A Pilot Study to Examine the Feasibility and Effects of a Home-Based Aerobic Program on Reducing Fatigue in Children With Acute Lymphoblastic Leukemia

Background: Fatigue is one of the most frequent symptoms experienced by children with cancer during treatment. Effective management of fatigue is essential for improving children’s quality of life. Objective: The aim of this study was to examine the feasibility of a home-based aerobic exercise intervention to reduce fatigue in children with acute lymphoblastic leukemia (ALL).

Methods: A 6-week home-based aerobic exercise intervention was implemented for children who were in the intervention group, whereas patients in the control group received routine care. Multivariate analysis was used to examine the effects of the aerobic exercise intervention on the children’s self-reported levels of fatigue at posttest and 1-month follow-up. Two types of analysis were used: intent-to-treat analysis and per-protocol analysis. Results: This study was conducted with 22 children with ALL: 12 in the intervention group and 10 in the control group who were matched by age and sex. For per-protocol analysis, the finding indicated that children who received the exercise intervention reported significantly lower “general fatigue” subscale than those in the control group at the 1-month follow-up measurement. For intent-to-treat analysis, the findings indicated that there were no intervention and time effect for any of the 3 fatigue subscales at either posttest.

KEY WORDS
Adherence
Cancer-related fatigue
Exercise program

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The finding indicated that the exercise program is feasible and warrants being tested in a clinical trial with a much larger sample of children for ALL. Implications for Practice: It suggests that a home-based exercise program may reduce fatigue for ALL children who are undergoing maintenance chemotherapy.

Cancer-related fatigue (CRF) is one of the most frequent and severe symptoms experienced by pediatric oncology patients during treatment and continuing even after treatment has ended. The occurrence of fatigue in pediatric oncology patients has been reported to range from 35.6% to 93%. Cancer-related fatigue is more intense in the first few days after chemotherapy and then gradually abates or fluctuates until the next course of chemotherapy. Fatigue has resulted in physical and psychosocial alterations and also impacts future life plans and self-performance. The management of fatigue is an important clinical issue because fatigue is recognized as having a greater impact on the patient’s physical well-being and quality of life than other mental or physical consequences of cancer or its treatment. Treatment of pediatric oncology patients is aggressive and focused on curing the disease; therefore, adverse effects, such as fatigue that result from treatments, may be ignored by clinicians or considered to be unavoidable symptoms that need to be endured. Evidence of effective options to manage CRF during cancer treatment is still limited. Nonpharmacological management, including counseling and education, or pharmacological interventions (for pain, sleep medication, or treatment of anemia) are general strategies for the management of fatigue. Research using exercise as a nonpharmacological intervention has shown promise in reducing fatigue in adult patients during and after cancer treatment and is more effective than psychosocial interventions. Exercise has shown more promising results than other strategies, such as sleep promotion, education and counseling, or distraction and relaxation, in reducing fatigue in adults.

Hinds and colleagues conducted a feasibility study testing an enhanced physical training program for hospitalized children with cancer (n = 25) and indicated that there were no differences reported in fatigue during the hospitalization or between intervention and control groups. However, sleep duration was higher in the intervention group. Also indicated that their exercise training program did not have an effect on muscle strength, exercise capacity, functional mobility, or fatigue between pretraining and posttraining. However, these 2 studies were limited to either testing the feasibility of exercise when patients were hospitalized on a 3- to 4-day basis or a small sample size (only 4 children completed the intervention).

Structured, supervised exercise training has shown to increase functional capacity and the improvement of Health-Related Quality of Life (HRQL) in adult cancer survivors. Several pilot studies using aerobic training have been conducted in children with cancer and have shown improved functional mobility. In summary, aerobic exercises in particular are recommended as a model for an exercise program that the parents can follow with their children because it has been shown to improve physical function or reduce fatigue. However, motivating children and adolescents to adhere to an exercise program is a tremendous challenge because of the high dropout rate. Therefore, the purpose of this study was to examine the feasibility and effect of a home-based aerobic exercise intervention on fatigue in children with acute lymphoblastic leukemia (ALL) during the maintenance stage of chemotherapy.

## Conceptual Framework

The conceptual framework used to guide the home-based aerobic exercise intervention designed to reduce fatigue in children with cancer was developed from an integration of the Human Response Model and the Transtheoretical Model for this study. From the Human Response Model, personal factors, such as demographics and physiological factors (hemoglobin), have an impact on individual adaptation to the therapeutic intervention (exercise in this study). Individual adaptation refers to human response, including experiential (fatigue, sleep quality, HRQL, and cardiorespiratory fitness) or behavioral (sleep duration, physical activity) adaptation. The major component of Transtheoretical Model is stage of change, which refers to a person’s readiness to engage in regular exercise. This process involves progress through 5 stages of change: precontemplation, contemplation, preparation, action, and maintenance. When individuals reach a point where they realize that an activity offers more benefits than disadvantages, a person will move forward from contemplation into preparation or action to engage in a behavior. For the purpose of this article, we reported only patients’ CRF and stage of change as the adaptation outcome and patients’ hemoglobin level as its personal factor that may have an impact on the individual adaptation (Figure 1).

## Methods

A quasi-experimental study was conducted with 12 pediatric oncology patients in the intervention group and 10 in control group who were matched by age and sex. A 6-week home-based aerobic exercise intervention was implemented for
children who were in the intervention group, whereas patients in the control group received usual care.

Participants and Setting

Patients who were recruited for this feasibility study included children and adolescents who had been diagnosed with ALL and were being treated with chemotherapy. The treatment protocols that children received including standard risk (TPOG-2002-SR), high risk (TPOG-2002-HR), and very high risk (TPOG-2002-VHR) were developed by the Taiwan Pediatric Oncology Group (TPOG). Eligible patients received maintenance chemotherapy after 20 weeks because their treatment protocols were for repeat cycles at this time point. All patients received daily 6-mercaptopurine and weekly methotrexate with pulses of dexamethasone (5 days) and vincristine every 4 weeks. Intrathecal therapy with cytarabine (Ara-C), methotrexate, and hydrocortisone were given every 8 weeks. We recruited patients after the week of completion of dexamethasone treatment to avoid treatment bias. Additionally, participants were physically and developmentally able and willing to practice the aerobic exercise and were all younger than 18 years. Thirty patients with ALL were approached for this study from June 2006 to July 2008. Six of these patients did not participate in this study because of the following reasons: The child died before the baseline assessment (n = 2), and declined participation (n = 4) (rejection rate = 14%). In this study, we recruited 24 patients who completed the baseline assessment of the study. However, 2 patients in the intervention group decided to drop out because they did not think they were able to practice the aerobic program at home. Thus, there were a total of 22 patients who completed the study, with 12 in the intervention group and 10 in control group (Figure 2).

The Home-Based Aerobic Exercise Intervention

The home-based aerobic exercise intervention consisted of following the steps detailed in a video, specifically designed for the study, 3 days a week, for 30 minutes each session, for 6 weeks. The same exercise video was used by all subjects in the intervention group, it was developed by an exercise specialist for this study. The content of the home-based aerobic exercise intervention included 3 sections: a warm-up (5 minutes), aerobic exercise (25 minutes), and cooldown (5 minutes), which is recommended by the American College of Sports Medicine. The warm-up and the cooldown exercise sections in this home-based aerobic exercise intervention were aimed to increase 10% to 30% of the participant's heart rate reserve (HRR), which is defined as the difference between the maximum heart rate and the resting heart rate (examined during the maximal exercise test). The aerobic exercise section was designed as a 25-minute exercise section that aimed to increase the participant's target HRR of 40% to 60%. This allowed the participants to modify the exercise time based on their physical ability. Before data collection, we invited 2 children with ALL to test the exercise video. Both children were able to complete the exercises and reach the target heart rate.

Figure 2: The enrollment of participants in the 2 groups.
rate. The exercise prescription, including duration and intensity in this study, was individualized to each patient in the intervention group after baseline assessment had been completed. For example, the exercise duration ranged from 10 to 30 minutes in the beginning of the exercise, depending on patient’s physical function for the first 2 weeks, but gradually increased to 30 minutes for the third week and after. They were instructed to practice the exercises at least 3 times weekly during the 6 consecutive weeks.

Measures

Data collected in this study included both self-reported measures and objective data. Self-reported instruments included the PedsQL Multidimensional Fatigue Scale, the physical activity log, the Children’s OMNI-Walk/Run Scale, and Stage of Change—Exercise Behavior. The objective measures used were the maximal exercise test for assessing cardiorespiratory fitness. For the purpose of this study, only subjective data were reported.

Self-reported Measures

PedsQL MULTIDIMENSIONAL FATIGUE SCALE

The Chinese version of the PedsQL multidimensional Fatigue Scale was used for children in this study. The scale was originally designed and tested in the United States by Varni and colleagues. It includes “general fatigue” (6 items), “sleep/rest fatigue” (6 items), and “cognitive fatigue” (6 items). All items used a 5-point Likert response set, ranging from 1 = “not at all” to 5 = “always.” The Chinese version of the PedsQL Multidimensional Fatigue Scale was developed and tested.

The reliabilities of the original PedsQL Multidimensional Fatigue Scale for subscales and total scale were .83 to .93 (Cronbach α coefficient), and the validity was also evident with high correlation with the Chinese version of Fatigue Scale—Children (Pearson correlation was from −0.36 to −0.56). In the original instrument, all items use a 5-point Likert response set, ranging from 1 = not at all to 5 = always; higher scores indicated fewer symptoms of fatigue. To compare the fatigue change patterns for patients during the intervention period, the PedsQL Multidimensional Fatigue Scale used in the current study was scored so that higher scores indicated that patients had increased fatigue. Cronbach α for each subscale ranged from .78 to .95, as established in our previous study.

THE PHYSICAL ACTIVITY LOG

The 24-hour physical activity assessment for participants was recorded using the physical activity log. The physical activity log was modified by from Bouchard and colleagues a 3-day activity record, which divided each day into 24 one-hour blocks instead of dividing each day into 96 periods of 15 minutes each as in the original version. The participants were called by the data collector via phone weekly to collect the physical activity data. For each 1-hour period, the physical activity was quantified on a scale from 1 to 9 on 9 categories, which included sleeping or resting in bed, sitting, light activity or standing, slow walking, light manual work, leisure activities and sports in a recreational environment, manual work at a moderate pace, leisure and sport activities of higher intensity (not competitive), and intense manual work, high-intensity sport activities, or sport competition, respectively. Participant’s activity were recorded as a value (ranging from 1 to 9), corresponding to activity that was dominant during that period. A patient was categorized as “physically active” if he/she had reported the exercise category of 6 (leisure activities and sports in a recreational environment) or above for at least 3 periods per week and at least for 30 minutes each period. This criterion was also used as the indicator for whether the participant adhered to the intervention program.

THE CHILDREN’S OMNI-WALK/RUN SCALE

The participants’ subjective, or perceived exertion during exercise and exercise testing period was assessed using the Children’s OMNI-Walk/Run Scale. The Children’s OMNI Scale combines both pictorial and verbal descriptors positioned along a numerical response range of 0 to 10 to assist the younger children’s ability to assign numbers to words or phrases that described their perceived exertion during exercise. Utter et al have found that the Children’s OMNI-Walk/Run Scale has demonstrated strong and significant correlation that was strongly significant correlated with their rating of perceived exertion, heart rate, and VO_{2max}.

STAGE OF CHANGE—EXERCISE BEHAVIOR

The participants’ intention of practicing home-based aerobic exercise as well as their intention to change their exercise behavior was assessed using the stage of change: exercise behavior, which was developed by Marcus and colleagues. The questionnaire assessed participants’ current physical activity status and their intention to start exercising. The response was divided into 5 stages, including precontemplation (participants who did not want to engage in any physical activity), contemplation (participants who did not engage in physical activity; however, they intended on changing their behavior within the next 6 months), preparation (participants who engaged in physical activity, but were irregular), action (participants who engaged in regular physical activity for <6 months), and maintenance (participants who sustained their physical activity for >6 months).

Procedures

After permission was obtained from the hospital’s institutional review board, data collection was begun. Parental consent and children’s assent were obtained after the children and their parents received verbal and written explanations of the study purpose and the data collection procedures and indicated their willingness to participate in the study. All participants were scheduled for a baseline assessment including the maximal exercise test and were given a questionnaire package (this included
characteristics of the participants. The intervention effects of the home aerobic exercise, during the 8 time points, were analyzed using the mixed-effects model (using the MIXED procedure in SAS; SAS Institute, Cary, North Carolina). The model included fixed-effects for time, group, interaction between group and time, baseline fatigue level, and hemoglobin level. Model effects were tested at a significance level of .05. To examine the true effect of the intervention, 2 types of analyses were conducted: intent-to-treat (ITT) analysis, used the data of all patients, and the per-protocol (PP) analysis, which included only those patients who adhered to the exercise prescription.

### Findings

#### Characteristics of the Participants

Table 1 presents the patients in the intervention and control groups for ITT analysis and PP analysis. Twelve participants were recruited for the ITT analysis, including 6 boys (50%) and 6 girls (50%); the average age of the children was 11.01 (SD, 3.56) years. Participants in the control group (n = 10) included 6 boys (60%) and 4 girls (40%); the average age of the children was 12.48 (SD, 3.86) years. The most common chemotherapy protocol for the 2 groups of children was TPOG-2002-HR, followed by TPOG-2002-VHR, and TPOG-2002-SR (TPOG, 2002).

Among these participants, 10 patients in the intervention group, 5 boys (50%) and 5 girls (50%), adhered to the exercise prescription. In the control group, only 5 patients reported that they did exercises of any type, according to their weekly physical activity log; therefore, only 5 patients, 3 boys (60%) and 2 girls (40%), in the control group were used for PP analysis.

#### The Feasibility for Patients to Practice Home-Based Aerobic Exercise

The adherence rate was used to calculate the feasibility of patients to practice the aerobic exercise at home. The adherence rate was defined as participants who were able to follow at least two-thirds of the exercise prescription during the intervention program. Table 2 presents the adherence rate that patients adhered to the home-based aerobic exercise intervention in the intervention group. The results indicated that the adherence rate during the 6-week intervention for the patients in ITT analysis was in a range of 67% to 83% (mean, 76% [SD, 6.02]), and 80% to 100% (mean, 90%...
Table 2 * Patient’s Adherence Rate of Home-Based Aerobic Exercise Program*  

<table>
<thead>
<tr>
<th>Time (Week)</th>
<th>Int (83)</th>
<th>Con (75)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Week</td>
<td>9 (90)</td>
<td>9 (90)</td>
<td>.02</td>
</tr>
<tr>
<td>Second Week</td>
<td>8 (80)</td>
<td>9 (90)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Third Week</td>
<td>8 (76)</td>
<td>10 (100)</td>
<td>&lt;.05</td>
</tr>
</tbody>
</table>

*Values are presented as n (%).

Table 3 • Group Differences in Fatigue Scores in Each Time Point ITT and PP  

<table>
<thead>
<tr>
<th>Time*</th>
<th>General Fatigue</th>
<th>Sleep/Rest Fatigue</th>
<th>Cognitive Fatigue</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Con, Mean (SD)</td>
<td>Int, Mean (SD)</td>
<td>P</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ITT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pretest</td>
<td>4.90 (4.01)</td>
<td>5.17 (5.44)</td>
<td>.97</td>
</tr>
<tr>
<td>T1</td>
<td>3.70 (3.71)</td>
<td>4.25 (3.60)</td>
<td>.79</td>
</tr>
<tr>
<td>T2</td>
<td>2.70 (3.74)</td>
<td>4.42 (4.10)</td>
<td>.23</td>
</tr>
<tr>
<td>T3</td>
<td>3.70 (4.52)</td>
<td>4.17 (3.64)</td>
<td>.84</td>
</tr>
<tr>
<td>T4</td>
<td>2.60 (3.75)</td>
<td>3.92 (4.03)</td>
<td>.38</td>
</tr>
<tr>
<td>T5</td>
<td>3.00 (4.14)</td>
<td>3.42 (4.48)</td>
<td>.87</td>
</tr>
<tr>
<td>T6</td>
<td>3.40 (3.92)</td>
<td>3.25 (3.14)</td>
<td>.77</td>
</tr>
<tr>
<td>T7</td>
<td>4.20 (3.79)</td>
<td>2.17 (2.89)</td>
<td>.07</td>
</tr>
<tr>
<td>PP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pretest</td>
<td>3.20 (3.03)</td>
<td>6.00 (5.62)</td>
<td>.59</td>
</tr>
<tr>
<td>T1</td>
<td>2.80 (2.28)</td>
<td>4.70 (3.80)</td>
<td>.99</td>
</tr>
<tr>
<td>T2</td>
<td>2.00 (2.45)</td>
<td>5.10 (4.15)</td>
<td>.47</td>
</tr>
<tr>
<td>T3</td>
<td>3.60 (4.83)</td>
<td>4.80 (3.65)</td>
<td>.65</td>
</tr>
<tr>
<td>T4</td>
<td>2.00 (1.87)</td>
<td>4.50 (4.17)</td>
<td>.72</td>
</tr>
<tr>
<td>T5</td>
<td>2.80 (3.35)</td>
<td>3.90 (4.77)</td>
<td>.61</td>
</tr>
<tr>
<td>T6</td>
<td>2.20 (2.49)</td>
<td>3.70 (3.23)</td>
<td>.79</td>
</tr>
<tr>
<td>T7</td>
<td>4.20 (2.95)</td>
<td>2.60 (2.99)</td>
<td>.03</td>
</tr>
</tbody>
</table>

Abbreviations: Con, control group; Int, intervention group; ITT, intent-to-treat analysis; PP, per-protocol analysis.

*Time: T1: first week; T2: second week; T3: third week; T4: fourth week; T5: fifth week; T6: after the completion of intervention; T7: 1 month after completion of intervention.

The The Effect of the Home-Based Aerobic Exercise on Fatigue  

The descriptive characteristics of 3 subscales of fatigue in the control group and the intervention group with different time points are presented in Table 3. The sleep/rest fatigue mean scores have generally higher values than general fatigue mean scores and cognitive fatigue mean scores in either ITT analysis or PP analysis. The results of ITT analysis present no intervention and time effect differences in most fatigue subscales at posttest and 1-month follow-up, whereas the mean difference of general fatigue score between the control group and the intervention group is moderate significant, with $P = .06$, which may expect that larger sample size can increase its power and make the $P$ value less than .05. The same group comparison in PP analysis is also statistically significant, with $P = .02$, but the significant results still do not happen in the other mean differences between the 2 groups in PP analysis. The change patterns for expected mean scores of general fatigue, sleep/rest fatigue, and cognitive fatigue are shown in Figures 3–5, respectively. It is explicit that the change patterns of general fatigue and sleep/rest fatigue are uniformly decreased behind weeks 2 and 3, whereas general fatigue in the control group decreased, and even flat in sleep/rest fatigue. It is concluded that the trend of intervention group is more robust in either ITT or PP analysis. In addition, compared with posttest and 1-month follow-up, the expected mean scores of general fatigue in the control group are increased obviously. Unlike general fatigue and sleep/rest fatigue, the descending trend of cognitive fatigue in experimental group defers to week 5, and the following trend is not monotone any more; nonetheless, the expected mean score of cognitive fatigue in the control group started to increase in week 3 early and showed a totally reversed trend with the intervention group from week 3 to 1-month follow-up, especially in PP analysis. Similar situation also appears in general fatigue in ITT analysis from week 4 to 1-month follow-up. Generally speaking, most of the expected

[SD, 6.32]) for PP analysis. The lowest adherence rate occurred at week 3 (67%) in ITT analysis.
mean scores of 3 fatigues in the control group are smaller than those in the intervention group before week 3 or 4, but the trend of 3 subscales in the control group surpasses that in the intervention group until 1-month follow-up. More importantly, the expected mean scores of 3 fatigue subscales are all consistently decreased from posttest to 1-month follow-up; however, this situation never appears in the control group, either in ITT or PP analysis.

Factors Related to Fatigue
To examine if there were other confounding variables that may affect fatigue, hemoglobin was used. The result indicated the hemoglobin level was not related to fatigue change pattern for either ITT or PP analysis (Table 4).

Intention to Practice Home-Based Aerobic Exercise
Table 5 presents the patients’ intention to practice home-based aerobic exercise for both ITT and PP analyses. In ITT analysis, in the intervention group, the pretest data indicated that 4 patients in the intervention group were in the stage of contemplation (34%), that these patients were not doing any physical activity at that time; 7 patients were at “preparation stage” (58%) who are doing irregular physical activity, and 1 patient (8%) was doing regular physical activity within 6 months. At the posttest, 25% patients (n = 3) were at the “action stage,” and 17% (n = 2) were at “maintenance stage” (sustained their physical activity for >6 months). However, the majority of the patients (n = 11; 92%) were changing back to the stage of “preparation stage” at 1-month follow-up. In PP analysis, the result indicated similar change pattern with those patients in the ITT analysis.

Discussion
This is the first study to examine the effect of the a home-based aerobic exercise intervention in reducing fatigue in children with ALL. Except for the subscale of general fatigue, there were no differences in the 3 subscales of fatigue at pretest, posttest, and 1-month follow-up for ITT analysis, for both groups. The results indicated that children who received the home-based aerobic exercise intervention reported significantly lower “general fatigue” than did children in the
control group at the 1-month follow-up only. The interpretation for this study may be limited by the small sample size. According to the adherence of patients in the intervention, it yields important information that the home-based aerobic exercise intervention is feasible for children with ALL at the maintenance stage at least for short periods.

To examine the true effects of the intervention, we used ITT and PP analyses. For the ITT analysis, there were no significant statistical differences between the 3 subscales of fatigue at pretest, posttest, and 1-month follow-up between the 2 groups. However, for the PP analysis, only patients who adhered to the prescribed exercise were analyzed. The results indicated that patients in the intervention group tended to have lower "general fatigue" level than did patients in the control group at 1-month follow-up.

We believe that the high adherence rate of this home-based aerobic program (86%) is due to parental involvement. In this study, parents had to agree to participate while the patient practiced the aerobic program. Evidence has shown that parental involvement in the lifestyle-change approach of children has positive effects on persistent reduction of body mass index in overweight children. The most recent meta-analyses of family-based interventions for management of overweight children found that family-based behavioral treatments were more effective (effect size of −0.89; 95% confidence interval, −1.06 to −0.73) than other treatments (effect size of −0.52; 95% confidence interval, −1.49 to 0.44). Family involvement with organized activities is an effective way to increase physical activity among children.

In this study, we used the structured, parental involvement home-based aerobic program to reduce fatigue. Structured, supervised exercise training has been shown to increase functional capacity and the improvement of HRQL in adult cancer survivors. Several pilot studies using aerobic training have been conducted in children with cancer and have shown improved functional mobility. In the current study, 2 patients who enrolled in the intervention program were dropped out because of nonadherence to the research protocol of aerobic

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**Table 4 • Mixed-Models Parameter Estimates for Fatigue in Children With Acute Lymphoblastic Leukemia**

<table>
<thead>
<tr>
<th>Primary Outcome Model</th>
<th>Num df</th>
<th>Den df</th>
<th>General Fatigue</th>
<th>Sleep/Rest Fatigue</th>
<th>Cognitive Fatigue</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>F</td>
<td>P</td>
<td>F</td>
<td>P</td>
</tr>
<tr>
<td>ITT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline fatigue</td>
<td>1</td>
<td>19</td>
<td>129.44 &lt;.0001</td>
<td>73.03 &lt;.0001</td>
<td>120.42 &lt;.0001</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>1</td>
<td>139</td>
<td>0.04 .84</td>
<td>0.10 .76</td>
<td>0.00 .96</td>
</tr>
<tr>
<td>Group</td>
<td>1</td>
<td>19</td>
<td>0.01 .91</td>
<td>0.02 .88</td>
<td>0.05 .83</td>
</tr>
<tr>
<td>Time</td>
<td>7</td>
<td>139</td>
<td>1.39 .21</td>
<td>1.40 .21</td>
<td>0.52 .82</td>
</tr>
<tr>
<td>Group × time</td>
<td>7</td>
<td>139</td>
<td>1.74 .10</td>
<td>0.25 .97</td>
<td>0.91 .50</td>
</tr>
<tr>
<td>PP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline fatigue</td>
<td>1</td>
<td>12</td>
<td>86.32 &lt;.0001</td>
<td>38.57 &lt;.0001</td>
<td>75.77 &lt;.0001</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>1</td>
<td>90</td>
<td>1.98 .16</td>
<td>0.00 .98</td>
<td>0.25 .62</td>
</tr>
<tr>
<td>Group</td>
<td>1</td>
<td>12</td>
<td>0.38 .55</td>
<td>0.00 .97</td>
<td>0.10 .75</td>
</tr>
<tr>
<td>Time</td>
<td>7</td>
<td>90</td>
<td>0.66 .71</td>
<td>0.53 .81</td>
<td>0.80 .59</td>
</tr>
<tr>
<td>Group × time</td>
<td>7</td>
<td>90</td>
<td>1.29 .27</td>
<td>0.14 1.00</td>
<td>1.37 .23</td>
</tr>
</tbody>
</table>

Abbreviations: Den df, denominator degrees of freedom; ITT, intent-to-treat analysis; Num df, numerator degrees of freedom; PP, per-protocol analysis.

*Group is coded as 0 for the control group and 1 for the intervention group; time, 1 for baseline, 2 for first week, 3 for second week, 4 for third week, 5 for fourth week, 6 for sixth week, 7 for immediately after intervention, 8 for 1-month follow-up; baseline fatigue was mean centered.

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![Figure 5](image-url) Unadjusted mean score change pattern for cognitive fatigue over time.
exercise. According to these patients’ physical activity logs, the durations of their exercise sessions were varied and did not meet the research protocol that they agreed on (ie, 3 times a week, 30 minutes per time). In summary, aerobic exercises in particular are recommended as a model for an exercise program that the parents can follow with their children because it has been shown to improve physical function or reduce fatigue. However, motivating children and adolescents to adhere to an exercise program is a tremendous challenge because of the high dropout rate.\(^\text{19,20}\) During the subject enrollment, 2 of the 14 patients (14%) from the intervention group did not participate in the study because they thought their physical strength was not good enough to practice during randomization. Although this feasibility study reported positive findings using an individualized prescription for exercise intensity and duration, motivating children with cancer to exercise continues to be challenging and needs further exploration.

The issue of motivating children to continue to exercise after the study has ended is a serious one for researchers and parents. During the intervention, patients in the intervention group had moved their “intention to practice” the physical activity from the contemplation stage and preparation stage to “action and maintenance” stage. However, when the study ended, patients moved back to their pretest behavior stage by 1-month follow-up. Parent and family can also influence children’s physical activity through modeling and reinforcement.\(^\text{36,37}\) The survival rates of childhood cancer have increased dramatically in the past decades;\(^\text{38}\) therefore, encouraging and guiding the survivors as well as the current patients to be more engaged in exercise are important, but knowing how to do this is a challenge for families, health care providers, and researchers.

### Conclusions

In summary, this study was conducted to determine the feasibility and effectiveness of a program to reduce fatigue in children who were diagnosed with ALL. The preliminary study has shown that home-based aerobic exercise intervention is feasible for children with ALL to practice at home. Because of the sample size, the improvement of the fatigue was moderated. We believe that replicating this study in a randomized clinical trial with a larger sample size is the next step. A much larger study could include children with other cancer-related illness who also experience fatigue.

### ACKNOWLEDGMENT

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### References


| Table 5 • Stage of Change of Practicing Home-Based Aerobic Exercise for ITT and PP Analysis* |
|---------------------------------|-------|-------|-------|-------|
|                                | Pretest | Posttest | 1-mo Follow-up |
|                                | ITT  | PP   | ITT  | PP   | ITT  | PP   |
| Precontemplation               | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Contemplation                  | 4 (34) | 4 (40) | 1 (8) | 0 (0) | 0 (0) | 0 (0) |
| Preparation                    | 7 (58) | 5 (50) | 6 (50) | 4 (40) | 11 (92) | 9 (90) |
| Action                         | 1 (8) | 1 (10) | 3 (25) | 3 (30) | 1 (8) | 1 (10) |
| Maintenance                    | 0 (0) | 0 (0) | 2 (17) | 2 (20) | 0 (0) | 0 (0) |

Abbreviations: ITT, intent to treat; PP, per protocol.
*Values are presented as n (%).
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