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Changes in Fatigue, Functional Status, and Sarcopenia Risk in Patients With Cancer: A Prospective Cohort Study

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CHANGES IN FATIGUE, FUNCTIONAL STATUS, AND SARCOPENIA RISK IN PATIENTS WITH CANCER: A PROSPECTIVE COHORT STUDY

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ABSTRACT

Purpose: To analyze changes in cancer-related fatigue, sarcopenia risk, and functional status in patients undergoing chemotherapy and investigate associations among these outcomes. **Methods:** A prospective cohort study was conducted with 104 patients undergoing chemotherapy with taxanes and/or platinum-based agents at an oncology outpatient clinic in northern Rio Grande do Sul, Brazil. Three assessments were performed at the beginning, midpoint, and end of treatment using the Revised Piper Fatigue Scale, SARC-CalF, and Thirty-Second Sit-to-Stand Test. Data were analyzed using descriptive and inferential statistics, with a significance level of 5%. **Results:** Of the 104 patients initially assessed, 62 completed all three assessments. Fatigue increased from 2.83 ± 1.90 to 4.96 ± 1.93 points ($p < 0.001$). Sarcopenia risk ($p = 0.965$) and functional status ($p = 0.219$) remained stable. At the first assessment, fatigue was weakly positively correlated with sarcopenia risk ($r = 0.270$; $p = 0.006$), with no significant correlation thereafter. Fatigue was weakly negatively correlated with functional status at the first ($r = −0.310$; $p = 0.001$) and second assessments ($r = −0.345$; $p = 0.002$*), but not at the third. **Conclusion:** Cancer-related fatigue increased during chemotherapy, whereas sarcopenia risk and functional status remained stable. The association between higher fatigue and lower functional status at the first two assessments highlights the importance of monitoring fatigue and functional status throughout cancer treatment.

Keywords: Neoplasms; Antineoplastic Agents; Fatigue; Sarcopenia; Functional Status.

Introduction

Cancer is a major public health concern, with approximately 35 million new cases per year projected worldwide by 2050, representing a 77% increase compared with 2022 (1). Advances in early detection and treatment have contributed to increased survival, with chemotherapy remaining one of the main therapeutic modalities. Among the widely used agents are taxanes and platinum-based agents, which are associated with various adverse effects during cancer treatment (2–4).

Among these effects, cancer-related fatigue (CRF) is characterized by a persistent feeling of physical, emotional, and/or cognitive exhaustion that is disproportionate to the activity performed and is not relieved by rest, potentially impairing quality of life and functional capacity (5, 6). Its occurrence results from the interaction of inflammatory, metabolic, and neuroendocrine alterations associated with the disease and its treatment, as well as factors such as malnutrition, cachexia, muscle mass loss, and physical inactivity (7, 8). CRF may remain underdiagnosed and is associated with poorer functional status, lower treatment adherence, and worse clinical outcomes (9, 10).

In this context, sarcopenia, characterized by progressive reductions in muscle mass and function, is an important factor associated with functional decline and CRF in patients with cancer. Its prevalence varies widely, ranging from 8% to 84.9%, depending on tumor type and the diagnostic criteria used (11, 12). Muscle loss may impair physical performance and the ability to perform activities of daily living, contributing to greater dependence, reduced autonomy, and lower treatment tolerance (13).

Despite the relevance of these outcomes, few studies have jointly examined their evolution throughout chemotherapy and the relationships among fatigue, risk of sarcopenia, and functionality. Understanding these

changes is relevant given their association with poorer quality of life, greater vulnerability, and unfavorable clinical outcomes (14).

Therefore, this study aimed to analyze the evolution of cancer-related fatigue, risk of sarcopenia, and functionality, as well as to investigate the associations among these outcomes in patients undergoing chemotherapy.

Methods

This was a prospective observational cohort study with a quantitative approach, conducted in the oncology outpatient clinic of a hospital in a city in northern Rio Grande do Sul, Brazil, from October 2025 to April 2026.

This study is part of a larger project entitled *"Incidence of fatigue and risk of sarcopenia in individuals with cancer"* which was approved by the Research Ethics Committee of the University of Passo Fundo, Brazil, under CAAE No. 91883625.3.0000.5342. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki of 1964 and its subsequent amendments, as well as the ethical guidelines established by Resolution No. 466/2012 of the Brazilian National Health Council.

The sample size calculation was based on the parent research project from which this study was derived. Based on the literature, it was estimated that approximately 90% of individuals with cancer undergoing chemotherapy would experience cancer-related fatigue (15). Considering a 10% confidence interval width and an additional 10% to account for potential losses and refusals, the required sample size was estimated at 155 participants. The calculation was performed using the online version of the PSS Health software (16).

Eligibility criteria included individuals of either sex, aged ≥18 years, with a cancer diagnosis and undergoing chemotherapy regimens containing taxanes and/or platinum-based compounds. Participants were recruited using a non-probability convenience sampling method. Individuals with a history of previous chemotherapy and those with physical limitations that prevented them from performing the assessment tests were excluded.

Data were collected at three time points: at the beginning of treatment, at the midpoint of the planned number of cycles, and at the end of chemotherapy. Participants were recruited through active case finding and selected according to the eligibility criteria. After receiving information about the study objectives and procedures, those who agreed to participate signed the informed consent form. Assessments were performed at all three time points using the same instruments and previously established procedures to ensure standardized measurement of outcomes throughout follow-up.

The interval between assessments varied according to the chemotherapy regimen, taking into account cycle frequency, the planned number of cycles, and the type of treatment administered for each diagnosis. Therefore, no fixed chronological interval was established between assessments; instead, follow-up time points were determined according to the course of chemotherapy for each participant.

At the initial assessment, sociodemographic variables (age, sex, and skin color) and clinical characteristics were collected, including cancer diagnosis, presence of metastases, chemotherapy class, nutritional and/or physiotherapy follow-up, treatments received, and physical activity. Data were obtained through

consultation of electronic medical records, in accordance with the ethical and confidentiality principles established by the Brazilian General Data Protection Law (LGPD).

For the assessment of the primary outcomes, validated instruments were used, including the Revised Piper Fatigue Scale to assess cancer-related fatigue, the SARC-CalF scale for sarcopenia screening, and the Thirty-Second Sit-to-Stand Test (30STS) to assess functional performance. The presence of metastasis was considered a secondary clinical variable and was used for comparative analysis of outcomes between participants with and without metastasis. Clinical and sociodemographic variables were considered potential characteristics associated with the outcomes. No specific models were defined or assessed to control for confounding factors or effect modifiers.

The Revised Piper Fatigue Scale is a multidimensional instrument validated for assessing fatigue in patients with cancer. It consists of 22 items distributed across three dimensions: behavioral, affective, and sensory/psychological, encompassing aspects related to functional capacity, the meaning attributed to fatigue, and the emotional and cognitive consequences of this symptom (17). Each item is scored on a Likert-type scale ranging from 0 to 10, with the total score calculated as the mean of the assessed items; higher scores indicate greater fatigue intensity.

Risk of sarcopenia was assessed using the SARC-CalF scale, a screening instrument consisting of the five SARC-F items (strength, walking, chair transfer, stair climbing, and falls), combined with calf circumference measurement. The total score ranges from 0 to 20 points, with scores ≥11 indicating risk of sarcopenia (18).

Finally, functionality was assessed using the Thirty-Second Sit-to-Stand Test (30STS), a simple and validated instrument for assessing lower-limb muscle strength and endurance and functional capacity (19). Participants began the test seated on an armless chair, with their arms crossed over the chest and their hips and knees flexed at 90°. Following a verbal command, they stood up completely and returned to the seated position, repeating the movement for 30 seconds. Performance was determined by the total number of repetitions completed within 30 seconds.

Considering the longitudinal design of the study and the need to perform three assessments throughout chemotherapy, participant recruitment was conditioned by the time available for data collection and the feasibility of following individuals through the different stages of the study. Therefore, the initially estimated sample size of 155 participants could not be reached during the established data collection period.

To minimize potential measurement bias, the same instruments and standardized procedures were used at all three follow-up assessments. Clinical information was collected through consultation of electronic medical records, and participants were assessed according to the previously established eligibility criteria.

The collected data were analyzed using IBM SPSS Statistics version 20.0. The sample was characterized using descriptive statistics, with means and standard deviations for numerical variables and absolute and relative frequencies for categorical variables. Sphericity was assessed using Mauchly's test.

Changes in CRF, risk of sarcopenia, and functionality over time were assessed using repeated-measures analysis of variance (ANOVA), followed by Bonferroni post hoc testing. Pearson's correlation coefficient was used to assess the association between CRF and SARC-CalF scores and between CRF and 30STS performance at each assessment time point. Means were compared between groups with and without metastasis using the independent-samples t test. A significance level of 5% ($p < 0.05$) was adopted. The effect size of the observed differences was estimated using Cohen's d.

Fatigue, risk of sarcopenia, and functionality were analyzed as continuous scores. For presentation of the distribution of fatigue, the classification categories established for the instrument were used, with fatigue classified as mild (score <4), moderate (score ≥4 and <6), and intense (score ≥6). Risk of sarcopenia was categorized according to the SARC-CalF cutoff of ≥11 points, and 30STS performance was presented according to the number of repetitions completed during the test.

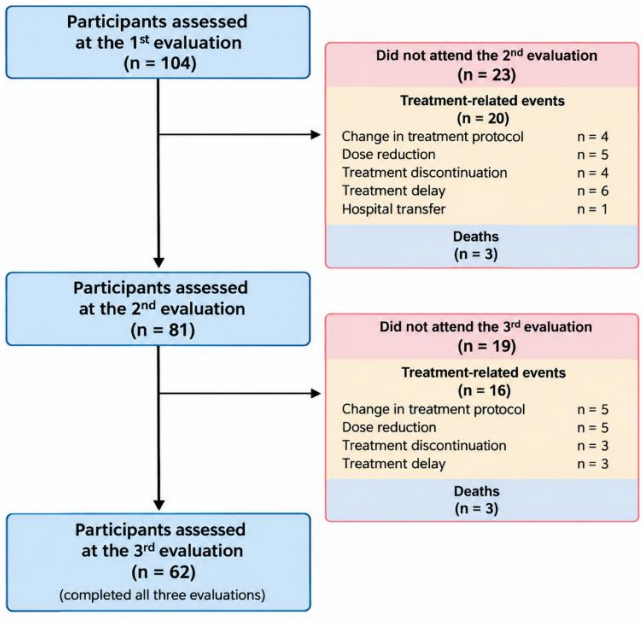
For longitudinal analyses of the outcomes, participants with available data from all three assessments were included, allowing within-subject comparisons between the first, second, and third assessment time points. Participants who did not complete follow-up were not included in the repeated-measures analysis. For comparative analyses performed separately at each assessment time point, the data available from the first, second, and third assessments, respectively, were used, and participation in all three time points was not required. No imputation was performed for missing data.

Results

Initially, 104 participants were assessed at the first evaluation. At the second evaluation, 81 participants remained, corresponding to 23 losses between assessments, of which 20 were due to treatment-related events and three were deaths. The treatment-related events included changes in treatment protocol (n = 4), dose reduction (n = 5), treatment discontinuation (n = 4), treatment delay (n = 6), and hospital transfer (n = 1).

At the third evaluation, 62 participants were assessed, corresponding to 19 losses from the second evaluation, of which 16 were due to treatment-related events and three were deaths. The treatment-related events included changes in treatment protocol (n = 5), dose reduction (n = 5), treatment discontinuation (n = 3), and treatment delay (n = 3). Thus, 62 participants completed all three planned evaluations, as shown in the flowchart below.

Figure 1. Flowchart of participant recruitment, follow-up, and attrition throughout the study. Passo Fundo, Rio Grande do Sul, Brazil, 2026.



The results presented in Table 1 describe the sociodemographic and clinical characteristics of the sample at the three assessment time points.

Table 1: Sociodemographic and clinical characteristics of the participants during the study. Passo Fundo, Rio Grande do Sul, 2026.

Variables	1st assessment (n = 104)	2nd assessment (n = 81)	3rd assessment (n = 62)
Age (mean ± SD)	58.42 ± 13.27	56.99 ± 12.53	58.31 ± 11.74
Sex [n (%)]			
Male	44 (42.3)	33 (40.7)	26 (41.9)
Female	60 (57.7)	48 (59.3)	36 (58.1)
Skin color [n (%)]			
White	91 (87.5)	71 (87.7)	55 (88.7)
Non-white	13 (12.5)	10 (12.3)	7 (11.3)
Diagnosis [n (%)]			
Breast cancer	28 (26.9)	24 (29.6)	20 (32.3)
Colon and rectal cancer	29 (27.9)	21 (25.9)	18 (29.0)
Stomach or esophageal cancer	13 (12.5)	11 (13.6)	8 (12.9)
Lung cancer	7 (6.7)	6 (7.4)	5 (8.1)
Gynecologic cancer	13 (12.5)	12 (14.8)	9 (14.5)
Head and neck cancer	8 (7.7)	3 (3.7)	1 (1.6)
Other types	6 (5.8)	4 (4.9)	1 (1.6)
Metastasis [n (%)]			
Yes	33 (31.7)	21 (25.9)	13 (21.0)
No	71 (68.3)	60 (74.1)	49 (79.0)
Chemotherapy class [n (%)]*			
Taxanes	53 (51.0)	46 (56.8)	35 (56.5)
Platinum-based compounds	77 (74.0)	59 (72.8)	46 (74.2)
Treatments received [n (%)]			
None	30 (28.8)	27 (33.3)	21 (33.9)
Surgery	44 (42.3)	37 (45.7)	29 (46.8)
Radiotherapy	18 (17.3)	10 (12.3)	9 (14.5)
Hormone therapy	2 (1.9)	2 (2.5)	1 (1.6)
More than one treatment	9 (8.7)	4 (4.9)	1 (1.6)
No response	1 (1.0)	1 (1.2)	1 (1.6)
Physical exercise [n (%)]			
Yes	17 (16.3)	13 (16.0)	11 (17.7)
No	87 (83.7)	68 (84.0)	51 (82.3)
Physical therapy [n (%)]			
Yes	4 (3.8)	2 (2.5)	2 (3.2)
No	100 (96.2)	79 (97.5)	60 (96.8)
Nutritionist [n (%)]			
Yes	16 (15.4)	10 (12.3)	5 (8.1)
No	88 (84.6)	71 (87.7)	57 (91.9)

Note: SD, standard deviation; n, number of participants; %, percentage. *Percentages may exceed 100% because participants could receive more than one chemotherapy class.

A predominance of female participants and individuals with white skin color was observed at all assessment time points. Mean age remained similar throughout follow-up, at approximately 58 years. The most frequent diagnoses were colon and rectal cancer and breast cancer, followed by gynecologic, stomach and esophageal, lung, and head and neck cancers. Metastases were present in 31.7% of participants at the initial assessment and in 21.0% of those assessed at the third time point.

Regarding treatments received, surgery was the most frequent modality, followed by no treatment at the time of assessment and radiotherapy. A low proportion of participants reported engaging in physical exercise throughout follow-up. Similarly, multidisciplinary care was limited, as indicated by the small proportion of participants receiving physiotherapy and nutritional care during the assessment period.

The results presented in Table 2 show the evolution of fatigue, risk of sarcopenia, and functionality across the three assessments performed during follow-up.

Table 2: Changes in fatigue, risk of sarcopenia, and functionality scores during follow-up (n = 62). Passo Fundo, Rio Grande do Sul, Brazil, 2026.

Variables	1st assessment	2nd assessment	3rd assessment	F (2.53)	*p*-value	d*
Fatigue	2.83 ± 1.90	3.90 ± 1.99	4.96 ± 1.93	40.827	**<0.001**	1.100**
R. sarcopenia	5.94 ± 5.37	5.06 ± 5.21	4.87 ± 5.08	0.024	0.965	0.205***
Functionality	8.58 ± 4.87	9.81 ± 4.92	9.80 ± 5.20	2.589	0.219	0.253

Note: R. sarcopenia, risk of sarcopenia; *d*, Cohen's *d* coefficient; **large effect size; ***small effect size; **bold**, $p < 0.05$.

Regarding fatigue, a progressive increase was observed across the assessments, with mean scores increasing from the first to the third assessment. This difference was statistically significant. In contrast, risk of sarcopenia showed low mean scores and remained stable throughout follow-up ($p = 0.965$). Similarly, functionality did not show statistically significant variation across the assessments.

The distribution of participants according to fatigue classification at the three assessment time points is presented in Table 3.

Table 3: Fatigue severity classification at the three assessment time points. Passo Fundo, Rio Grande do Sul, Brazil, 2026.

Fatigue severity	1st assessment	2nd assessment	3rd assessment
Mild fatigue	75 (72.1)	36 (44.4)	12 (11.5)
Moderate fatigue	17 (16.3)	31 (38.3)	20 (32.3)
Severe fatigue	12 (11.5)	14 (17.3)	30 (48.4)

Note: n, number of participants; %, percentage·

A change in the distribution of fatigue severity was observed over time, with a progressive decrease in the proportion of participants with mild fatigue and an increase in moderate and severe fatigue. Notably, severe fatigue increased substantially at the third assessment, accounting for 48.4% of the participants assessed at that time point.

Table 4 presents the pairwise comparisons between assessment time points for fatigue scores obtained using the Bonferroni post hoc test.

Table 4: Pairwise comparisons of fatigue scores between assessment time points using the Bonferroni post hoc test (n = 62). Passo Fundo, Rio Grande do Sul, Brazil, 2026.

Variables	Comparison		ΔM	SE	95% CI		*p*-value
					Lower limit	Upper limit	
Fatigue	1st assessment	2nd assessment	-1.411	0.244	-2.011	-0.812	**<0.001**
	2nd assessment	3rd assessment	-1.108	0.273	-1.780	-0.437	**<0.001**
	1st assessment	3rd assessment	-2.519	0.317	-3.300	-1.739	**<0.001**

Note: ΔM, mean difference; SE, standard error; CI, confidence interval; **bold**, $p < 0.05$.

The Bonferroni post hoc analysis showed statistically significant differences between all assessment time points. An increase in fatigue scores was observed from the first to the second assessment, from the second to the third assessment, and from the first to the third assessment, with the latter representing the largest difference observed.

The associations between fatigue and the other variables investigated at the different assessment time points are presented in Table 5.

Table 5: Correlations between fatigue and study variables at the three assessment time points. Passo Fundo, Rio Grande do Sul, Brazil, 2026.

	1st assessment		2nd assessment		3rd assessment	
Correlations	R	*p*-value	R	*p*-value	R	*p*-value
Fatigue X Risk of sarcopenia	0.270	**0.006**	0.105	0.353	-0.120	0.356
Fadiga X Functionality	-0.310	**0.001**	-0.345	**0.002**	-0.198	0.123

Note: *r*, Pearson's correlation coefficient; **bold**, $p < 0.05$.

At the first assessment, a weak positive correlation was observed between fatigue and risk of sarcopenia. At the second and third assessments, no statistically significant correlations were observed between these variables. Regarding functionality, a weak negative correlation with fatigue was identified at the first and second assessments. At the third assessment, the correlation between fatigue and functionality was not statistically significant.

Considering the clinical relevance of disease progression to the outcomes assessed, a comparative analysis was performed between participants with and without metastasis, considering fatigue, risk of sarcopenia, and functionality (Table 6).

Table 6: Comparison of outcomes according to the presence of metastasis. Passo Fundo, Rio Grande do Sul, Brazil, 2026.

	1st assessment			2nd assessment			3rd assessment		
Variables	Yes (n = 33)	No (n = 71)	*p*-value	Yes (n= 21)	No (n= 60)	*p*-value	Yes (n= 13)	No (n=49)	*p*-value
Fatigue	3.86 ± 2.103	2.36 ± 1.601	**<0.001**	4.46 ± 2.486	3.71 ± 1.772	0.140	6.02 ± 1.356	4.68 ± 1.980	**0.008**
Risk of sarcopenia	7.15 ± 5.580	5.37 ± 5.226	0.118	5.86 ± 5.516	4.78 ± 5.123	0.420	5.38 ± 5.853	4.73 ± 4.920	0.684
Functionality	7.27 ± 4.817	9.18 ± 4.818	0.063	9.66 ± 4.871	9.86 ± 4.986	0.873	6.84 ± 5.698	10.59 ± 4.834	**0.020**

Note: Values are presented as mean ± standard deviation; *p*-values based on valid observations; **bold**, $p < 0.05$.

Fatigue levels were significantly higher among participants with metastasis at the first and third assessments. At the second assessment, although fatigue levels were also higher in this group, no statistically significant difference was observed.

Regarding functionality, lower scores were observed among participants with metastasis at the third assessment, whereas no statistically significant differences were identified at the earlier assessments. Risk of sarcopenia did not differ significantly between the groups.

Discussion

The results of the present study demonstrated a progressive increase in fatigue and its severity throughout chemotherapy, whereas the risk of sarcopenia and functionality remained stable across the assessment time points. A weak negative correlation was also observed between fatigue and functionality at the first and second assessments, indicating an association between higher levels of fatigue and lower levels of functionality at these time points.

These findings are consistent with studies that identified a significant increase in fatigue throughout chemotherapy in patients with colorectal cancer, particularly in the physical domain and total fatigue score (20). Similarly, another study identified an association between greater fatigue intensity and poorer nutritional status during chemotherapy (21). This pattern may be related to treatment-related systemic toxicity, chronic inflammation, metabolic alterations, and reduced physical conditioning (7, 8).

Despite this convergence, the literature also describes heterogeneous trajectories of fatigue throughout treatment. In patients with breast cancer, different patterns of change have been observed, including stable symptom levels and even symptom improvement in some patients (22). Similarly, psychosocial factors, such as anxiety and depression, have been strongly associated with fatigue, reinforcing its multifactorial nature and suggesting that it is not determined exclusively by treatment progression (23).

In this context, another relevant finding was the change in the distribution of fatigue severity over time, characterized by a progressive reduction in the proportion of individuals with mild fatigue and an increase in moderate and severe fatigue, culminating in a predominance of severe fatigue at the third assessment, affecting

nearly half of the sample. A similar finding was described in a longitudinal study of more than 4,000 women with stage I to III breast cancer, in which different fatigue trajectories were identified, including a group with progressive worsening of symptoms throughout follow-up (24).

Although fatigue progressively worsened throughout chemotherapy, it is noteworthy that the sample already presented some degree of mild fatigue at the initial assessment. A systematic review and meta-analysis including more than 34,000 patients with cancer demonstrated that this symptom may be present before treatment initiation, indicating the influence of disease-related characteristics and physical and psychosocial factors (25). In addition, metabolic and inflammatory alterations may contribute to its persistence, as demonstrated by a study that identified an association between persistent fatigue and alterations related to energy metabolism and inflammation (26). Therefore, cancer-related fatigue should be understood as a multifactorial symptom rather than merely a transient effect of chemotherapy (27).

Unlike fatigue, the risk of sarcopenia remained stable, with low mean scores throughout follow-up. This finding is similar to that observed in a study that identified heterogeneous patterns of muscle mass during chemotherapy, with some patients maintaining stable muscle parameters (28). In addition, changes in body composition may be masked by increased body fat or the presence of edema, making their identification more difficult. Studies comparing SARC-CalF with computed tomography have demonstrated limited sensitivity of the instrument for identifying sarcopenia (29). Thus, the absence of changes in SARC-CalF does not exclude the possibility of muscle alterations not detected by the instrument used, particularly given its limitations as a screening tool.

Although fatigue and sarcopenia share mechanisms related to inflammation, metabolic alterations, and reduced physical activity, their trajectories may differ. The association between greater risk of sarcopenia and higher levels of fatigue has been reported in other studies, suggesting the presence of common mechanisms between these conditions (30). However, evidence also indicates reductions in muscle mass during systemic treatment, with substantial heterogeneity across studies, cancer types, and treatment modalities (31). In the present study, fatigue increased significantly, whereas SARC-CalF remained relatively stable, and a weak positive association between the two was observed only at the initial assessment. This pattern may be related to the multidimensional nature of fatigue, which, although it may involve muscular and functional alterations, is also influenced by clinical and treatment-related factors that are not reflected by the SARC-CalF (32).

Functionality also remained stable throughout follow-up, despite evidence indicating that chemotherapy may be associated with functional decline. Previous studies have shown that physical function may remain stable or even improve during treatment, particularly among individuals with better baseline functional performance (33). However, despite the absence of significant longitudinal changes, fatigue showed a weak negative correlation with functionality at the first and second assessments. These findings indicate that higher levels of fatigue were associated with poorer functional performance at the time points at which this relationship was identified, without necessarily implying a longitudinal decline in functionality.

This relationship is consistent with studies associating higher levels of fatigue with reduced muscle strength, poorer performance on the sit-to-stand test, and poorer physical function (34, 35). These findings reinforce the close relationship between fatigue and functionality, particularly with regard to mobility, exercise tolerance, and the performance of daily activities.

The higher levels of fatigue observed among participants with metastasis may be related to greater disease extent and systemic involvement. Previous studies have reported a higher frequency and prevalence of fatigue among patients with advanced or metastatic disease, as well as an association between higher levels of fatigue and poorer functional performance (36, 37). In the present study, the poorer functionality observed at the third assessment among participants with metastasis may be related to greater disease burden and greater clinical complexity in these patients. This interpretation is consistent with studies associating advanced cancer with reduced physical activity and functional capacity, and higher levels of fatigue with poorer objective measures of physical function (38, 39).

Another relevant finding was the low participation of patients in physiotherapy and nutritional care during treatment. Given the multifactorial nature of fatigue, multidisciplinary strategies may contribute to its management. Studies have highlighted supervised exercise, physiotherapy rehabilitation, and nutritional care as relevant strategies in oncology care (40), while other investigations have demonstrated benefits of physical exercise on function, fatigue, and quality of life during treatment (41–43). In this context, the low participation observed in the sample should also be considered when interpreting the results, as limited access to multidisciplinary supportive care strategies may have influenced patients' experiences during treatment.

Several methodological aspects should be considered when interpreting the results. The risk of sarcopenia was assessed using the SARC-CalF, a screening instrument that may have limitations in identifying early muscle alterations when compared with more specific methods, such as imaging-based assessments (29). In addition, the reduction in the number of participants during follow-up may have introduced attrition bias, as individuals who did not complete all three assessments experienced treatment-related clinical intercurrent events. The reduced sample size at the final assessment may also have limited the precision of the estimates and the ability to detect associations of smaller magnitude. The clinical heterogeneity of the sample, which included different cancer types, may likewise have influenced the results. The absence of multivariable analysis limits the simultaneous control of potential confounding factors.

The generalizability of the findings should be considered with caution given the convenience sampling, the single oncology center setting, and the heterogeneity of the diagnoses and chemotherapy regimens evaluated. Despite these limitations, the longitudinal design allowed the evolution of fatigue, risk of sarcopenia, and functionality to be monitored throughout chemotherapy. Future studies with larger samples, longer follow-up periods, and more specific methods for assessing body composition and sarcopenia may further clarify the interaction among these outcomes.

Conclusion

The results of this study demonstrated a progressive increase in cancer-related fatigue throughout chemotherapy, accompanied by worsening fatigue severity. In contrast, the risk of sarcopenia and functionality remained stable during follow-up. However, higher levels of fatigue were associated with lower functionality at the earlier assessment time points, whereas the association between fatigue and risk of sarcopenia was observed only at the initial assessment.

These findings reinforce the importance of continuous monitoring of fatigue in patients with cancer undergoing chemotherapy, as well as the provision of multidisciplinary strategies aimed at symptom management and preservation of functionality during treatment. In addition, they highlight the need for complementary and

more specific methods to assess muscle composition and sarcopenia, as well as studies with longer follow-up periods, to further understand the evolution of sarcopenia and its interaction with fatigue and functionality during cancer treatment.

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DECLARATIONS

Ethics approval

This study was approved by the Research Ethics Committee of the University of Passo Fundo, Brazil, under CAAE No. 91883625.3.0000.5342, in accordance with Resolution No. 466/2012 of the Brazilian National Health Council.

Consent to participate

Written informed consent was obtained from all participants prior to their inclusion in the study through the signing of the Informed Consent Form (ICF).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Author contributions

Bianca Piriz Latorre: Conceptualization, data collection, statistical analysis, interpretation of results, writing of the original manuscript, and critical revision of the manuscript.
Dayana Cristina Kafer: Conceptualization, data collection, statistical analysis, and approval of the final version of the manuscript.
Lia Mara Wibelinger: Conceptualization, interpretation of results, writing of the original manuscript, critical revision of the manuscript, supervision, and approval of the final version of the manuscript.
Siomara Regina Hahn: Conceptualization, critical revision of the manuscript, supervision, and approval of the final version of the manuscript.
All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Data availability

The datasets generated and/or analyzed during the current study are not publicly available due to the confidentiality of participant information and ethical restrictions. Data may be made available by the corresponding author upon reasonable request, subject to applicable ethical and institutional requirements.