microliter) of blood to avoid the possibility of internal bleeding. This criterion was adopted as a recommendation from the hematology/oncology unit physicians members of the research team to insure that the exercise intervention would not cause any harm to the patients. This measure seemed to be appropriate; however, future investigations should explore the possibility of lowering this recommendation to perhaps 10 000 platelets/mm$^3$ of blood to

minimize the number of missing sessions, and thus maximize participation in the exercise protocol.

In conclusion, this is one of the first studies to administer an in-hospital exercise protocol to adults with acute myelogenous leukemia undergoing chemotherapy. This is also apparently the only study that used a combined aerobic and resistance training exercise intervention in acute leukemia patients during treatment. The results of our study suggest that a supervised controlled exercise intervention is feasible and can positively affect cardiovascular and muscular endurance, reduce fatigue and depression, and maintain QOL during treatment.

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