Biol Blood Marrow Transplant 23 (2017) 659–669

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

ASBMT American Society for Blood and Marrow Transplantation

Clinical Research: Supportive Care

# Strength Training to Enhance Early Recovery after Hematopoietic Stem Cell Transplantation

Eileen Danaher Hacker [1,*], Eileen Collins [1], Chang Park [1], Tara Peters [1], Pritesh Patel [2], Damiano Rondelli [2]

[1] College of Nursing, University of Illinois at Chicago, Chicago, Illinois
[2] College of Medicine, University of Illinois at Chicago, Chicago, Illinois

*Article history:*
Received 24 October 2016
Accepted 23 December 2016

*Key Words:*
Exercise
Fatigue
Physical activity
Functional ability
Stem cell transplantation
Strength training

A B S T R A C T

Intensive cancer treatment followed by hematopoietic stem cell transplantation (HCT) results in moderate to severe fatigue and physical inactivity, leading to diminished functional ability. The purpose of this study was to determine the efficacy of an exercise intervention, strength training to enhance early recovery (STEER), on physical activity, fatigue, muscle strength, functional ability, and quality of life after HCT. This single-blind, randomized clinical trial compared strength training (n = 33) to usual care plus attention control with health education (UC + AC with HE) (n = 34). Subjects were stratified by type of transplantation and age. STEER consisted of a comprehensive program of progressive resistance introduced during hospitalization and continued for 6 weeks after hospital discharge. Fatigue, physical activity, muscle strength, functional ability, and quality of life were assessed before HCT hospital admission and after intervention completion. Data were analyzed using split-plot analysis of variance. Significant time × group interactions effects were noted for fatigue ($P = .04$). The STEER group reported improvement in fatigue from baseline to after intervention whereas the UC + AC with HE group reported worsened fatigue from baseline to after intervention. Time ($P < .001$) and group effects ($P = .05$) were observed for physical activity. Physical activity declined from baseline to 6 weeks after hospitalization. The STEER group was more physically active. Functional ability tests (timed stair climb and timed up and go) resulted in a significant interaction effect ($P = .03$ and $P = .05$, respectively). Subjects in the UC + AC with HE group were significantly slower on both tests baseline to after intervention, whereas the STEER group's time remained stable. The STEER group completed both tests faster than the UC + AC with HE group after intervention. Study findings support the use of STEER after intensive cancer treatment and HCT. Strength training demonstrated positive effects on fatigue, physical activity, muscle strength, and functional ability. The exact recovery patterns between groups and over time varied; the STEER group either improved or maintained their status from baseline to after intervention (6 weeks after hospital discharge) whereas the health education group generally declined over time or did not change.



## INTRODUCTION

Intensive cancer treatment followed by hematopoietic stem cell transplantation (HCT) is considered curative for a number of hematological malignancies [1] but it is associated with high 100-day treatment-related mortality [1] and devastating complications [2,3]. These complications result in highly distressing symptoms, significantly impaired functional status, and diminished quality of life (QOL) that can last for years after treatment [4-7]. A marked reduction in physical activity after intensive cancer treatment and HCT has been documented [8]. Up to 90% of HCT recipients report severe persistent fatigue [9-12]. Although the relationship between physical activity and fatigue is not completely understood, sustained physical inactivity after HCT is sufficient to cause loss of muscle mass with resulting decreases in strength. Muscle mass losses during the first 6 months after HCT are frequently not regained even 5 years after transplantation [13-15].

This clinical picture of impaired recovery after intensive cancer treatment and HCT closely resembles the clinical syndrome of frailty in older adults. Using Fried's Clinical Phenotype of Frailty in Older Adults [16] as a guide and adapted for HCT, we hypothesized that muscle strength plays a crucial role in preventing the development of physical deconditioning/frailty and eventual progression to disability in HCT recipients (Figure 1). The working hypothesis is that

*Financial disclosure:* See Acknowledgments on page 667.
* Correspondence and reprint requests: Eileen Danaher Hacker, PhD, Department of Biobehavioral Health Science, University of Illinois at Chicago, 845 S. Damen Avenue, (M/C 802), Room 760, Chicago, IL 60612.
*E-mail address:* ehacker@uic.edu (E.D. Hacker).

http://dx.doi.org/10.1016/j.bbmt.2016.12.637
1083-8791/

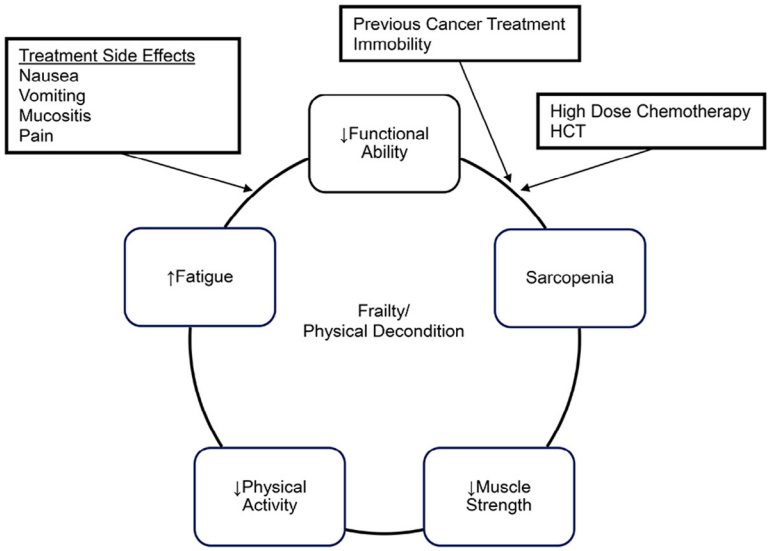


**Figure 1.** Model of frailty/physical decondition (adapted from Fried's Clinical Phenotype of Frailty in Older Adults, 2001).

muscle strength is needed to break the negative cycle of physical deconditioning/frailty that begins with loss of muscle mass leading to decreased strength→ reduced physical activity→ fatigue→ decreased functional ability→ even further loss of muscle mass. Without intervention, frailty and long-term disability ensue even though the HCT survivors are free of cancer [17]. Thus, there is a tremendous need to break this negative cycle and develop effective interventions to reduce loss of muscle mass and enhance early recovery.

This study focuses on strength training to enhance early recovery (STEER) after intensive cancer treatment and HCT. Exercise is widely promoted as a means for improving physical functioning in people with cancer [18,19]. Strength training, in comparison to all other exercise modalities, most effectively builds muscle mass [20]; however, few studies have evaluated strength training in the HCT population. Most HCT studies combined strength training with aerobic exercises [21-27], making it difficult to disentangle the individual effects of strength training. Only 1 small HCT study, besides our pilot work, employed single-modality strength training [28]. Although beneficial effects were demonstrated, fatigue, physical activity, and functional ability were not assessed. Our pilot studies demonstrated that (1) strength training using elastic resistance bands has potential positive effects on physical activity, fatigue, and QOL; and, (2) strength training is feasible during the early recovery period if the intervention is tailored to the individual's capabilities, making subject burden reasonable [29,30].

A strength training intervention to block or reverse physical deconditioning after HCT is vitally important for maintaining physical independence, as demonstrated by the ability to perform everyday activities. From a cost and subject burden perspective, it is imperative that the independent effects of strength training be established in this challenging population. Furthermore, strength training after HCT may be more important than aerobic exercise, according to the American College of Sports Medicine [31]. Given the importance of maintaining muscle mass and reducing the debilitating effects of intensive cancer treatment and HCT, there is a clear need for a randomized clinical trial (RCT) to evaluate a strength training intervention in the early recovery period after HCT. The purpose of this single-blind RCT was to compare STEER to usual care plus attention control with health education (UC + AC with HE) after intensive cancer treatment and HCT on physical activity, fatigue, muscle strength, functional ability, and QOL. This study addresses the following question, "Does strength training enhance recovery from baseline to 6 weeks after hospital discharge after HCT?"

## METHODS

### *Design*

This study employed a single-blind RCT to test the efficacy of the STEER invention compared with UC + AC with HE after HCT. Subjects were stratified by type of transplantation (allogeneic or autologous) and by age (≤60 years of age or > 60 years of age). Random allocation to treatment and allocation concealment were achieved using sequentially numbered, opaque, sealed envelopes [32].

STEER consisted of a comprehensive program of progressive resistance using elastic resistance bands to strengthen the upper body, lower body, and abdominal muscles. UC + AC with HE consisted of a standardized health education program. Both study arms contained an in-hospital component followed by a 6-week post–hospital discharge phase (described in detail below). Dependent variables included physical activity, fatigue, muscle strength, functional ability, and QOL. Variables were measured before admission to the hospital for the HCT to provide baseline information and during the seventh week after hospital discharge to provide information regarding the efficacy of the intervention and recovery after HCT. The study was approved by the institutional review board.

### *Sample and Setting*

Consecutively eligible patients 18 years of age or older scheduled to undergo HCT at a Midwestern academic medical center were invited to participate. Patients who were initially eligible for inclusion were scheduled to undergo HCT for an underlying malignancy and cognitively able to understand the purpose of the research. Patients contemplating HCT undergo an extensive medical work-up before transplantation. All of the pretesting procedures are standard of care and were not considered part of the research. The medical work-up generally includes a history and physical; multigated acquisition scans to assess heart function; spirometry to assess pulmonary function; various blood tests to assess kidney, liver, and blood cell function and exposure to viruses; chest x-rays; urinalysis; and a dental exam. The treating physicians reviewed all the pretests and provided approval for subjects to participate in this study. Subjects were excluded if they presented with a significant comorbidity, such as impending pathological fracture, that would be make it potentially unsafe to exercise if randomized to STEER. To continue to participate in the study after hospital discharge, subjects were required to be ambulatory.

Enrollment was open from May 2013 through August 2015. One hundred eighteen people scheduled for HCT were eligible to participate. Eighty-four (71%) agreed to participate. Multiple reasons for declining to participate