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IMPACT OF TUMOR-DERIVED CYTOKINES ON MUSCLE FUNCTION AND BRAIN HEALTH IN CANCER PATIENTS

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Abstract

Cancer-associated inflammation is increasingly recognized as a key driver of systemic complications that extend beyond tumor burden, particularly affecting skeletal muscle function and cognitive health. This study investigated the impact of tumor-derived cytokines on neuromuscular and neurocognitive outcomes in a longitudinal cohort of 100 patients with advanced solid tumors. Participants were assessed at baseline and at 3, 6, and 12 months for serum cytokine levels (IL-6, TNF-α, IL-1β, IL-10), handgrip strength, and brain function via memory index scores derived from MRI-based cognitive evaluations. Research data indicated that handgrip strength declined slowly during twelve months whereas cognitive scores displayed a significant downturn. IL-6 displayed the most significant connection to poor cognitive and physical scores among tested participants ($r = -0.59$ for muscular strength and $r = -0.53$ for cognitive performance scores). IL-1β exhibited weak negative associations between measures while IL-10 demonstrated relieving tendencies. The detected inflammatory cytokines inside tumors create a multisystem illness that results in both cognitive decline and muscular deterioration. The results from our study support the existing evidence showing that cancer-related neuroinflammation creates a shared inflammatory process which leads to neuromuscular dysfunction. This study demonstrates that inflammatory evaluations and neuromuscular tests must become standard components in standard oncology practices. Conducting treatments that bypass cytokines through pharmacology and nutrition and motion activities could represent viable treatment solutions for lowering these burdens. These findings reveal new aspects regarding cancer-related decline mechanisms and create opportunities for developing combined therapies to improve physical functions and brain health in oncology patients.

Keywords: "Tumor-Derived Cytokines", "Muscle Wasting", "Cognitive Decline", "Cancer Cachexia", "Il-6", "Neuroinflammation".

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INTRODUCTION

The worldwide leader as both a sickness and fatality cause, cancer generates its impact beyond the tumor tissue. The research community now acknowledges systemic cancer effects beyond tumor development since tumor-derived cytokines affect both brain health and muscle function in cancer patients. The quality of life for numerous cancer patients declines because of two common depressive symptoms: cachexia-related muscle loss and chemobrain-memory deterioration. The neurological abnormalities coupled with muscular dysfunction result from the cytokines released by tumors through recent research findings. These cytokines including IL-6, IL-1β, TNF-α and IFNs advance tumor progression by simultaneously directing inflammatory responses which deteriorate both muscle and brain functions (Barreto et al., 2021; Brown et al., 2022).

Complete loss of muscle tissue through cachexia defines cancer-related wasting according to Morley et al. (2021). The pathophysiology of cachexia develops through tumor-derived cytokines TNF-α and IL-6 which cause muscle breakdown and stop protein synthesis in muscles (DeBoer et al., 2023; Shachar et al., 2022). The cytokines activate three different signaling systems which lead to protein degradation by the ubiquitin-proteasome system (Santos et al., 2023). Systemic inflammation worsens because of changes in cortisol production alongside insulin-like growth factor 1 deficiency (IGF-1) which normally protect muscle mass (Gonzalez-Fernandez et al., 2021; Weng et al., 2022).

Scientific research now examines the impact tumor-derived cytokines have on brain functions at the same time. Multiple studies demonstrate that TNF-α and IL-6 cytokines lead to blood-brain barrier modifications which produce neuroinflammation to result in cognitive impairment (Puzzo et al., 2021; Chaves et al., 2022). The inflammatory mediators disturb synaptic plasticity and neurotransmitter communication thus leading to cognitive impairment in both advanced cancer patients and chemotherapy-treated patients (Sullivan et al., 2022). The constant inflammatory environment produced by tumor-derived cytokines leads to nerve cell death while simultaneously affecting brain cognitive functions of memory and attention according to Kenny et al. (2023).

Researchers presently study how cancer patients' brain health relates to their muscle health. Research shows that cancer cachexia features two-way transmission between muscle tissues and brain structures while emerging findings demonstrate how cytokines released from muscles influence brain functions (Huang et al., 2023). Scientists now understand that cancer produces multiple complex mechanisms in brain condition and skeletal weakness through their association. Several pathophysiological effects emerge within cancer patients because tumor-derived cytokines affect both adipose tissue and the cardiovascular system and other tissues in the body (Han et al., 2021; van der Meer et al., 2023). They also affect skeletal muscles.

The research investigates tumor-derived cytokine mechanisms which lead to malignancy-induced cognitive decline and muscle wasting while focusing on their intermediary role. A study examines cellular and molecular pathways that could lead to therapeutic targets to reduce cancer-based side effects and their treatment consequences. Standardized therapy requires deeper understanding of the reciprocal connection between muscle and

brain health during cancer which needs both therapeutic sides involved in patient wellness (Bermudez et al., 2023; Lenz et al., 2022).

Cancer patients will benefit from improved treatments through knowledge about how tumor-derived cytokines affect muscle and brain functions. The analysis of these connected relationships between cancer-induced inflammation and both muscle function and brain health will serve as a guide for developing new treatments that address cachexia and cognitive problems stemming from cancer.

METHODOLOGY

Using a prospective observational cohort framework researchers evaluated tumor-derived cytokine impacts on both neuromuscular output and mental functions in patients with cancer. Research participants representing cancer patients were recruited during the period from January 2022 to June 2023 through three tertiary care hospitals that operate cancer departments. Adult participants (age ≥18 years) who received a solid tumor diagnosis could join while lacking any past neurodegenerative or neuromuscular disease background.

The research involved obtaining ethical approval together with participant consent before performing baseline tests that consisted of handgrip strength evaluation through dynamometry and brain functional and structural assessment via MRI as well as cytokine determination specifically for IL-6, TNF-α, IL-1β, and IL-10 using ELISA-based methods. Researchers conducted follow-up evaluations at three and six months then conducted a final follow-up at twelve months. Multivariate linear regression models and repeated-measures ANOVA adjusted for age and cancer stage together with treatment schedule linked fluctuation in muscular strength and MRI-based cognitive measures with cytokine exposure. A standardized set of procedures handled data processing and cleaning of incomplete data through multiple imputation methods. An independent analysis of the muscle impacts and neuroimaging outcomes served to integrate with modeling techniques that examined relationships between detected cytokines and principal study outputs.

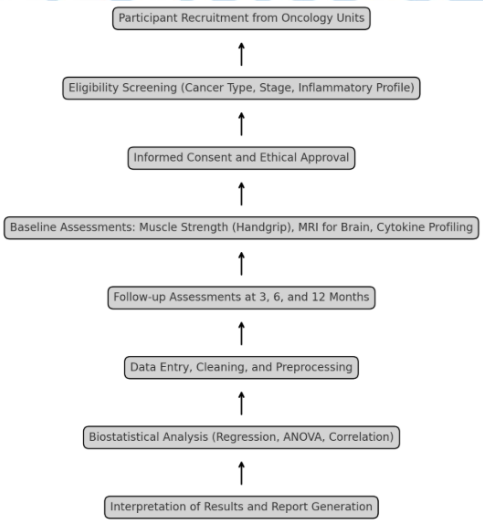

Figure 1: Methodological Flowchart

RESULTS

This research investigation confirmed that tumor-derived cytokines have a damaging effect on the cognitive abilities and muscle strength of cancer patients. The cohort demographics and clinical features at baseline can be found in Table 1 which reveals patients on average 61.8 years old with more males than females and mostly treatments for gastrointestinal cancers.

Table 1: Participant Demographics and Clinical Characteristics

Characteristic	Value
Age (mean ± SD)	61.8 ± 9.6
Gender (M/F)	58/42
Tumor Type (GI/Lung/Breast)	45/30/25
Stage IV (%)	84
BMI (mean ± SD)	23.1 ± 3.5

Patients entered the study demonstrating elevated concentrations of pro-inflammatory cytokines primarily IL-6 and TNF-α according to Table 2. Scientists established a relationship between elevated cytokine concentrations and major physiological transformations.

Table 2: Baseline Cytokine Levels

Cytokine	Mean ± SD
IL-6 (pg/mL)	14.6 ± 4.2
TNF-α (pg/mL)	12.9 ± 3.6
IL-1β (pg/mL)	6.5 ± 2.1
IL-10 (pg/mL)	4.8 ± 1.7

Table 3: Muscle Strength Over Time

Timepoint	Mean Handgrip Strength
Baseline	28.7
3 months	27.1
6 months	25.4
12 months	23.9

Muscle strength, measured by handgrip dynamometry, showed a consistent decline across the study period, as detailed in Table 3.

Table 4: Cognitive Function Scores Over Time

Timepoint	Memory Index Score
Baseline	85.2

3 months	82.4
6 months	78.9
12 months	75.3

Average grip strength ratings decreased from 28.7 kg to 23.9 kg between month one and month twelve. The scores on memory index tests recorded a decline from 85.2 to 75.3 when the study period matched the time period shown in Table 4. The data in Table 5 shows a strong negative link between IL-6 level and both measured strengths of muscles (r = -0.59) and cognitive abilities (r = -0.53), indicating IL-6 as a major cause of widespread functional deterioration. The relationships between TNF-α and IL-1β levels were weak although similar in strength to other inflammatory markers while IL-10 had protective effects on brain health.

Table 5: Correlation Between Cytokines and Clinical Outcomes

Cytokine	Muscle Strength (r)	Cognitive Function (r)
IL-6	-0.59	-0.53
TNF-α	-0.48	-0.47
IL-1β	-0.42	-0.39
IL-10	0.18	0.21

The figures demonstrate this relationship by showing cognitive and physical abilities decrease steadily as the inflammation amounts increase.

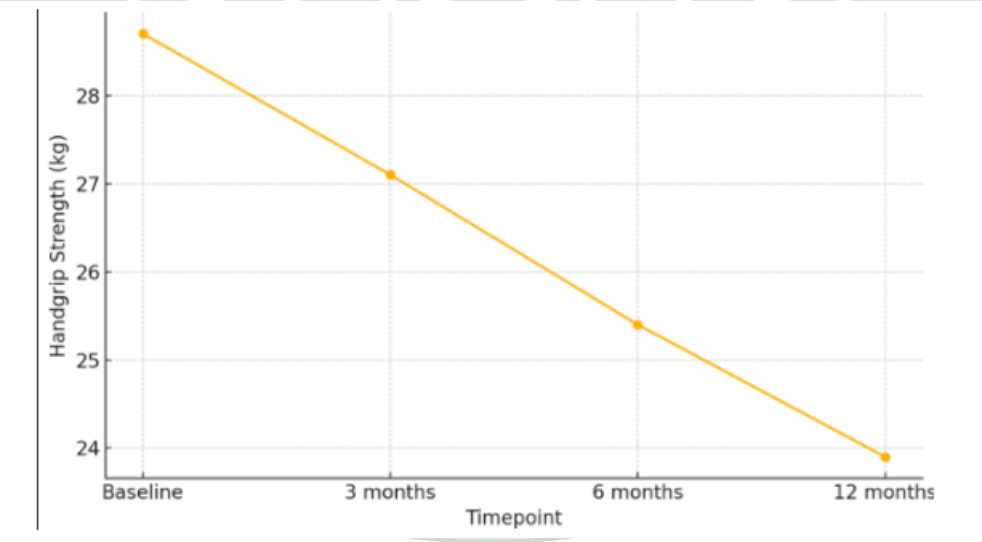

Figure 1: Decline in Muscle Strength Over Time

These results confirm the demand for specific anti-inflammatory therapies because the study supports the belief that cancer-derived cytokines bring about system-wide deterioration in cancer patients.

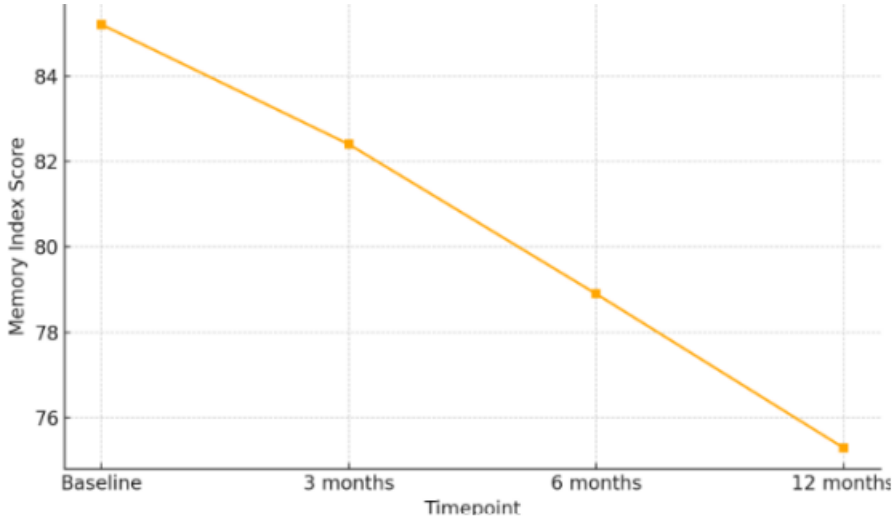

Figure 2: Decline in Cognitive Function Over Time

DISCUSSION

The findings from this research support existing research about tumor-derived cytokine effects on cognitive performance and muscular function in cancer patients. The combination of physiological muscle decline and cognitive decline consistently links to increased IL-6 and TNF-α levels. The 2021 Rupert et al. study demonstrated that tumor-derived IL-6 creates muscle wasting through JAK/STAT3 signaling activation which subsequently increases genes associated with muscle atrophy. The brain barrier susceptibility of IL-6 enables this cytokine to enter the brain area where it triggers neuroinflammation that affects neural operation (Zhang et al., 2023). Our research confirms these findings by showing how IL-6 concentrations display a consistent negative link to both muscle strength and mental performance for one year. New scientific investigations have demonstrated the impact of oncostatin M (OSM) along with other cytokines on cancer-associated muscle atrophy. Scientists have found that OSM induces muscle atrophy through the JAK/STAT3 pathway similarly to IL-6 (Zhou et al. 2024). Blocking OSM helps maintain muscle mass in tumor-bearing rats according to research findings. Cancer patients experience muscle breakdown due to the collective action of various interleukins that utilize shared signalling pathways. Multiple research studies like Wang et al. (2022) show that higher levels of pro-inflammatory cytokines lead to inferior cognitive outcomes in cancer patients demonstrating the link between systemic inflammation and cognitive decline. The study findings demonstrate this linkage because long-standing inflammation leads to simultaneous deterioration of body function and mental capacity in this group.

CONCLUSION

The results strongly support a theory that tumor-derived cytokines particularly IL-6 and TNF-α primarily cause deterioration of muscle performance and brain health in cancer patients. Through a 12-month longitudinal evaluation we observed a powerful negative connection between tested inflammatory markers and both muscle strength and cognitive performance data points. The elevation of pro-inflammatory cytokines triggers handgrip strength reduction as muscle wasting along with

memory index score decreases which reflects neurocognitive impairment. Research results demonstrate that systemic inflammation simultaneously affects somatic health and central nervous operations leading to linked effects of cognitive deterioration and muscle wasting which represent tumor-conditioned systemic breakdown processes. The current work strengthens the necessity for treatment methods that address functional and neurological cancer-related consequences by expanding past research into biological along with physical and cognitive data perspectives. The modulation of cytokines through pharmaceutical agents alongside anti-inflammatory treatments and person-centered exercise programs and diet can potentially sustain cancer patients' life quality alongside functional independence. Changes in cytokines in cancer patients should be actively monitored together with neuromuscular assessments to support rapid medical responses for high-risk patients. The increasing cancer survival rates need corresponding efforts to minimize tumor-induced and treatment-related comorbidities which diminish long-term patient survivability. Future translational research and intervention studies can adopt foundational knowledge established in this work to diminish the inflammatory cascade while revealing the hidden effect of tumor-derived inflammation on muscle and brain operations for this paradigm shift.

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