

# Multidirectional Walking in Hematopoietic Stem Cell Transplant Patients

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## ABSTRACT

POTIAUMPAI, M., S. CUTRONO, T. MEDINA, M. KOEPEL, D. L. PEREIRA, W. F. PIRL, K. A. JACOBS, M. ELTOUKHY, and J. F. SIGNORILE. Multidirectional Walking in Hematopoietic Stem Cell Transplant Patients. *Med. Sci. Sports Exerc.*, Vol. 53, No. 2, pp. 258–266, 2021. **Background:** The effect of a peritransplant multidirectional walking intervention to target losses in physical function and quality of life (QOL) has not been investigated. **Purpose:** This study examined the effects of a novel multidirectional walking program on physical function and QOL in adults receiving a hematopoietic stem cell transplant (HSCT). **Methods:** Thirty-five adults receiving an autologous or allogeneic HSCT were randomized to a multidirectional walking (WALK) or usual care (CONT) group. The WALK group received supervised training during hospitalization; the CONT group received usual care. Patients were assessed at admission ( $t_0$ ), 3 to 5 d post-HSCT ( $t_1$ ), and 30 d post-HSCT ( $t_2$ ). Physical function measures included the 6-min walk test (6MWT), the Physical Performance Test, and the Timed Up and Go test. Health-related QOL was collected using the Functional Assessment of Cancer Therapy–Bone Marrow Transplant (FACT-BMT) questionnaire. **Results:** There were no significant between-group changes for physical function or QOL. However, after the intervention ( $t_1$  to  $t_2$ ), the WALK group showed significant improvement in aerobic capacity (6MWT,  $P = 0.01$ ), physical ( $P < 0.01$ ) and functional well-being ( $P = 0.04$ ), and overall QOL scores ( $P < 0.01$ ). The CONT group saw no significant changes in physical function or QOL. Effect sizes showed the WALK group had a larger positive effect on physical function and QOL. Minimal clinically important differences in the 6MWT and FACT-BMT were exceeded in the WALK group. **Conclusion:** A multidirectional walking program during the transplant period may be effective at increasing aerobic capacity and QOL for patients receiving HSCT compared with no structured exercise. **Key Words:** PHYSICAL FUNCTION, QUALITY OF LIFE, PHYSICAL ACTIVITY, STEM CELL TRANSPLANTATION, EXERCISE ONCOLOGY, CANCER

Hematopoietic stem cell transplant (HSCT) is used as a treatment for a number of hematologic malignancies such as multiple myeloma, Hodgkin's and non-Hodgkin's lymphoma, and acute/chronic myeloid leukemia (1). By 2020, the number of HSCT survivors is projected to grow to 242,000, leading to a compounding number of survivors living with long-standing detriments to their physical functioning and health-related quality of life (QOL) due to the aggressive nature of HSCT (2).

Treatment-related complications such as chronic graft versus host disease, pain, unyielding fatigue, and steroid myopathy

contribute to a reported 58% decrease in physical activity levels after HSCT (3). A combination of HSCT therapy-related toxicity to the cardiovascular and musculoskeletal systems and reduced physical activity increases the risk of developing comorbidities such as increased body fatness, cardiometabolic risk factors, and sarcopenia (4,5). Further, physical function significantly declines during HSCT treatment and continues after hospital discharge. In as little as 1 wk post-HSCT, patient-reported physical function can significantly decrease, corresponding with declines in objectively measured physical function (6). Similarly, QOL significantly decreases in HSCT recipients. El-Jawahri et al. (7) reported a 12% decrease in QOL scores over the HSCT treatment period, which is double the change that is considered clinically significant. Decreases in QOL also resulted in a commensurate worsening of symptoms such as fatigue, depression, insomnia, and nausea (7). Unfortunately, the deleterious effects of HSCT have a prolonged effect on QOL that can extend several years beyond the end of treatment and discharge from the hospital (8).

There is a need to develop and provide evidence-based supportive care options to reduce treatment-related side effects and provide recuperation post-HSCT. The current literature

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proposes exercise as a viable intervention, with strong reports of increased aerobic capacity (9–11), muscle strength (12–14), physical function (15), and decreased fatigue levels (12), and improved immunologic parameters (16). Aerobic exercise interventions consist of hallway or treadmill walking and ergometer cycling. Although walking is a basic yet effective intervention, it may not address increases in physical function that transfer to activities of daily living (ADL). Activities that measure ADL physical function require movement in the sagittal, frontal, and transverse planes of motion; however, aerobic exercise interventions only cover the sagittal direction. Multidirectional training covers all movement planes and challenges foot–eye coordination and standing and dynamic balance (17). Studies evaluating multidirectional training report significant gains in balance, movement velocity, and reaction times (17,18). Baumann et al. (15) reported using ADL-specific training in HSCT patients and found that patients in the exercise group were able to maintain their aerobic capacity and muscle strength with corresponding increases in QOL. Although the ADL-specific program was successful, the authors did not specify what type of drills were used, making it difficult to determine whether training was provided in all directional planes. In addition, physical function was not tested using ADL-specific measures, making it difficult to conclude whether the intervention was successful at improving ADL-specific physical function.

To our knowledge, there have been no additional studies that have used ADL-specific or multidirectional training in HSCT recipients during the transplant period. To identify the benefits of peritransplant multidirectional exercise, we conducted a preliminary randomized controlled trial beginning when patients were admitted for their scheduled HSCT and ending 30 d post-HSCT. The purpose of the study was on physical function and health-related QOL in HSCT patients. We hypothesized that participants in the multidirectional walking program would exhibit attenuated losses in physical function and QOL during the inpatient treatment phase and would have higher levels of physical function and QOL post-HSCT compared with a usual care group.

## METHODS

**Participants.** We conducted a single-center, stratified, randomized controlled trial at the University of Miami's Sylvester Comprehensive Cancer Center (NCT 03103308). To be eligible for participation, patients had to have been diagnosed with a form of hematopoietic cancer, be between the ages of 40 and 80 yr, and be scheduled to receive an autologous (AUTO) or allogeneic (ALLO) transplant. Participants were excluded from the study for the following reasons: 1) a diagnosis of dementia, altered mental status, or severe psychiatric conditions; 2) preexisting comorbid conditions that would contraindicate exercise testing; and 3) concurrent non-transplant-related chemotherapy or radiation. A CONSORT flow diagram of the study is provided in Figure 1.

All forms, questionnaires, and protocols were approved by the university's institutional review board. Study staff explained all aspects of the study to participants, and written informed consent was obtained from all participants before participation.

After the informed consent process, a total of 35 patients were stratified according to their treatment type (AUTO or ALLO) and then randomized into the intervention or usual care group using a computer-generated randomization list. Assessments were administered at three time points: 1) at baseline, 1–3 d before admission for HSCT ( $t_0$ ); 2) 3–5 d post-HSCT ( $t_1$ ); and 3)  $30 \pm 3$  d post-HSCT ( $t_2$ ). Figure 2 illustrates the flow of study assessments.

Study data were collected and managed using Research Electronic Data Capture (REDCap) hosted at the University of Miami (19,20). REDCap is a secure, Web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources.

**Physical function measures.** Physical function was measured using the 6-min walk test (6MWT), the Timed Up and Go (TUG) test, and the Physical Performance Test (PPT). The 6MWT is a safe, easy to administer, and widely used tool that measures the maximum distance a patient can walk within the given time frame and has been strongly correlated with  $\dot{V}O_{2\max}$  (21).

The TUG is an assessment of physical mobility and dynamic balance and is strongly correlated with the Berg balance score and gait speed (22). The PPT is a valid tool used to objectively measure ADL physical function (23). The modified battery consists of seven tasks that encompass upper fine and coarse motor functions, balance, coordination, and endurance. A numerical score, dependent on time for completion, is assigned to each task.

**Patient-reported outcomes.** HSCT-specific health-related QOL was measured using the Functional Assessment of Cancer Therapy–Bone Marrow Transplant (FACT-BMT) questionnaire. The FACT-BMT consists of 27 items that measure health-related QOL in patients with cancer and 23 additional items specific to QOL in HSCT recipients (24). Statements on the FACT-BMT pertain to the patient's feelings from the past 7 d and responses are presented using a five-point forced-choice Likert format.

## INTERVENTION

**Multidirectional walking (WALK).** The WALK group began the preparatory phase of the intervention 1 d after being admitted to the HSCT unit, which continued until their transplant. The goal was to familiarize patients with the multidirectional drills and to help patients adapt to the physical stress they may encounter during treatment. The duration and complexity of the program progressed based on the patient's performance and comfort level.

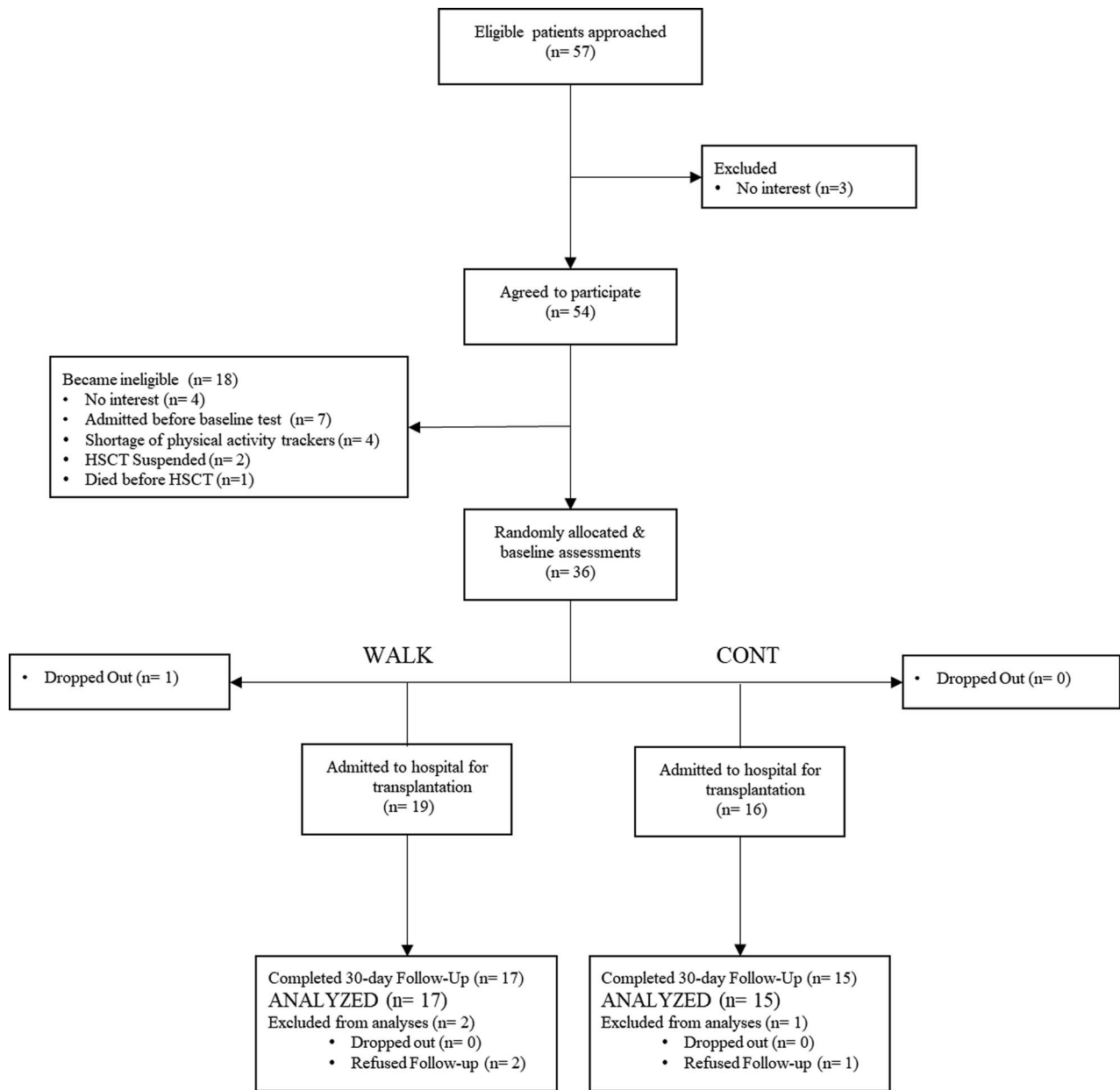


FIGURE 1—CONSORT participant flow.

After the scheduled HSCT, study staff administered the physical function assessments and QOL questionnaire. The WALK group then scheduled three weekly sessions (F: frequency) with an exercise and cancer specialist to complete the walking program and multidirectional drills (T: type). Throughout an exercise session, patients provided their RPE based on a 0 to 10 scale. Patients were encouraged to maintain an exertion level of moderate intensity (5,6) during the multidirectional drills and a high intensity (7,8) during the walking portion (I: intensity).

Currently, there is no universal protocol for progression during a walking program in HSCT. In this study, progression heavily relied on the patient’s consent, current health, and volitional effort. The walking program gradually increased in

duration from 5 to 30 min or when the patient asked to end the session (T: time). If the patient-reported treatment-related symptom severity that interfered with participation or a member of the treatment team advised against physical activity participation, the session was rescheduled with approval from the treating physician. Because of the low-intensity nature of the intervention, no specific criteria were used to determine the commencement of the exercises, and participation in the exercises was up to the discretion of the treating physician.

The multidirectional drills were performed inside patients’ rooms using a weighted eight-rung agility ladder. Drills incorporated forward, backward, sideways, and diagonal walking. Each drill was demonstrated before the patient completing the drill. Five drills were performed for four sets of six

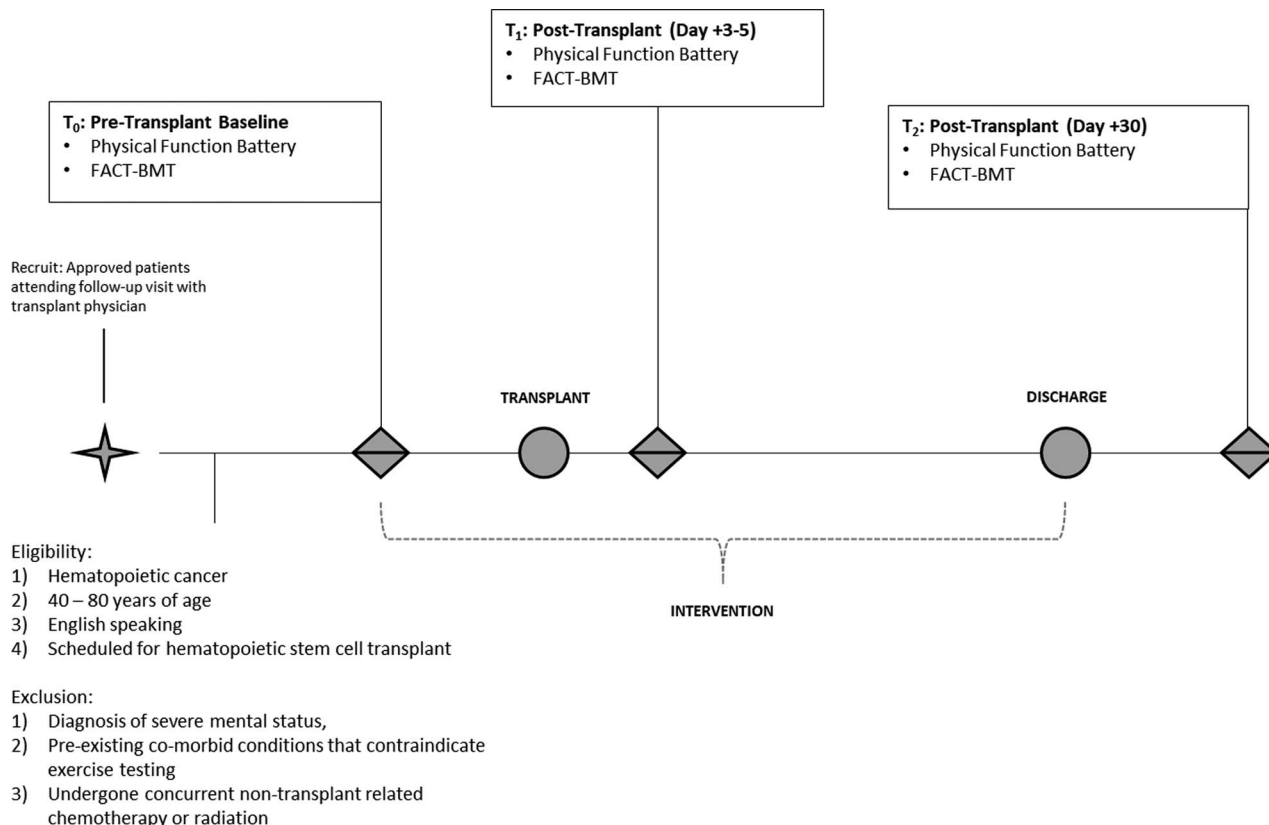


FIGURE 2—Study time line.

repetitions. The multidirectional drills took approximately 20 min to complete (T: time). On days that patients did not meet with an exercise and cancer specialist, patients were instructed to try and complete at least 30 min of unsupervised walking.

**Usual care group (CONT).** Once patients in the CONT group were admitted for HSCT, an exercise and cancer specialist provided physical activity counseling regarding the benefits of activity for HSCT. Patients were encouraged to be physically active during their admission for HSCT. Patients were also given a pedometer to track their daily steps as a means to self-monitor their physical activity. However, the CONT group did not receive supervised walking or multidirectional walking sessions.

**Statistical analysis.** Statistical analyses were conducted in R (R Core Team, 2019). Descriptive statistics were used to calculate participants’ characteristics. A mixed effect model with random intercepts and fixed slopes was used to adjust for baseline differences. Independent group comparisons at measurement points  $t_0$  to  $t_1$  to  $t_2$  for physical function and patient-reported outcomes were analyzed using a two-way repeated-measures ANOVA. All tests were two-tailed, and an alpha level of  $<0.05$  was considered statistically significant.

In addition, group-specific effect size was calculated between two fixed timed points ( $t_1$  and  $t_2$ ). A Hedge’s  $g$  estimate was used because it includes a correction for sample size and is more appropriate to use with small samples. To calculate Hedge’s  $g$ , we use the adjusted means and pooled SD as

standardizers. The interpretation of Hedge’s  $g$  is as follows: 0.80 is considered a large effect, 0.50 is considered a medium effect, and 0.20 is considered a small effect.

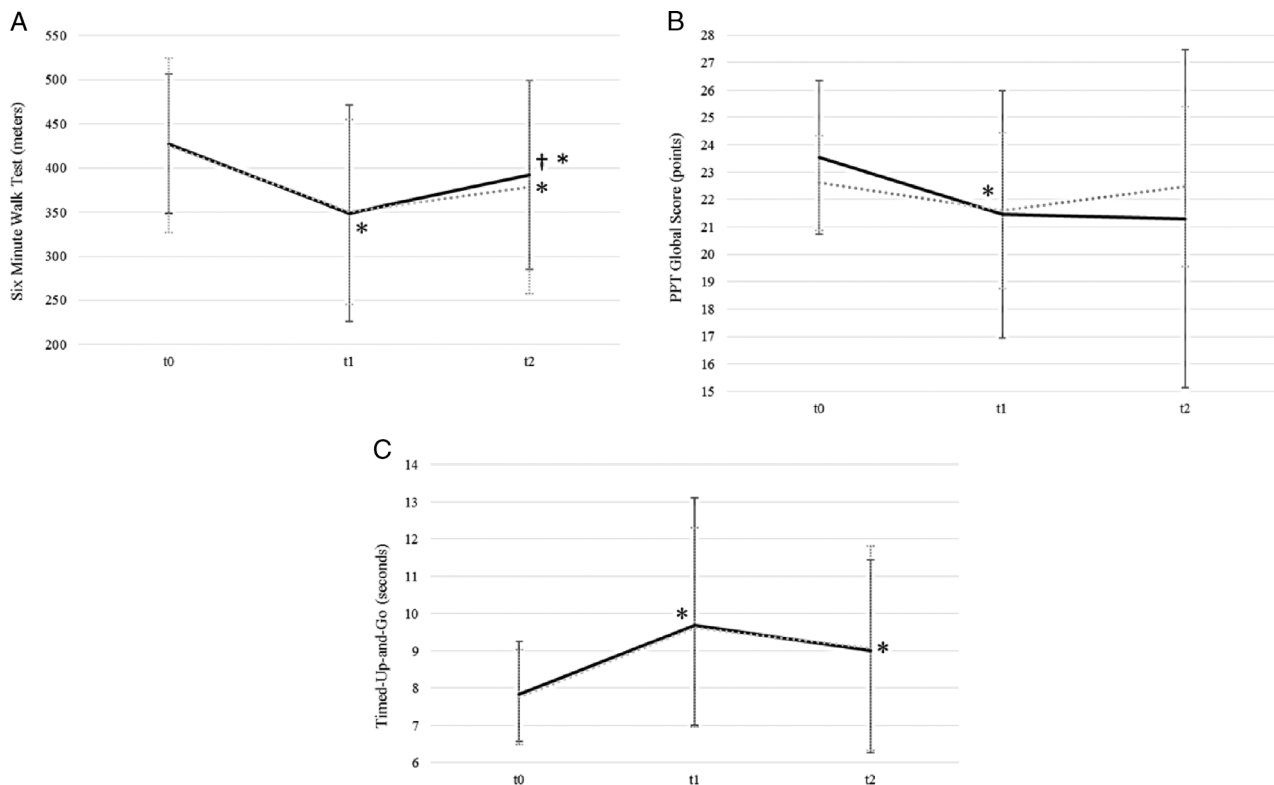
## RESULTS

Patients’ demographic and medical characteristics are presented in Table 1. There were no statistically significant

TABLE 1. Patient characteristics.

|                              | All (n = 35)  | WALK (n = 19) | CONT (n = 16) | P    |
|------------------------------|---------------|---------------|---------------|------|
| Age (yr)                     | 58.77 (7.55)  | 59.26 (7.87)  | 58.19 (7.37)  | 0.68 |
| Sex, n (%)                   |               |               |               | 0.12 |
| Male                         | 19 (54.3)     | 11 (57.9)     | 5 (31.3)      |      |
| Female                       | 16 (45.7)     | 8 (42.1)      | 11 (68.8)     |      |
| Race                         |               |               |               |      |
| Asian                        | 1             | 1             | 0             |      |
| Black or African American    | 6             | 3             | 3             |      |
| Hispanic                     | 8             | 3             | 5             |      |
| White                        | 19            | 12            | 7             |      |
| More than one race           | 1             | 0             | 1             |      |
| Height (cm)                  | 169.92 (8.97) | 168.37 (9.01) | 171.77 (8.84) | 0.27 |
| Weight (kg)                  | 82.48 (16.83) | 82.33 (18.01) | 82.65 (15.90) | 0.96 |
| Body mass index              | 28.61 (5.67)  | 29.12 (6.41)  | 28.01 (4.79)  | 0.57 |
| Diagnosis                    |               |               |               |      |
| Acute myeloid leukemia       | 11            | 6             | 5             |      |
| Acute lymphoblastic leukemia | 1             | 1             | 0             |      |
| Chronic lymphocytic leukemia | 1             | 1             | 0             |      |
| Myelodysplastic syndrome     | 3             | 2             | 1             |      |
| Multiple myeloma             | 16            | 7             | 9             |      |
| Other lymphomas              | 3             | 2             | 1             |      |
| Transplant                   |               |               |               | 0.24 |
| AUTO                         | 18            | 9             | 10            |      |
| ALLO                         | 17            | 10            | 6             |      |

Values are presented as mean (SD).



**FIGURE 3—Changes in physical function: 6MWT distance (A), PPT total score (B), and TUG performance time (C). Black solid line, WALK; gray dotted line, CONT; \*Significantly different than  $t_0$ ,  $P < 0.05$ . †Significantly different than  $t_1$ ,  $P < 0.05$ . Error bars represent SD.**

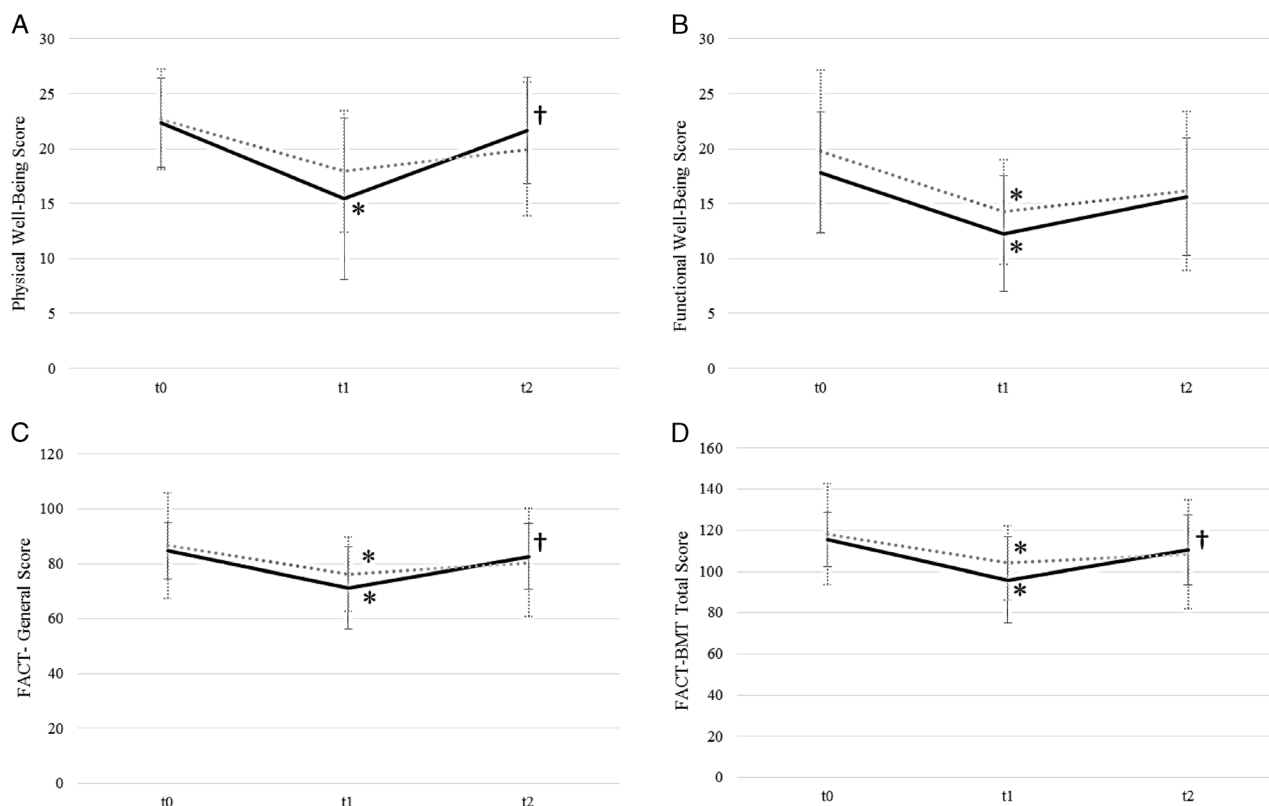
differences between groups at baseline. Figure 3 illustrates changes in PPT scores, 6MWT, and TUG performance time. No significant changes between groups were seen in the 6MWT, TUG performance time, or PPT global score after the intervention. The FACT-BMT and its subscales are presented in Figure 4. There were no significant differences in scores between groups. Hedge's  $g$  effect sizes for each physical function measure and the FACT-BMT and its subscales are presented in Figure 5.

The average time between  $t_0$  and  $t_1$  for the WALK group was  $12.85 \pm 4.31$  d and  $11.71 \pm 4.03$  d for the CONT group. The difference in days between the WALK and the CONT group was not significant ( $P = 0.41$ ). The average time between discharge and  $t_2$  for the WALK group was  $15.10 \pm 3.74$  d and  $16.27 \pm 2.69$  d for the CONT group. The difference in days between groups was not significant ( $P = 0.31$ ). Adherence to the multidirectional walking program was calculated by the number of sessions a patient completed versus the number of scheduled sessions based on the hospitalization period. On average, patients in the WALK group achieved a 78.68% adherence to the WALK program, with an average of 1.95 missed sessions per person. On an RPE scale of 0–10, patients rated the multidirectional drills a  $6.01 \pm 0.70$  difficulty and the walking program a  $5.83 \pm 0.98$  difficulty. There was a 0% contamination rate, that is, the extent to which the CONT group adopted the intervention and started to exercise on their own. Of the 15 participants in the CONT group, six participants returned exercise logs recording their pedometer readings. The main reasons the nine remaining participants cited

for not returning exercise logs included not participating in physical activity during their hospitalization ( $n = 5$ ), forgetting to wear the pedometer ( $n = 2$ ), or forgetting to record their steps ( $n = 2$ ). Of the six participants who returned exercise logs, the average daily steps were 1924 (SD = 754).

Despite the absence of significant group–time interactions, repeated-measures analyses revealed significant main effects for time for the 6MWT ( $P < 0.001$ ) and the TUG ( $P < 0.001$ ). Further analyses showed that both the WALK and the CONT groups saw significant decreases in physical function performance in the 6MWT (Fig. 3A), PPT (Fig. 3B), and TUG (Fig. 3C) from  $t_0$  to  $t_1$ . However, the WALK group showed significant changes from  $t_1$  to  $t_2$ . After the intervention, the WALK group showed significant improvement in cardiovascular capacity via the 6MWT (MD = 43.66, SD = 63.10,  $P = 0.04$ , 12.5% improvement, power = 0.97,  $g = 0.37$ ) (Fig. 3A), whereas the CONT group showed no significant changes from  $t_1$  to  $t_2$  (MD = 27.75, SD = 78.08,  $P = 0.41$ , power = 0.53, 7.92% improvement,  $g = 0.24$ ). Although both the WALK and the CONT groups could not reach pretransplant 6MWT distances at  $t_2$ , only the CONT group exhibited significantly lesser distance walked (MD = 47.62, SD = 59.83,  $P = 0.01$ ) (Fig. 3A). Independent group comparisons showed no significant changes from  $t_1$  to  $t_2$  for the TUG.

QOL scores showed no significant interaction effects, yet a significant effect for time was seen for physical well-being ( $P < 0.001$ ), functional well-being ( $P < 0.001$ ), HSCT-related QOL ( $P < 0.001$ ), general QOL ( $P < 0.001$ ), and total QOL



**FIGURE 4—Changes in QOL: physical well-being (A), functional well-being (B), FACT general (C), and FACT-BMT total score (D). Black solid line, WALK; gray dotted line, CONT; \*Significantly different than  $t_0$ ,  $P < 0.05$ . †Significantly different than  $t_1$ ,  $P < 0.05$ . Error bars represent SD.**

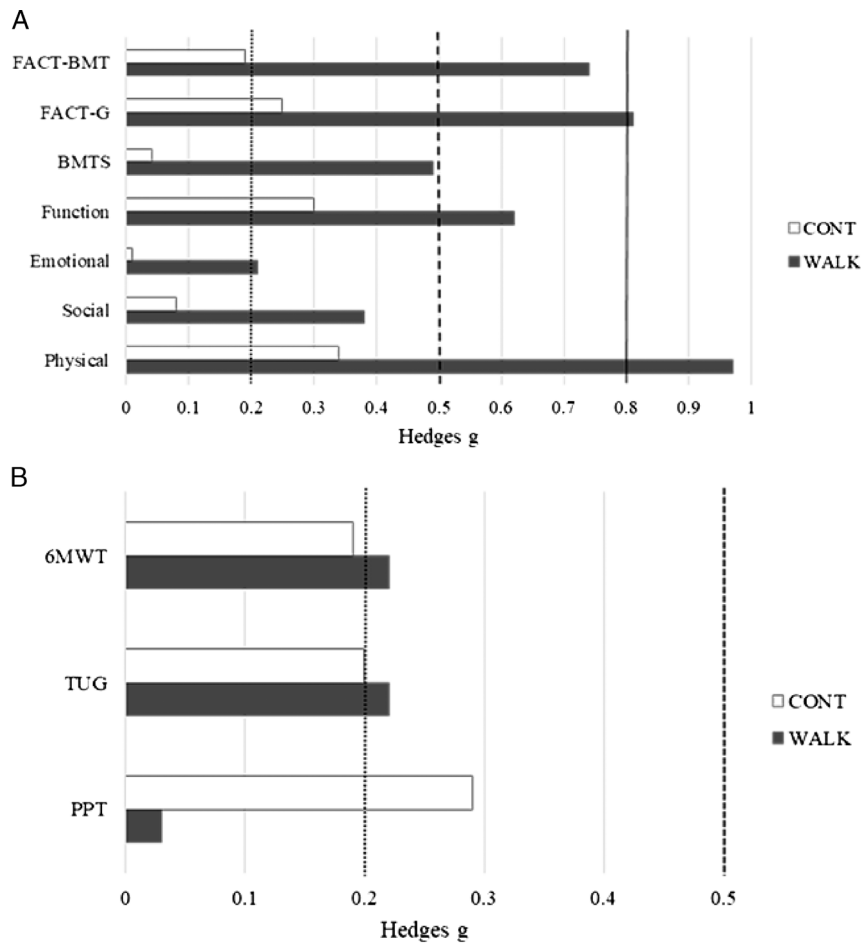
( $P < 0.001$ ). The WALK and the CONT groups saw significant decreases in multiple domains of the FACT-BMT from  $t_0$  to  $t_1$  (Fig. 4). At  $t_2$ , only the WALK group exhibited significant increases in physical well-being (MD = 6.16, SD = 7.38,  $P < 0.01$ , power = 0.99, 39.82% improvement,  $g = 0.97$ ) (Fig. 3A), functional well-being (MD = 3.37, SD = 6.54,  $P = 0.04$ , power = 0.84, 27.49% improvement,  $g = 0.62$ ) (Fig. 3B), HSCT-related QOL (MD = 3.32, SD = 5.46,  $P = 0.01$ , power = 0.94, 13.47% improvement,  $g = 0.49$ ), general QOL (FACT-G) (MD = 11.21, SD = 14.92,  $P < 0.01$ , power = 0.99, 15.71% improvement,  $g = 0.81$ ) (Fig. 3C), and total QOL (FACT-BMT) (MD = 14.53, SD = 19.38,  $P < 0.01$ , power = 0.99, 15.13% improvement,  $g = 0.74$ ) (Fig. 3D). The CONT group showed no significant improvements in physical well-being (MD = 2.00, SD = 6.21,  $P = 0.76$ , power = 0.46, 11.15% improvement,  $g = 0.34$ ), functional well-being (MD = 1.88, SD = 4.40,  $P = 0.59$ , power = 0.69, 13.19% improvement,  $g = 0.30$ ), HSCT-related QOL (MD = 0.25, SD = 3.53,  $P = 1.00$ , power = 0.07, 0.90% improvement,  $g = 0.04$ ), general QOL (FACT-G) (MD = 4.25, SD = 11.42,  $P = 0.65$ , power = 0.57, 5.58% improvement,  $g = 0.25$ ), and total QOL (FACT-BMT) (MD = 4.50, SD = 13.58,  $P = 0.89$ , power = 0.48, 4.21% improvement,  $g = 0.19$ ).

## DISCUSSION

Although there were no significant group by time interactions, the WALK group significantly improved their 6MWT

distance from  $t_1$  to  $t_2$  (12.5% difference), whereas the CONT group exhibited no significant changes. Although the effect seen by both groups is small to moderate, there are clinical implications of the observed improvements. The suggested minimally important difference (MID) for the 6MWT is 47 to 49 m (25). The WALK group showed a significant increase of  $43.66 \pm 63.10$  m compared with the CONT group with a nonsignificant increase of  $27.75 \pm 78.08$  m. Although both the WALK and the CONT groups do not exceed the average MID, the multidirectional walking intervention shows more promise as an effective peritransplant intervention to address the significant decreases in cardiovascular capacity post-HSCT compared with not providing a physical intervention. These findings carry clinical relevance in this population due to increased risk of developing premature comorbidities such as cardiovascular disease and characteristics associated with metabolic syndrome and an increased mortality risk (26,27).

The use of the 6MWT has been suggested as a predictor of clinical outcomes in HSCT patients and increases in the distance walked are associated with lower risk of nonrelapse mortality and higher overall survival (28). Calculated walk distances for age- and gender-matched healthy adults produced 6MWT distances that ranged between 417.76 and 582.22 m for women and 416.69–713.94 m for men (29). This sharply contrasts with the women in the study who walked between 91.44 and 487.68 m and men who walked between 243.84 and 655.32 m. The sizeable discrepancy in meters walked versus the predicted walk distance supports 1) how



**FIGURE 5**—Within-group effect sizes from  $t_1$  to  $t_2$ : FACT-BMT (A); physical function measures (B). *Gray bar, WALK; white bar, CONT; dotted line, small effect size; dashed line, moderate effect size; Solid line, large effect size.*

hematologic malignancies contribute to physical deconditioning in HSCT recipients, 2) the need for interventions with the ability to improve cardiovascular capacity, and 3) a low-intensity intervention such as combined multidirectional drills and walking can still have a positive impact on cardiovascular capacity. These results concur with previous studies demonstrating that submaximal aerobic endurance is malleable to change regardless of the exercise modality (10,30–32). To our knowledge, there are currently no other studies that have used multidirectional walking in HSCT patients. The novel finding from the present study is that a multidirectional walking intervention was able to elicit improvements despite improved aerobic endurance being a secondary rather than a primary target of multidirectional walking.

The novelty of the present study lies in the use of ADL-based tests to measure changes in physical function and the use of a multidirectional walking intervention. Currently, no other studies evaluating changes in physical function involving cancer patients or survivors have used the PPT; rather, they relied on assessments that indirectly translate physical function. In contrast to our hypothesis, there was no significant between-group or within-group differences. However, previous studies in older adults with mobility impairment and metabolic risk factors showed significant improvements in

PPT performance after 10–12 wk of structured resistance and multimodal exercise (33,34). We theorize that the absence of significant changes in the current study may have been due to the truncated intervention period (13 to 31 d), compared with previous interventions in other populations. Also, the intervention did not span the entire hospitalization period due to treatment-related complications such as neutropenia, fatigue, pain, and gastrointestinal issues that may have prevented participation in the training sessions. In addition, the training intensity may not have been sufficient to elicit the physiological adaptations needed to improve performance. Because of environmental constraints, our patients performed light- to moderate-intensity walking and agility drills tailored to their volitional effort. Regardless of the lack of significant change in PPT scores, it is important to note the low level of physical function performance in HSCT patients. Based on categories developed by Brown et al. (35), to determine frailty, our patients would be categorized as mildly frail nearing the threshold of moderately frail.

Performance on the TUG also significantly decreased from  $t_0$  to  $t_1$  for WALK and CONT; both WALK and CONT increased the time to complete the TUG and did not exhibit changes from  $t_1$  to  $t_2$ . This may be due to the increased sedentary activity post-HSCT (3,36). In addition, linear and multidirectional walking do not directly target muscle strength, so

lower limb strength development, preservation, and recovery was not directly addressed. Based on normative values for the TUG, our results show that our patients' performance times were comparable with adults 10–20 yr older than the average age reported in the study, providing further insight into the functional status of HSCT patients and the need to intervene on the physical capabilities of HSCT patients (37).

Patients also reported significant increases in QOL. Although there was an absence of between-group differences, calculated effect sizes revealed differences between groups (Fig. 5A). Reported scores showed significant decreases for both WALK and CONT in physical and functional well-being, BMT subscale, FACT general, and FACT-BMT scores immediately after transplant ( $t_0$  to  $t_1$ ). These significant declines confirm that the severe nature of HSCT is detrimental to QOL (7). The effect sizes of the WALK group showed greater improvements for the FACT-BMT and its subscales than in the CONT group (Fig. 5A). The WALK group displayed large effect sizes indicating its potential to improve physical well-being ( $g = 0.97$ ) and general QOL ( $g = 0.81$ ), whereas the effect sizes for the CONT group were small ( $g = 0.34$  and  $g = 0.25$ , respectively). In addition, the WALK group had moderately large effect sizes for improving functional well-being ( $g = 0.62$ ), HSCT-related QOL ( $g = 0.49$ ), and overall QOL ( $g = 0.74$ ), whereas the CONT group displayed weak effects. The moderate to large effect sizes point to increases in QOL scores that correspond to MID. The WALK group reported a  $6.16 \pm 7.38$ -point increase in physical well-being and a three-point increase in functional well-being, which is over the two- to three-point MID (7,38). The WALK group also reported an  $11.21 \pm 14.92$ -point increase in the FACT-G, which is well over the MID range of three to seven points (38). In addition, because a 5-point change in FACT-BMT total score is suggested as clinically significant, our findings in the WALK group scores from  $t_1$  to  $t_2$  highlight the positive impact of the intervention (7,39).

Our results align with previous studies that have used exercise to address QOL in patients undergoing HSCT. A number of other exercise studies opted to use the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30), which has been found to be highly correlated to the FACT-BMT (40). Studies that used the EORTC QLQ-C30 also showed improvements in physical functioning (9,10), emotional well-being (15), fatigue (13), and global QOL scores after interventions using resistance training, aerobic training, or a combination of both.

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Similar to the present study, Brassil et al. (32) implemented a motivational walking program using physical activity monitors to evaluate its effects on performance status and QOL using the FACT-BMT. Researchers found that FACT-BMT scores were significantly lower immediately after HSCT compared with pretransplant scores, and postintervention scores were higher than posttransplant scores but still did not reach pretransplant levels. The pattern of results in the present study mirror those of Brassil et al. (32), suggesting that despite the steep decline in QOL, a targeted walking intervention has the ability to restore QOL in HSCT patients.

**Study limitations.** No between-group effects were found for the measures reported, which was likely due to the small sample size. As a result, we calculated effect sizes to provide a quantification of the impact of the interventions. A larger study, consisting of more patients allocated into each intervention arm, might help further elucidate the effects of the intervention. In an effort to study a more general population of HSCT patients, this study included patients receiving an AUTO or ALLO transplant. Because the course of treatment and recovery varies between the two types of transplant, the results cannot distinguish responses based on patients' transplant type. In addition, conditioning regimens before HSCT were not considered as inclusion or exclusion criteria for the present preliminary study; rather, all patients were included to determine feasibility of the intervention.

## CONCLUSION

Outcome measures of general health-related and HSCT-specific QOL showed moderate to large effect sizes and MID after patients completed the multidirectional walking program. Although there were no significant between-group differences in physical function status, the WALK group exhibited significant increases in aerobic capacity after the intervention. This study demonstrated that a peritransplant walking intervention may be effective at targeting select physical function measures and health-related QOL in HSCT patients.

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