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Exploring the Functional and Psychosocial Impacts of CAR T-Cell Therapy from an Occupational Therapy Perspective

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Abstract

Background

Chimeric antigen receptor (CAR) T-cell therapy is an immunotherapy with preliminary success in treating blood cancers, however, it is associated with adverse side effects that can impact patients' functional statuses. There is a need to further explore side effects associated with CAR T-cell therapy and the role that occupational therapy may serve in addressing affected areas. The purpose of this study was to explore the functional and psychosocial effects patients experience while undergoing CAR T-cell therapy to better understand the rehabilitation needs from an occupational therapy perspective.

Methods

A retrospective chart review was completed to collect data from patients who underwent CAR T-cell therapy at a cancer hospital between February 2024 and July 2024. Patients were included if they received occupational therapy services throughout their inpatient stay, including completion of selected assessments prior to infusion, day +3 following infusion, day +6 following infusion, and day +9 following infusion.

Results

Trends between assessment scores prior to infusion and prior to discharge were explored with each patient. Although with varied results, this study found that CAR T-cell therapy may affect patients' cognition, psychosocial wellbeing, grip strength, balance, and fatigue levels.

Discussion

Occupational therapy practitioners in acute care oncology can focus on the areas identified in this study to support evaluation and intervention planning for patients undergoing inpatient CAR T-cell therapy.

Keywords: acute care, cancer, CAR T-cell therapy, occupational therapy, oncology, rehabilitation

Introduction and Background

Approximately every three minutes, one person in the United States is diagnosed with one of the three main types of blood cancers, leukemia, lymphoma, or myeloma, amounting to an estimated total of ~180,000 individuals per year (Leukemia and Lymphoma Society, 2023). While chemotherapy, surgery, and radiation remain the most common forms of cancer treatment, chimeric antigen receptor (CAR) T-cell therapy is an emerging immunotherapy that has had preliminary success in treating relapsed or refractory forms of blood cancers and preventing long-term remissions since its Food and Drug Association (FDA) approval in 2017 (National Cancer Institute, 2022). While initial clinical trials show promising results, there are various limitations of this newer therapy. Approximately half of patients treated with CAR T-cell therapy achieved a complete response, where no cancer cells were detected after treatment (Sermer et al., 2020). However, rates of relapse in the following years highly vary across different studies, and increasingly more research is being conducted to determine more accurate initial response rates and relapse rates for each type of blood cancer. An additional drawback is that CAR T-cell therapy is associated with various adverse side effects (National Cancer Institute, 2022).

Common side effects of CAR T-cell therapy include fever and chills, shortness of breath, nausea and vomiting, dizziness, severe fatigue, muscle and joint pain, confusion, tremors, and loss of balance (American Cancer Society, 2022). Additionally, one of the most serious anticipated side effects is cytokine release syndrome (CRS), which causes neurologic symptoms such as severe confusion and altered mental status, seizure-like activity, and trouble speaking and understanding speech (National

Cancer Institute, 2022). These side effects can impact patients' short-term and long-term functional status, specifically in the following areas: sleep, coping, balance, physical functioning, and cognition (Stenson et al., 2021; Wang, et al., 2021). These identified functional deficits are all key areas that occupational therapy practitioners (OTPs) can evaluate and intervene upon.

Occupational therapy currently plays a role in cancer rehabilitation, showing efficacy in addressing areas such as memory and attention, cancer-related fatigue, upper extremity impairments, and activities of daily living (ADL)/ instrumental activities of daily living (IADL) participation (Pergolotti et al., 2016) for individuals with various types of cancer. However, the current literature investigating the impact of CAR T-cell therapy on an individual's ability to engage in their daily routine and meaningful occupations is limited (Kamal et al., 2021). Using primarily self-reported outcome measures, the literature posits that many patients experience physical, psychological, and cognitive symptom burden that affect functional status and quality of life after CAR T-cell therapy (Wang et al., 2021). Fatigue is the most common and most distressing symptom self-reported by patients after CAR T-cell therapy (Ruark et al., 2020), contributing to impaired physical functioning such as decreased exercise capacity, muscle weakness, tremors, and balance impairments (Obaisi et al., 2020). Patients report that physical symptoms interfere with many aspects of physical functioning that occupational therapy can address, including interference with daily activities, work, walking, and social activities (Stenson et al., 2022; Whisenant et al., 2021).

Additionally, approximately 40% of patients self-report cognitive difficulties post-CAR T-cell therapy that have a negative impact on mental and physical health (Kamal

et al., 2021; Ruark et al., 2020). The cognitive difficulties most commonly reported are memory deficits and difficulty finding words (Kamal et al., 2021; Stenson et al., 2022). More specifically, the most common cognitive deficits identified in the acute stage are confusion and disorientation, language disturbance, attention deficits, memory deficits, and executive dysfunction (Kazzi et al., 2023). Patients self-report that cognitive symptoms experienced after CAR T-cell therapy interfere with daily activities, work, relationships with others, mood, and quality of life (Whisenant et al., 2021).

Lastly, the physical and cognitive difficulties identified above are associated with decreased mental health and decreased enjoyment of life after CAR T-cell therapy (Ruark et al., 2020; Whisenant et al., 2021). Around 50% of patients report experiencing at least one negative neuropsychiatric outcome after CAR T-cell therapy, including anxiety and depression (Ruark et al., 2020). Specifically, patients describe the process as a challenging experience, causing disruption of daily life and future plans, contributing to difficulty planning for the future, and causing a loss of identity and normalcy (Stenson et al., 2022). The overall psychosocial symptom burden identified by patients interfered with ability to engage in daily routines, mood, relationships with others, and enjoyment of life (Whisenant et al., 2021).

Though sparse, the literature search performed by the authors yielded six areas of function that are potentially impacted by CAR T-cell therapy: cognition, psychosocial wellbeing, functional balance, functional strength, cancer-related fatigue, and ADL performance. There is need to further explore the associated side effects and the role OTPs may serve in addressing impacted areas. The purpose of this study was to explore the functional and psychosocial effects patients experience while undergoing

CAR T-cell therapy in an inpatient setting to better understand rehabilitation needs from an occupational therapy perspective. The secondary aim of this study was to provide insight into the lived experience of those who undergo CAR T-cell therapy, lending to foundations for future research on potential occupational therapy interventions to address the identified needs of this population.

Methodology

This study was submitted to the Institutional Review Board (IRB) and approved as exempt from further IRB review (UP-24-00712). A retrospective chart review was completed to collect patient data from the electronic medical record (EMR).

Study Population

The inclusion criteria of this study consisted of English or Spanish-speaking patients undergoing CAR T-cell therapy during inpatient stay from February 2024-July 2024 at a cancer hospital in a metropolitan area. Patients were included who received occupational therapy services throughout their admission, including completion of selected assessments during standard provision of occupational therapy services. Assessments were completed and scored prior to CAR T infusion, day +3 following infusion, day +6 following infusion, and day +9 following infusion prior to discharge. Patient scores were recorded in occupational therapy documentation in the Electronic Medical Record (EMR). Only patients who had complete data sets were included in this study. Initially twelve patients were identified as patients who underwent CAR T-cell therapy at the aforementioned cancer hospital between February 2024- July 2024. Reasons for patient exclusion included incomplete data sets due to inability to participate secondary to side effects, complications requiring higher level of care, or

completion of assessments on days other than criteria designated in study. In addition, the exclusion criteria consisted of patients who spoke neither English nor Spanish to ensure validity of outcome measures used. This selection process yielded a total number of participants of n=4.

Procedure

Three study investigators reviewed charts from the EMR to determine eligible participants, as designated by the study population inclusion and exclusion criteria. Investigators performed a retrospective chart review to gather study data, which included demographic information (age and gender), assessment scores from timepoints identified, length of stay, and Immune Effector Cell Encephalopathy (ICE) scores as documented daily by the medical team, which measures neurotoxicity after CAR T-cell therapy. Study investigators completed all phases of screening and data collection. Once data collection was complete, trends and comparisons between assessment scores prior to infusion and prior to discharge were explored for each patient. Due to the small sample size of this study, conclusions cannot be drawn from statistical analyses, however trends explored between data collection points provide useful insight into how the experience of CAR T-cell therapy may affect patients' functional status and the role occupational therapy may play in addressing areas of deficit.

Outcome Measures

The following assessments were incorporated into the standard provision of occupational therapy care for patients receiving CAR T-cell therapy during inpatient admission: Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005);

Depression, Anxiety, and Stress Scale (DASS-21) (Henry & Crawford, 2005); Cancer Fatigue Scale (CFS) (Okuyama et al., 2000); grip strength measured via dynamometer; Functional Reach Test (Duncan et al., 1990); and Activity Measure for Post-Acute Care "6 clicks" Daily Activity Inpatient Short Form (AM-PAC) (Haley et al., 2004). These measures were selected as they correspond to the specific functional areas of interest in this study: cognition, psychosocial well-being, fatigue levels, strength and frailty, balance, and ADL performance. Additionally, these measures are commonly used in occupational therapy practice in acute care, and have been shown to have high validity, test-retest reliability, and internal consistency. Patients' pre-test scores were obtained two to four days before each patient received their CAR T infusion, in order to compare each patient's status after CAR T-cell therapy to baseline scores. Post-test scores were obtained three days after infusion, six days after infusion, and nine days after infusion in order to gather a comprehensive picture of the symptoms and deficits each patient experienced in the days following infusion.

Cognition via Montreal Cognitive Assessment

The Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005) was completed with each patient to evaluate changes in patients' cognition from prior to infusion to prior to discharge. Version 8.1 was used as the pre-test measure, followed by use of Versions 8.2, 8.3, and repeating 8.1 on post-infusion day +3, post-infusion day +6, and post-infusion day +9 respectively. The MoCA yields scores out of the highest possible score of 30. Normal cognitive performance is defined by a score of 26 or above, mild cognitive impairment is defined by a score between 18-25, moderate

cognitive impairment is defined by a score between 10-17, and severe cognitive impairment is defined by a score between 0-9 (Nasreddine et al., 2005).

Psychosocial Well-being via Depression, Anxiety, and Stress Scale

The Depression, Anxiety and Stress Scale (Henry & Crawford, 2005) was selected to assess patients' psychosocial well-being throughout their inpatient stay. The Depression, Anxiety, and Stress Scale (DASS-21) is a self-report measure in which patients rate items using 0, 1, 2, or 3 in response to how much each statement applied over the past week, and yields scores for three subscales: depression, anxiety, and stress. The short form of this scale with 21 items was used in alignment with time constraints often experienced when providing occupational therapy services in acute care. Scores from the 21-item short form are multiplied by two during scoring in order to be compared to the severity ratings used in the 42-item long form. Scores are categorized as "normal", "mild", "moderate", "severe", and "extremely severe". For the depression subscale, scores between 0-9 indicate "normal" levels of depression, scores between 10-13 indicate "mild depression", scores between 14-20 indicate "moderate depression", scores between 21-27 indicate "severe depression", and scores 28+ indicate "extremely severe depression". For the anxiety subscale, scores between 0-7 indicate "normal" levels of anxiety, scores between 8-9 indicate "mild anxiety", scores between 10-14 indicate "moderate anxiety", scores between 15-19 indicate "severe anxiety", and scores 20+ indicate "extremely severe anxiety". For the stress subscale, scores between 0-14 indicate "normal" levels of stress, scores between 15-18 indicate "mild stress", scores between 19-25 indicate "moderate stress", scores between 26-33

indicate “severe stress”, and scores 34+ indicate “extremely severe stress” (Henry & Crawford, 2005).

Fatigue Level via Cancer Fatigue Scale

The Cancer Fatigue Scale (Okuyama et al., 2000) is a self-report measure that assesses cancer patients’ physical, affective, and cognitive fatigue with 15 items rated from 1 “no” to 5 “very much” based on the patient’s current state. The scale yields an overall score out of 60, with higher scores indicating more severe cancer-related fatigue.

Grip Strength via Dynamometer

Each patient’s grip strength was assessed using a dynamometer. The average of three trials on each hand was used for each patient at every data collection point. Grip strength was compared to normative data (norms) according to age and sex.

Functional Balance via Functional Reach Test

The Functional Reach Test (Duncan et al., 1990) was used to assess each patient’s balance. Two trials were completed with each patient and the average of the trials was calculated to yield pre-test and post-test scores. Scores are measured in centimeters. A score of 6 inches (or 15.24 cm) or less indicates a significantly increased risk for falls, and scores between 6-10 inches (15.24- 25.4 cm) indicate moderate risk for falls. The normative data for the 41-69 age group is 37.846 cm +/- 5.6 cm for men, and 35.05 cm +/- 5.6 cm for women.

ADL Performance via Activity Measure for Post-Acute Care

The Activity Measure for Post-Acute Care “6 clicks” Daily Activity Inpatient Short Form (AM-PAC) (Haley et al., 2004) was used to measure each patient’s overall ADL

performance. This outcome measure uses six questions to assess patients' functional outcomes in the area of daily activity. The six primary activities of daily living assessed include bathing, lower body dressing, upper body dressing, toileting, eating, and grooming. Assistance levels are divided into four categories: "total", "a lot", "a little", and "none". Scores between 6-8 indicate "total assistance", scores between 9-13 indicate "maximum assistance", scores between 14-19 indicate "moderate assistance", scores between 20-22 indicate "minimal assistance", a score of 23 indicates "stand-by assistance", and a score of 24 indicates independence. Higher scores indicate higher ADL performance.

Immune Effector Cell Encephalopathy (ICE) Score

The Immune Effector Cell Encephalopathy (ICE) score is a 10-point scale used to identify and measure neurotoxicity (Lee et al., 2019). This assessment is commonly used with the CAR T-cell therapy population, as cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) are closely associated with CAR T-cell therapy. The ICE assessment measures changes in a patient's speech, orientation, handwriting, attention, and receptive aphasia. Patients are scored twice daily by the medical team at the respective hospital in this study to assess changes in cognition that indicate development of ICANS. An ICE score of 10 is associated with no impairment. ICE scores between 7-9 are associated with grade 1 ICANS, between 3-6 are associated with grade 2 ICANS, and between 0-2 are associated with grade 3 ICANS. Lastly, an ICE score of 0 as a result of the patient being unarousable or unable to complete the ICE assessment is associated with grade 4 ICANS (Lee et al, 2019).

Results

Demographic Information

Table 1 summarizes the demographic information of the study population, including age, gender, and length of inpatient stay. The population consists of two male and two female participants, as self-identified in the EMR. The mean age of participants is 63.25, and the average length of inpatient stay was 13.5 days, with the typical expected length of inpatient stay during CAR T-cell therapy being fifteen days at this site. Table 2 includes assessment scores for all patients across all time points according to each assessment.

Table 1

Demographic Information

Participant	Age	Gender	Length of Stay
Patient 1	71	Male	10 days
Patient 2	52	Female	14 days
Patient 3	67	Female	15 days
Patient 4	63	Male	15 days

Cognition

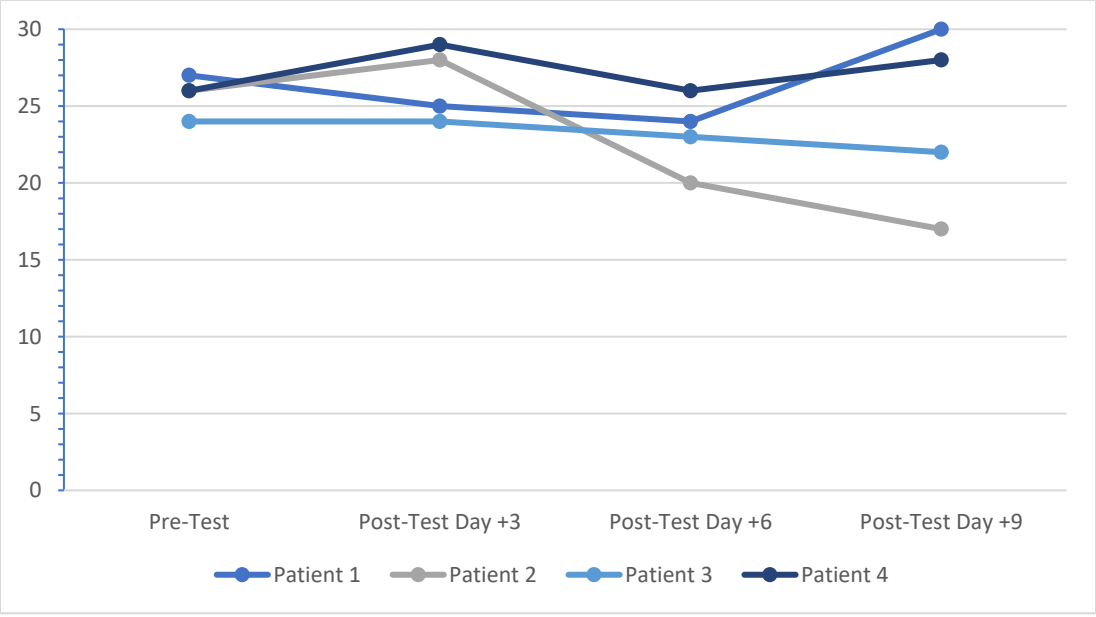
In regard to the MoCA, patient scores varied across all time points as seen in Figure 1. Patient 1's score on the MoCA steadily declined below normal range on post-infusion day +3 (25/30) and post-infusion day +6 (24/30). Patient 2's score on the MoCA decreased to below normal range on post-infusion day +6 (20/30) and continued to decline below normal on post-infusion day +9 (17/30). Patient 3's initial score on the

MoCA was below normal range (24/30), and continued to steadily decrease post-infusion, remaining at below normal range post-infusion day +9 (22/30) prior to discharge. Lastly, Patient 4's MoCA scores fluctuated, however remained above normal range at all data collection time points. Overall, from pre-infusion to pre-discharge, three out of four patients demonstrated a decrease in MoCA scores below normal range during CAR T-cell therapy. In addition, two out of four patients scored below the normal range on the MoCA prior to discharge, with one patient scoring 17/30, potentially indicating moderate cognitive impairment and one patient scoring 22/30, potentially indicating mild cognitive impairment.

Specifically, the most consistent and notable finding included scores on the attention subscale of the MoCA. Three of four patients demonstrated a one-to-four point score decrease in the attention subscale during CAR T-cell therapy. Only one patient's scores did not yield changes in attention throughout inpatient admission.

Figure 1

MoCA Scores

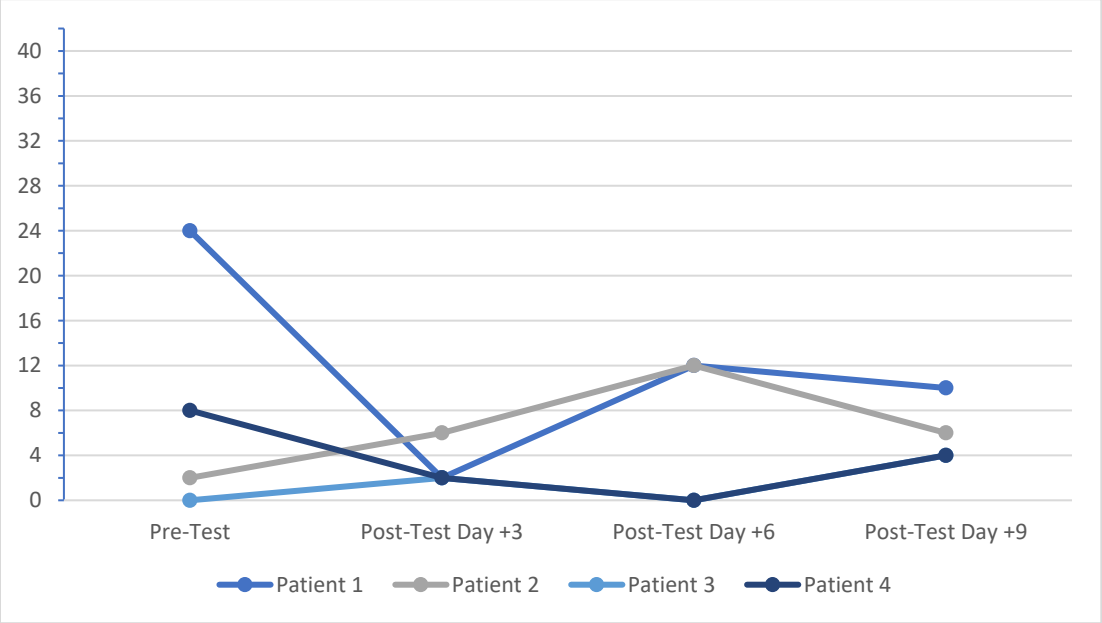


Psychosocial Well-being

Regarding the depression subscale scores from the DASS-21, the four patients' self-reported level of depressive symptoms varied, which is illustrated in Figure 2. Patient 1 reported depressive symptoms that indicated "severe depression" prior to infusion, followed by scores that indicated "mild depression" for all post-infusion measures. Both Patient 2 and Patient 3 ultimately reported increased depressive symptoms when comparing pre- and post-CAR T-cell therapy scores, however their final scores on post-test day +9 indicated a "normal" level. Lastly, Patient 4 maintained scores that indicated a "normal" range throughout their CAR T-cell therapy experience, with scores ultimately decreasing from pre-infusion to pre-discharge. Overall, from pre-infusion to post-infusion day +9, the scores of Patient 1 and Patient 4 decreased, whereas the scores of Patient 2 and Patient 3 increased. In summary, one patient out of four scored above the "normal" range for the depression subscale prior to their discharge.

Figure 2

Depression Subscale Scores

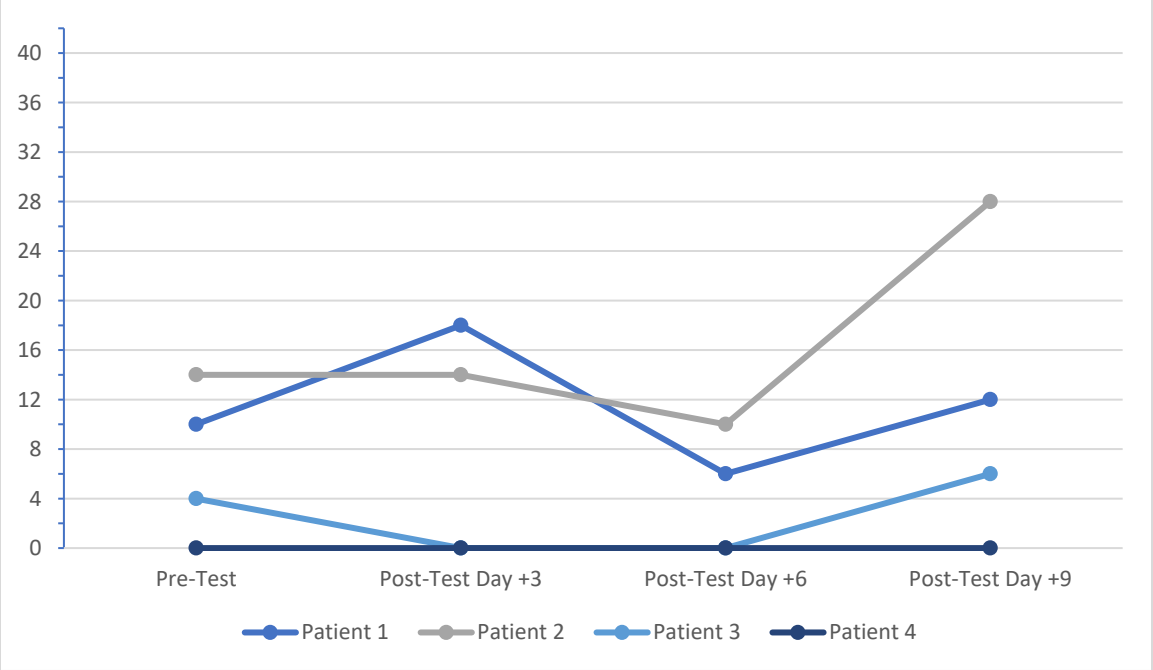


Regarding the anxiety subscale, each of the patients' scores fluctuated throughout their inpatient stay as shown in Figure 3. Patient 1 reported anxiety symptoms that indicated "moderate" anxiety pre-infusion, which then increased to indicate "severe anxiety" three days after infusion. This patient then reported anxiety symptoms that indicated a "normal" range of anxiety symptoms on day +6, and ultimately reported anxiety symptoms in the "moderate" range on day +9 after CAR T infusion. Patient 2 experienced "moderate" anxiety symptoms pre-infusion, on post-infusion day +3, and post-infusion day +6. This patient's final score on post-infusion day +9 indicates "extremely severe anxiety" prior to discharge. Patient 3 reported anxiety symptoms in the "normal" range pre-infusion, followed by no anxiety symptoms on day +3 and day +6. This patient then reported anxiety symptoms in the "normal" range again prior to discharge. Patient 4 reported no anxiety symptoms throughout CAR T-cell therapy during inpatient admission. Overall, Patient 1, Patient 2, and Patient 3 reported

an increased number of anxiety symptoms from pre-infusion to post-infusion day +9, with two out of four patients scoring within the range for “moderate” anxiety or “extremely severe” anxiety.

Figure 3

Anxiety Subscale Scores

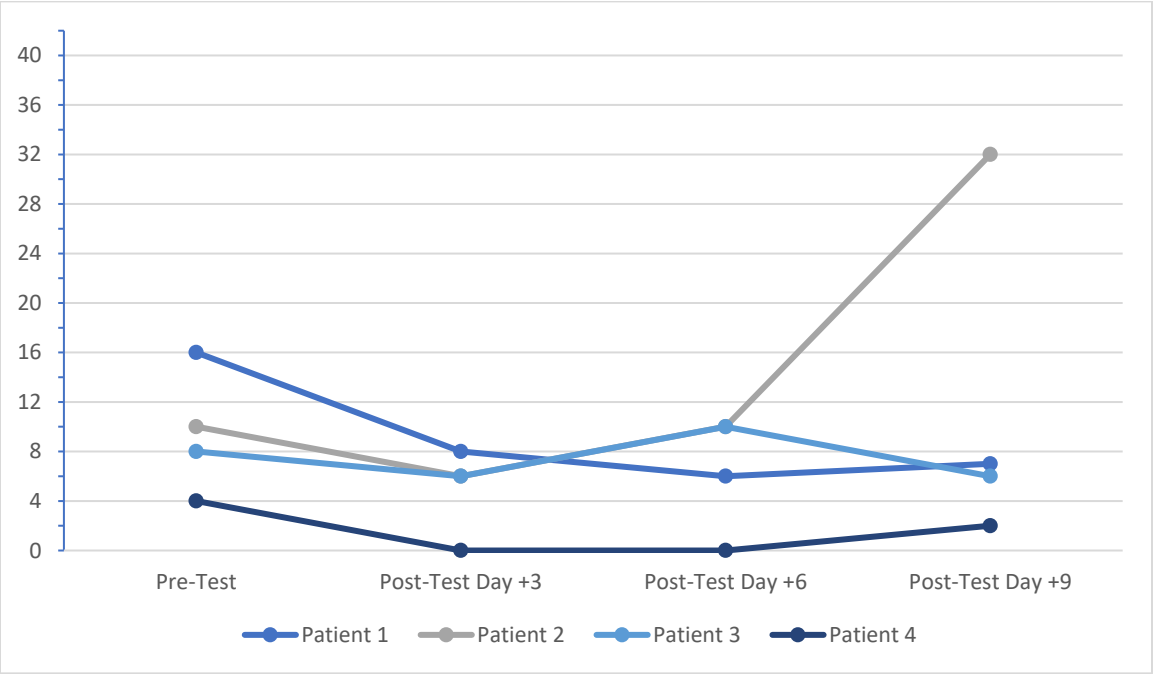


Similarly to the other subscales of the DASS-21, the stress subscale scores varied amongst patients, demonstrated by Figure 4. Patient 1 reported stress symptoms that indicated “mild stress” pre-infusion, then decreased to the “normal” range at all post-infusion data points. Patient 2’s stress scores initially indicated “normal” levels of stress, however ultimately increased to indicate “severe stress” levels on post-infusion day +9. Patient 3 and Patient 4 reported stress symptoms in the “normal” range throughout inpatient admission. Overall, Patient 1, Patient 3, and Patient 4 experienced a decrease in stress scores from pre-infusion to post-infusion day +9. However, Patient

2 experienced a significant increase in stress symptoms resulting in “severe stress” from pre-infusion to post-infusion day +9.

Figure 4

Stress Subscale Scores

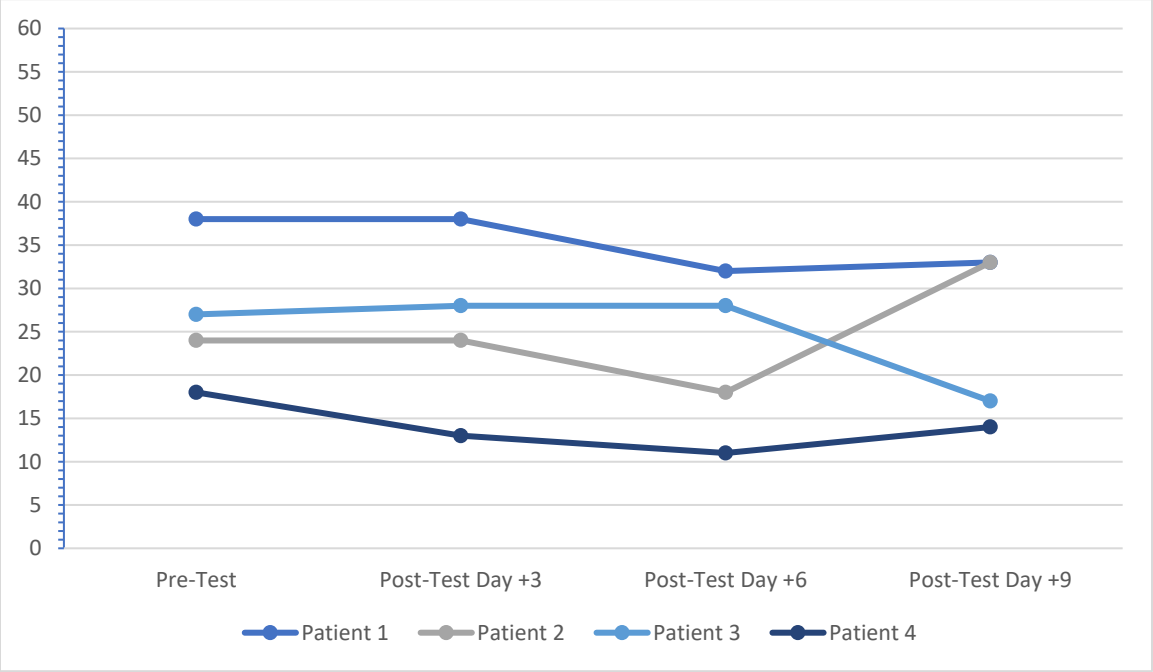


Fatigue Levels

Figure 5 depicts the participants’ cancer-related fatigue levels according to their composite scores on the Cancer Fatigue Scale. Each patient’s experience of their perceived fatigue levels varied throughout their inpatient experience with CAR T-cell therapy. Patient 1, Patient 3, and Patient 4 reported decreased fatigue levels from pre-infusion to post-infusion day +9, however scores varied throughout. In contrast, Patient 2 reported increased fatigue levels from pre-infusion to post-infusion day +9 by nine points on the Cancer Fatigue Scale.

Figure 5

Cancer Fatigue Scale Scores



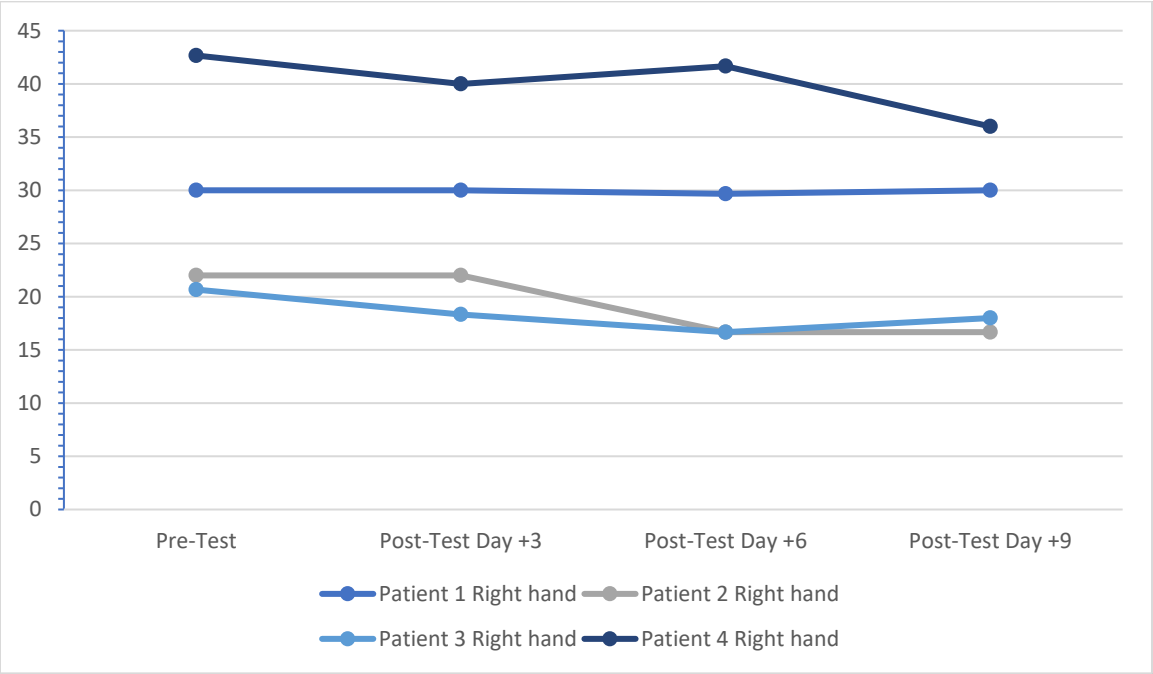
Grip Strength

Figure 6 summarizes participants' average scores for right-hand grip strength as measured using a dynamometer, as all patients were right-hand dominant. Changes in grip strength yielded the most consistent results of all outcome measures used, with a decrease in grip strength in three of four patients. Patient 1 is the only patient observed with no change in grip strength with the right hand. Patient 2, Patient 3, and Patient 4 all experienced a decrease in grip strength from their initial score. Regarding normative data for age and gender, three of four patients scored between one to three standard deviations below the mean. Specifically, prior to discharge, Patient 2's grip strength was two standard deviations below the mean with her right hand and three standard deviations below the mean with her left hand, respective to normative data for age and gender (Wang et al., 2018). Grip strength scores for Patient 3 and Patient 4 prior to

discharge were one standard deviation below the mean with both hands, respective to normative data on age and gender (Wang et al., 2018).

Figure 6

Grip Strength Scores



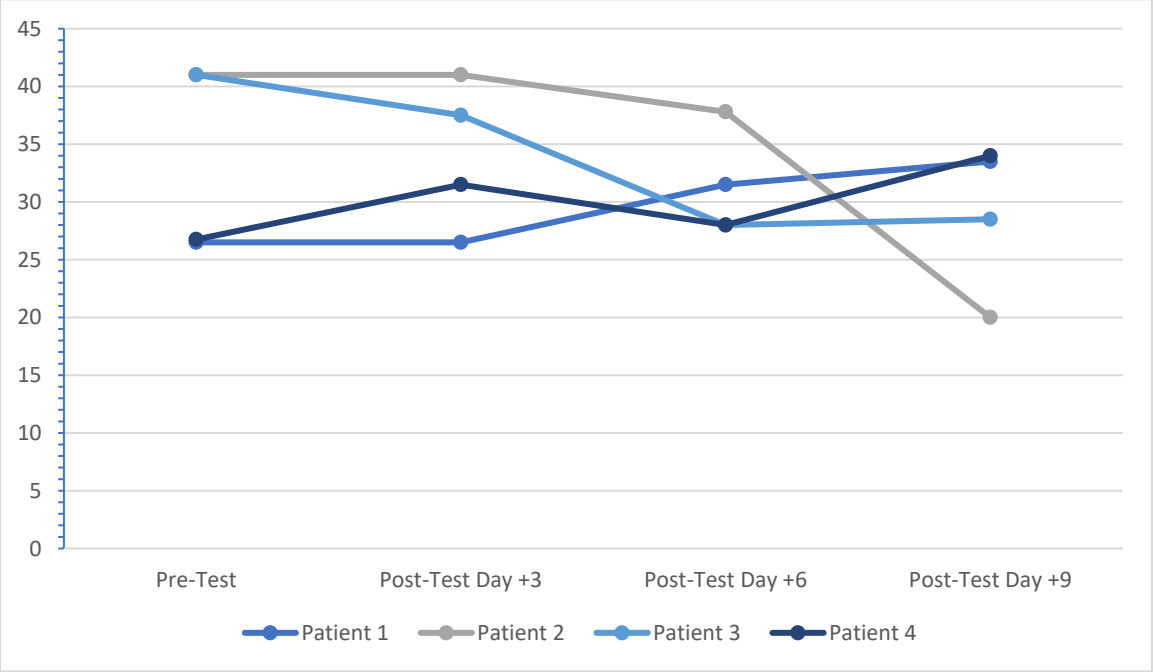
Functional Balance

Consistent with other outcome measures used in this study, scores on the Functional Reach Test varied, as illustrated by Figure 7. Patient 1's Functional Reach Test scores fell below the normal range when outcome measures were assessed pre-infusion, post-infusion day +3, and post-infusion day +6. However, this patient's Functional Reach Test score ultimately fell within the norms for age and gender on post-infusion day +9. Patient 2's scores were above or within the norms for age and gender pre-infusion, post-infusion day +3, and post-infusion day +6, however fell significantly below the norms by post-infusion day +9. Patient 3's scores fell within the norms pre-infusion and post-infusion day +3, however fell below the norms on post-infusion day +6

and post-infusion day +9. Patient 4's Functional Reach Test scores fell below the norms for age and gender pre-infusion, post-infusion day +3, and post-infusion day +6, however ultimately fell within the normal range for age and gender on post-infusion day +9. To summarize overall trends, Patient 1 and Patient 4's scores on the Functional Reach Test increased from pre-infusion to post-infusion day +9, whereas Patient 2 and Patient 3's scores on the Functional Reach Test decreased from pre-infusion to post-infusion day +9 and fell below norms for gender and age.

Figure 7

Functional Reach Test Scores



ADL Performance

Overall, patient ADL performance showed little change throughout CAR T-cell therapy as scored on the AM-PAC. Patient 1 required stand-by assistance (score of 23 out of 24) pre-infusion and on post-infusion day +3, and ultimately was independent with ADLs on post-infusion day +6 and post-infusion day +9. The remaining three patients

were all independent with basic ADL performance throughout their inpatient stay according to the AM-PAC scale.

ICE Score

As measured daily by the medical team, each patient's ICE score remained a score of 10 out of 10 possible points throughout their inpatient admissions, which indicates "no impairment".

Discussion

While each patient's experience of CAR T-cell therapy differed, common trends in functional status were explored in this study. Due to the small sample size of this study, conclusions cannot be drawn from statistical analyses, however the trends drawn between pre-infusion and post-infusion day +9 provide insight into how the experience of CAR T-cell therapy may affect patients' functional status and psychosocial performance. To summarize trends in cognition, two patients experienced an increase in their MoCA score, while two patients experienced a decrease in their MoCA score that fell below the established normal range. More specifically, one patient's score was associated with mild cognitive impairment, and one patient's score was associated with moderate cognitive impairment at time of discharge. This finding supports the current literature investigating the potential impacts of CAR T-cell therapy, in which 40% of patients self-report cognitive difficulties that negatively impact their physical and mental health, as well as interfere with the ability to engage in their typical daily routine (Whisenant et al., 2021). Specifically, it has been found that cognitive symptoms are common following CAR T-cell therapy, especially in the acute stage (<2 weeks) following infusion (Kazzi et al., 2023). Furthermore, the findings in this study suggest

that attention is the area of cognition most affected by CAR T-cell therapy, and further studies with larger sample sizes should include additional exploration into the impact on each cognitive domain. Studies suggest that perceived cognition significantly worsens in multiple cognitive domains from 90 days to 360 days after CAR T-cell therapy, including global cognition, memory, language, organization, and divided attention (Barata et al., 2022), highlighting the need for further research on the long-term effects of CAR T-cell therapy. While the MoCA assesses these identified impacted areas of cognitive function, further research may be indicated to determine if the MoCA is the most appropriate cognitive assessment to be used with this population. Cognitive function is necessary to engage in daily activities, and this finding corroborates the current literature findings that the most commonly reported cognitive symptoms after CAR T-cell therapy include memory deficits, difficulty finding words, impaired attention, impulsivity, and emotional lability (Obaisi et al., 2022).

Most significantly, the findings of this study indicate that CAR T-cell therapy has the potential to affect cognition, which contrasts with the trend seen in ICE scores across patients, as assessed and measured by the medical team. Each patient maintained an ICE score throughout inpatient admission that indicates “no impairment” due to neurotoxicity (Lee et al., 2019). However, this study suggests that multiple areas of cognitive function have the potential to be significantly impacted by CAR T-cell therapy, which highlights why occupational therapy services and assessments are increasingly important to use with this population, as the measures used in this study identified impaired cognitive areas that the ICE assessment did not detect. The findings of this study are supported by the literature, which suggests that the ICE score can lack

sensitivity to cognitive deficits due to its brevity (Kazzi et al., 2023). Studies have shown that patients' ICE scores have the potential to be incongruent with the cognitive deficits experienced in the acute stage after CAR T-cell therapy, and the use of alternative cognitive screening tools such as the MoCA is indicated (Kazzi et al., 2023).

Additionally, this study found that several patients experienced increased depression, anxiety, and stress symptoms after CAR T infusion that were categorized as above the normal range, whether mild, moderate, severe, or extremely severe. These findings support the current literature, which has found that the physical and cognitive deficits experienced after CAR T-cell therapy are associated with decreased mental health, as evidenced by half of patients reporting at least one negative psychosocial/emotional symptom, including anxiety and depression, after CAR T infusion (Ruark et al., 2020). This highlights the importance of occupational therapy services for this population, as OTPs can evaluate and design interventions to address the psychosocial and emotional symptoms many individuals experience following cancer treatment, such as CAR T-cell therapy. Psychosocial interventions, as implemented by OTPs, have been shown to improve quality of life and reduce anxiety and depression in oncology patients and survivors (Hunter et al., 2017, Newman et al., 2024).

To summarize trends in cancer-related fatigue, three patients reported decreased cancer-related fatigue, while one patient reported increased cancer-related fatigue levels from pre-infusion to pre-discharge by nine points on the Cancer Fatigue Scale. This significant increase in cancer-related fatigue as seen with one patient is supported by the current literature base, which has found that fatigue is one of the most common

symptoms experienced after CAR T-cell therapy, and that cancer-related fatigue contributes to decreased physical functioning that interferes with the ability to engage in meaningful daily activities (Ruark et al., 2020; Stenson et al., 2022). The CFS has been validated to assess fatigue from a multi-dimensional standpoint, addressing the physical, affective, and cognitive dimensions of cancer-related fatigue. The physical subscale of the CFS has established convergent validity with the Eastern Cooperative Oncology Group (ECOG) Performance Status Scale, which describes a patient's level of function based on their physical ability, daily activity, and ability to care for oneself (Okuyama et al., 2000). Therefore, the finding that CAR T-cell therapy has the potential to increase an individual's cancer-related fatigue according to the CFS suggests that the resulting physical fatigue can interfere with an individual's physical functioning and daily activities. OTPs can address fatigue using evidence-based interventions, such as energy conservation strategies and exercise programs (Kim et al., 2022; Newman et al., 2024). The CFS has also established convergent validity with the Hospital Anxiety and Depression Scale (HADS), which indicates that cancer-related fatigue is associated with emotional distress (Okuyama et al., 2000). The trends explored in this study support the literature, as the patient with an increase in cancer-related fatigue after CAR T infusion also experienced anxiety levels in the "extremely severe" range and stress levels in the "severe" range. Additionally, other sources of literature demonstrate that patients identify fatigue as the most emotionally distressing symptom after CAR T infusion (Ruark et al., 2020). Further research with a larger sample size is necessary to explore this relationship.

One of the most notable and consistent findings in this study was grip strength, in which three patients experienced a decrease in grip strength when comparing their initial and final scores with both their dominant and non-dominant hands. Specifically, two of the patients' grip strength with both upper extremities fell below the mean for age and gender prior to discharge. Grip strength is highly correlated with length of hospital stay, frailty, and fall risk with patient populations other than the cancer population (Marano et al., 2022; Neri et al., 2021; Pham et al., 2023). Concerning the cancer population specifically, decreased grip strength has been associated with poorer outcomes including reduced functional status (Hadzibegovic et al., 2023; Xie et al., 2022), depression (Zhang et al., 2022), impaired health-related quality of life (Campos E Silva et al., 2022; Paek & Choi, 2019), and increased mortality risk (Hadzibegovic et al., 2023; López-Bueno et al., 2022). Therefore, patients whose grip strength falls below the norms for age and gender after CAR T-cell therapy may be at increased risk for poorer outcomes, contributing to potentially longer admissions and increased post-treatment complications. OTPs can play a key role in evaluating and addressing frailty in the oncology population in order to mitigate the effects that frailty may have on overall function and hospital admission, including length of stay (Goede, 2023; Welford et al., 2022).

According to the Functional Reach Test, a score of 6 inches or less indicates a significantly increased risk for falls, and a score between 6 and 10 inches indicates a moderate risk for falls. One patient in this study had a Functional Reach Test score of 7.87 inches on post-infusion day +9, indicating a significantly increased risk for falls. While none of the other patients' scores indicated moderate risk or significantly

increased risk for falls at discharge, the trends in functional balance according to the Functional Balance Test can be summarized as two patients were observed with an increase in scores from pre-infusion to post-infusion day +9, whereas two patients' scores decreased from pre-infusion to post-infusion day +9. Furthermore, two patients' scores on the Functional Balance Test fell below the norms for age and gender.

Lastly, to summarize trends in ADL performance, one patient experienced a small increase in AM-PAC scores from stand-by assistance to independent with basic ADL performance from pre-infusion to post-infusion. All other patients maintained independent scores on the AM-PAC scale throughout their admission. Although no major changes in basic ADL performance according to the AM-PAC scale were observed during inpatient admission, the aforementioned areas measured by each outcome measure impact a patient's ability to engage in activities that are meaningful and necessary. According to the current base of literature, patients self-report that the physical, cognitive, and mental health-related symptoms experienced after CAR T-cell therapy interfere with the ability to engage in daily activities, daily routines, social activities, and work (Whisenant et al., 2021), supporting the findings of this study that various areas of physical, emotional, and cognitive function can impact ability to engage in daily activities and routines.

While preliminary, the trends explored in this study support that CAR T-cell therapy has the potential to affect the following areas: cognition, psychosocial wellbeing, grip strength, balance, and fatigue—all of which can impact an individual's participation in everyday functioning and desired occupations. Although each patient's experience differed, patients reported high levels of symptoms both pre-infusion and post-infusion

that affected functional status, highlighting a need for evaluation and intervention in these areas throughout the entire process of CAR T-cell therapy in acute care, both before and after the infusion is administered.

There are various limitations in this study, most notably the small sample size. While additional patients underwent CAR T-cell therapy within the selected date range, many patients had incomplete data sets due to various reasons, which made these patients ineligible for this study. The inclusion criteria requiring patients to have complete data sets with data points from pre-infusion, post-infusion day +3, post-infusion day +6, and post-infusion day +9 specifically was necessary for standardization, however resulted in a small sample size of n=4. Therefore, conclusions using statistical analyses cannot be drawn from this study. Lastly, while the outcome measures selected have been established as valid and reliable in this practice setting, there is a possibility that the outcome measures were not sensitive enough to detect small changes in functional status for the purposes of this study. Despite these limitations, the findings of this study can serve as preliminary trends that explore the ways CAR T-cell therapy can affect functional and psychosocial well-being and highlight the need for continued research with a larger sample size. Additionally, there are indications for future research concerning the long-term functional impacts of CAR T-cell therapy by collecting outcome measures at follow-up appointments, as this study focused on short-term effects of CAR T-cell therapy during inpatient admission. This study preliminarily identified potential needs of this population and additional research is indicated to identify the best practices and interventions to be used by OTPs to address the aforementioned areas of need for this population.

Conclusion and Practice Implications

OTPs are currently involved in oncology settings and can have a profound impact in addressing cancer-related disability and improving quality of life. However, there is a lack of awareness and understanding of the role that occupational therapy can serve with the CAR T-cell therapy patient population specifically (Obaisi et al., 2022). The aim of this review was to explore the specific needs of the CAR T-cell therapy population and further highlight the role occupational therapy can have in addressing the areas of deficit explored by this study.

The findings of this study are valuable as they provide insight into the lived experience of individuals who undergo CAR T-cell therapy and provide further understanding of the functional and psychosocial impacts of this therapy. According to the trends explored in this study, CAR T-cell therapy affected several of the patients' cognition, psychosocial wellbeing, grip strength, balance, and fatigue levels. These areas are all primary areas of need that OTPs can evaluate and create tailored intervention plans to address across the continuum of care. This study established potential areas of focus that OTPs in the acute care oncology setting can focus on during evaluation and to support intervention planning.

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