

# Exploring the cooperation between rehabilitation medicine and CAR-T cell therapy for enhanced cancer treatment

**Boyuan Zhao**

The First Clinical Medical College, Harbin Medical University, Harbin, 150000, China

zhaoboyuan@mail.sdufe.edu.cn

**Abstract.** The most common cause of death worldwide is cancer, and the sophisticated and aggressive medications used to treat it can have serious side effects and limitations. Immunotherapy known as chimeric antigen receptor T-cell (CAR-T) therapy has become a viable treatment option for some cancers, notably hematologic malignancies. However, it is linked to a number of adverse effects that may have a detrimental influence on patients' quality of life and access to care. Because it focuses on recovering patients' functional abilities and enhancing their quality of life rehabilitation medicine is essential to the treatment of cancer. This literature review aims to explore the cooperation between them to achieve better cancer treatment outcomes. This literature review will analyze and evaluate the literature on side effects of CAR-T Cell Therapy, the role of rehabilitation medicine in cancer treatment, and the rationale behind combining these two approaches for improved cancer treatment.

**Keywords:** rehabilitation medicine, CAR-T cell therapy, physical therapy.

## 1. Introduction

Cancer is a leading cause of death worldwide, and its treatment often involves complex and aggressive therapies that can lead to significant side effects and impairments. CAR-T cell therapy, a form of immunotherapy, has emerged as a promising treatment option for certain types of cancer, particularly hematologic malignancies. However, it is associated with various side effects, which can negatively impact patients' quality of life and treatment affordability. Rehabilitation medicine plays a vital role in cancer treatment because it focuses on restoring patients' functional capabilities and improving their quality of life, as well as side effects that occur during CAR-T cell therapy. This literature review aims to explore the cooperation between them to achieve better cancer treatment outcomes. Combining two approaches for cancer care has recently gained attention. Evaluating the side effects of CAR-T cell therapy in cancer treatment and the role of rehabilitation medicine is essential in improving cancer care. This review analyzes the relevant literature to understand the rationale behind this combination.

## 2. Literature review

Helaine reviewed the case of a 62-year-old man who received CAR T-cell therapy for diffuse large B-cell lymphoma. The patient developed severe side effects from the medication, such as neurotoxicity and cytokine release syndrome (CRS), which necessitated hospitalization and extensive care. The research emphasizes the value of physical therapy in the care of CAR T-cell treatment patients.

Helaine explains how physical therapy therapies like mobility training, breathing exercises, and range-of-motion training can help avoid and manage treatment-related side effects like respiratory distress, exhaustion, and respiratory muscle weakness. The results of this patient's physical therapy interventions are also discussed in the publication. The Eastern Cooperative Oncology Group (ECOG) Performance state scale, which gauges a patient's capacity to carry out everyday tasks, was used to evaluate the patient's functional state. The patient's ECOG score prior to physical therapy was 4, meaning he was bedridden and unable to perform any activity. After physical therapy the patient's ECOG score increased to 2, indicating that he was able to perform some activities of daily living. The 6-minute walk test (6MWT) measures how far a patient can walk in 6 minutes and is also used to assess a patient's gait behavior. Prior to receiving physical therapy, the patient could barely walk 25 feet. The patient was able to walk 150 feet after physical treatment, an increase of 125 feet. This research emphasizes the value of early intervention and the necessity of patient care that is multidisciplinary. The improvements in this patient's functional status and walking abilities offer as further evidence of the potential advantages of physical therapy interventions in enhancing patient outcomes [1].

Michael Fediw examines the effects of rehabilitation medicine on CAR T-cell therapy. He starts by giving a general summary of CAR T-cell therapy, including its possible advantages as well as any difficulties or negative consequences that can arise. CAR T-cell therapy often results in adverse reactions such as cytokine release syndrome (CRS), leading to flu-like symptoms, fever, and exhaustion. However, rehabilitation medicine can help patients deal with these side effects and improve their general well-being. Physical therapy, occupational therapy, and other interventions are some of the ways that rehabilitation medicine can help manage these symptoms. CAR T-cell therapy can cause different adverse effects, including neurotoxicity, which can lead to neurological symptoms like disorientation and convulsions. Nevertheless, patients can benefit from physical therapy by recovering their strength and mobility, while occupational therapy can enhance overall functioning and help them perform daily tasks. Through cognitive and speech therapy as well as other therapies, rehabilitation medicine can assist in managing these symptoms. The study discusses the importance of early intervention in enhancing a patient's general quality of life by treating cognitive function and attention through cognitive therapy and improving speaking ability via speech therapy. Patients could benefit from cognitive therapy to regaining cognitive function and enhancing memory and attention, while speech therapy could assist in communication. Rehabilitation Medicine can assist patients in recovering more rapidly and successfully from this novel cancer treatment by offering early intervention and a wide range of services [2].

### **3. What is CAR-T cell therapy**

Immunotherapy, namely CAR-T cell therapy, has demonstrated encouraging outcomes in the treatment of some cancers [3]. The treatment entails genetically altering a patient's own T cells, a crucial type of white blood cell in the immune system that can identify and combat cancer cells.

The first step in CAR-T cell treatment is to draw T cells from patient's blood. Then, in a lab setting, these cells are genetically altered to express CARs. These CARs are made to target particular antigens, or proteins, that are found on the surface of cancer cells [3].

The T cells are altered and then put back into patient's bloodstream so that they can hunt down and kill cancer cells. It is hoped that these altered T cells will be better able to identify and eliminate cancer cells than the patient's own immune system.

The use of CAR-T cells in the treatment of leukemia and lymphoma, two kinds of blood cancer, has shown great promise. The therapy has been demonstrated in clinical trials to result in high percentages of remission in individuals who have not responded to prior therapies [3].

CAR-T cell therapy is a very young and experimental medicine, although it has great potential. Long-term safety and effectiveness of the treatment remain unresolved amidst the possibility of harmful consequences like neurotoxicity and cytokine release syndrome.

## **4. Side effects of CAR-T cell therapy**

### *4.1. Multiple toxicities*

Here are the negative influences of the therapy: cytokine release syndrome (CRS), neurotoxicity, and other effects which are of less incidence. 77% of patients receiving the treatment experienced CRS, with 46% experiencing grade 1 or 2 CRS and 31% experiencing grade 3 or higher CRS. Life-threatening complications can be caused by various side effects, including neurotoxicity. Up to 40% of individuals experience this type of toxicity, with roughly 13% of them experiencing grade 3 or higher severity [2]. Along with neurotoxicity, there are other potential side effects, such as immune-mediated, hematologic, and organ toxicity, which may also require immediate intervention and identification to avoid severe consequences [4, 5].

### *4.2. Cytokine release syndrome (CRS)*

The rapid release of cytokines by activated CAR-T cells causes CRS, an inflammatory response in the body that manifests as symptoms like fever, hypotension, and respiratory distress [6]. Immunosuppressive drugs like tocilizumab work to target the interleukin-6 receptor, which is crucial in severe CRS cases that can range from moderate to potentially fatal. Intensive care may be required for such cases [4].

### *4.3. Neurological toxicities*

In patients who have undergone the therapy, neurological toxicities have been identified [5]. These toxicities are thought to arise from the introduction of CAR-T cells into the central nervous system, which leads to inflammation and disruption of neuronal activity [7]. To address these neurotoxicities, possible solutions include administering corticosteroids, antiepileptic medications, and supportive care that entails hydration and replacement of electrolytes [5].

### *4.4. Hematologic, organ, and immune-mediated toxicities*

Patients receiving therapy may encounter various toxicities, including hematologic ones like anemia, neutropenia, and thrombocytopenia. These could raise the danger of infection or bleeding. Meanwhile, organ toxicities like nephrotoxicity and hepatotoxicity could happen to some patients, along with immune-mediated toxicities like graft-versus-host disease and autoimmune hemolytic anemia. It's important to catch these serious side effects early on for timely and life-saving intervention. These points are underpinned by sources [4, 5].

## **5. Role of rehabilitation medicine**

Cancer treatment can often result in physical, psychological, and social issues, and that's where rehabilitation medicine comes in. It's a crucial aspect of cancer care because it targets those impairments and works to make things better. A team of experts, including occupational, physical, and speech therapists, along with those providing psychosocial support and pain management, work together to provide the best care possible.

### *5.1. The role of physical therapy*

In the realm of cancer recovery, physical therapy is a crucial component as it serves to combat weaknesses in endurance, strength, and flexibility, as well as facilitate pain and lymphedema control. Physical therapists can develop individualized exercise programs to help patients regain their functional abilities and improve their quality of life [8]. In cancer patients and survivors, exercise interventions have been proven to reduce cancer-related fatigue and enhance emotional well-being, while also improving their physical functioning [9].

### *5.2. Occupational therapy*

Patients' ability to carry out activities of daily living, such as self-care, employment, and leisure time, is the primary aim of occupational therapy [10]. Occupational therapists can provide adaptive equipment, environmental modifications, and energy conservation techniques to help patients overcome their functional limitations and maintain their independence.

### *5.3. Speech therapy*

Speech therapy is essential for patients with communication and swallowing difficulties resulting from cancer or its treatment, such as head and neck cancer or neurotoxicities from CAR-T cell therapy. Speech therapists can provide strategies to improve speech clarity, voice quality, and swallowing function, as well as address cognitive-communication impairments.

### *5.4. Psychosocial support*

A cancer patient's journey requires a multifaceted approach whereby the physical, psychological, and social deficiencies resulting from cancer and its remedies are tackled. This necessitates rehabilitation medicine, which includes physical, occupational, and speech therapy. The process is an all-encompassing one and is supplemented by psychosocial support and pain management to ensure holistic care.

### *5.5. Pain management*

Pain management is another critical component of cancer rehabilitation, as pain is a common and debilitating symptom experienced by cancer patients. Examples of pharmacological interventions used in pain management strategies include analgesics and anti-inflammatory drugs. In addition, non-pharmacological methods such as meditation, acupuncture, and physical therapy are also utilized.

## **6. Integrating physical therapy with CAR-T cell therapy**

Physical therapy, as a vital component of rehabilitation medicine, is vital in assisting patients undergoing CAR-T cell therapy throughout their cancer treatment journey. The successful outcome of treatment can be improved by physical therapy as it targets the hinderance therapy causes to patients. Through addressing their physical impairments and functional limitations, physical therapy contributes to the betterment of patients' quality of life and expedites their recovery. The importance of rehabilitation medicine in cancer treatment and the justification for integrating rehabilitation medicine and CAR-T cell therapy in cancer treatment will be connected in this part, which will also provide examples of how physical therapy might support CAR-T cell therapy through cancer treatment.

### *6.1. Managing side effects with physical therapy*

Physical therapy can help patients manage the side effects of CAR-T cell therapy by providing targeted interventions to address the specific impairments caused by the treatment. For example:

*6.1.1. CRS.* The encouragement of functional recovery and the treatment of symptoms can be possible with physical therapy. It has the potential to be extremely important. To improve cardiovascular fitness and endurance, physical therapy has one of its primary aim for patients with CRS. All in all, the improvement of overall cardiovascular health, reducing inflammation, and increased blood flow can be achieved by aerobic exercise, such as cycling or walking. Additionally, it has been demonstrated that aerobic exercise improves immunological function, which may be especially advantageous for patients receiving CAR-T cell therapy. Impairments associated with CRS can be tackled through physical therapy, along with regular cardio workouts. For example, patients may experience muscle weakness and atrophy due to prolonged bed rest or the use of corticosteroids to manage CRS symptoms. Targeted strengthening exercises, such as resistance training, can help improve muscle strength and function, ultimately supporting patients' return to their daily activities.

*6.1.2. Hematologic toxicities.* CAR-T Cell Therapy can cause patients to experience reduced exercise tolerance, weakness, and fatigue due to anemia, thrombocytopenia, and neutropenia [4]. Physical therapists can develop individualized exercise programs to help patients regain their strength, endurance, and functional abilities. Improvement in cardiovascular fitness and reduction in fatigue can be achieved through aerobic exercises such as cycling or walking. Additionally, muscle strength can be enhanced and muscle wasting prevented by doing resistance training [8].

*6.1.3. Neurological toxicities.* Physical therapists can offer assistance to those with neurological setbacks such as seizures, encephalopathy, or aphasia, which can hinder mobility, coordination, and balance [5]. Through gait, balance, and proprioceptive exercises, they can help improve overall mobility and reduce the probability of falls to ensure greater stability.

*6.1.4. Immune-mediated toxicities.* Immune-mediated toxicities, such as graft-versus-host disease, which can cause joint discomfort, stiffness, and limited range of motion, can occasionally result from CAR-T cell therapy [5]. Physical therapists can offer joint mobilization, stretching exercises, and modalities such as heat or cold therapy to alleviate pain, improve joint mobility, and restore normal function.

#### *6.2. Promoting recovery and preventing long-term disabilities*

By including rehabilitation services early in the cancer care continuum, physical therapy can play a vital role in encouraging recovery and preventing long-term impairments in patients receiving CAR-T cell therapy. By providing early intervention and monitoring patients' functional abilities throughout the treatment process, physical therapists can help patients maintain their functional abilities and prevent the development of long-term disabilities [11].

*6.2.1. Pre-treatment assessments and baseline functional evaluations.* For example, physical therapists can provide pre-treatment assessments and baseline functional evaluations to identify patients' strengths and weaknesses before starting CAR-T Cell Therapy. In order to ensure that each patient receives the most suitable and efficient care possible throughout their treatment, this information can help build up personalized exercise plans that are suited to their individual needs.

*6.2.2. Collaborative approach in monitoring patients' progress.* Physical therapists can work closely with the oncology team to monitor patients' progress during CAR-T cell therapy and adjust their rehabilitation interventions as needed. This collaborative approach can help identify and address any emerging impairments or functional limitations early on, facilitating patients' recovery and enhancing their overall treatment outcomes.

In conclusion, physical therapy could be notably involved in assisting CAR-T cell therapy through cancer treatment by addressing the side effects of the treatment, promoting recovery, and preventing long-term disabilities. The integration of physical therapy into the cancer care continuum can contribute to the overall success of CAR-T Cell Therapy and improve patients' quality of life.

### **7. Rationale for combining rehabilitation medicine and CAR-T cell therapy in cancer treatment**

Incorporating both CAR-T Cell Therapy and rehabilitative medicine for the treatment of cancer could bring about positive results. Dealing with the adverse effects of CAR-T Cell Therapy can improve the quality of life and the treatment results of patients. Rehabilitation medicine can help manage the toxicities associated with CAR-T cell therapy by providing early intervention and targeted therapies to address the specific impairments brought on by the treatment. For instance, speech therapy helps treat communication and swallowing issues brought on by neurological toxicities, while physical therapy might assist patients in regaining their strength and stamina after enduring hematologic toxicities.

### *7.1. Integration*

Integrating rehabilitation into the cancer care continuum can help patients maintain their functional abilities and prevent the development of long-term disabilities [11]. Improving patients' quality of life is possible through early participation in rehabilitation activities, which hastens their recovery and boosts their ability to participate in daily activities like work and play.

### *7.2. Addressing psychosocial aspects*

Patients receiving CAR-T cell therapy must address the psychosocial components of cancer care because the process can be emotionally taxing and distressing [5]. With access to therapy, support networks, and stress-reducing techniques, patients can improve their emotional health and overall wellness.

### *7.3. Personalized cancer care*

Each patient's unique needs can be met with personalized cancer care, thanks to cooperation that can lead to tailored rehabilitation interventions [11]. By considering factors such as comorbidities, functional impairments, and treatment goals, individualized care plans can be developed to provide the most effective treatment possible. This level of personalized care is crucial for successful patient outcomes.

### *7.4. Improved cost-effectiveness*

Because early treatment of side effects and impairments can delay the emergence of long-term problems and lessen the need for more extensive and expensive interventions, combining rehabilitation medicine with CAR-T cell therapy in cancer treatment can increase cost effectiveness [11]. By enhancing patients' quality of life and functional abilities, the financial burden of cancer treatment can be lessened while also allowing them to participate in social activities and return to work.

## **8. Conclusion**

In conclusion, there is a lot of potential for improving cancer treatment outcomes and raising patients' quality of life through collaboration between rehabilitative medicine and CAR-T cell therapy. Rehabilitation medicine can be extremely helpful in speeding up patients' recovery and averting permanent disabilities by addressing the side effects of therapy and offering patients specialized therapies to control their impairments. By incorporating them into cancer care, they can help create individualized, affordable treatment plans that ultimately enhance patient outcomes and quality of life. Future research should focus on increasing the evidence-based evidence for the combination of rehabilitation medicine and CAR-T cell therapy in cancer treatment, expanding the sample size of such experimental cases, and applying them to formulate personalized strategies from the perspective of patients themselves. Research should also look into ways to use telemedicine and digital health technology to make rehabilitation programs more easily accessible and delivered to cancer patients getting CAR-T cell therapy.

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