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ORIGINAL ARTICLE

Assessment of pain and nutritional status in patients undergoing palliative radiotherapy

Avaliação da dor e estado nutricional em pacientes submetidos à radioterapia paliativa

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ABSTRACT

BACKGROUND AND OBJECTIVES: Cancer pain has a high prevalence and significant psychosocial impact. Nutritional analysis and instrumental assessment of pain in cancer patients provide guidelines for better control, as nutritional status is a prognostic factor. The objective of this study was to investigate the characteristics of pain and its association with nutritional status in patients undergoing antalgic radiotherapy in a public hospital in the Brazilian Amazon.

METHODS: This is a prospective, non-randomized, observational study that enrolled forty-eight patients for palliative antalgic treatment in the Radiotherapy Department of the *Hospital Regional do Baixo Amazonas* (HRBA - Lower Amazonas Regional Hospital), Brazil. Validated questionnaires were used to assess and exclude comorbidities and pain symptoms. Data collection included uni and multidimensional instruments for pain analysis before and after radiotherapy, and analysis of clinical, epidemiological, and nutritional data.

RESULTS: Half of the patients were cachectic; the other half, who were not cachectic, were overweight patients with low appendicular lean mass. Patients responded well to antalgic radiotherapy both immediately and after 1 month of treatment. Cachectic patients had a higher score by the Visual Analogue Scale with significantly lower numerical reduction. Response rates were lower and deterioration after radiation occurred more frequently in this group. Cachectic patients had more neuropathic pain and longer pain duration. This group also presented a higher score for catastrophic thoughts about pain and a higher rate of anxiety and depression symptoms.

CONCLUSION: Considering the results obtained, a negative influence of poor nutritional status is observed on the response to antalgic irradiation and pain symptoms. This fact that must be considered when planning the treatment of cancer patients.

KEYWORDS: Cachexia, Cancer pain, Radiotherapy.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A dor no câncer apresenta alta prevalência e impacto psicossocial significativo. À análise nutricional e a avaliação instrumental da dor em pacientes oncológicos fornecem diretrizes para um melhor controle, já que o estado nutricional é um fator prognóstico. O objetivo deste estudo foi investigar as características da dor e sua associação com o estado nutricional em pacientes submetidos à radioterapia antálgica em um hospital público na Amazônia Brasileira.

MÉTODOS: Este é um estudo observacional prospectivo, não randomizado, que envolveu 48 pacientes em tratamento paliativo antálgico no Departamento de Radioterapia do Hospital Regional do Baixo Amazonas (HRBA), Brasil. Questionários validados foram utilizados para avaliar e excluir comorbidades e sintomas de dor. A coleta de dados incluiu instrumentos unidimensionais e multidimensionais para análise da dor antes e após a radioterapia, além da análise de dados clínicos, epidemiológicos e nutricionais.

RESULTADOS: Metade dos pacientes apresentava caquexia; a outra metade, que não era caquética, era composta por pacientes com sobrepeso e baixa massa magra apendicular. Os pacientes responderam bem à radioterapia antálgica, tanto imediatamente quanto após um mês de tratamento. Pacientes caquéticos apresentaram uma pontuação na Escala Analógica Visual mais alta, com redução numérica significativamente menor. As taxas de resposta foram menores e a deterioração após a radiação ocorreu com mais frequência neste grupo. Pacientes caquéticos tiveram mais dor neuropática e maior duração da dor. Este grupo também apresentou uma pontuação mais alta para pensamentos catastróficos sobre a dor e uma maior taxa de sintomas de ansiedade e depressão.

CONCLUSÃO: Considerando os resultados obtidos, observou-se uma influência negativa do estado nutricional deficiente na resposta à irradiação antálgica e nos sintomas de dor. Esse fato deve ser considerado ao planejar o tratamento de pacientes com câncer.

DESCRITORES: Caquexia, Dor no câncer, Radioterapia.

HIGHLIGHTS

- Nutritional status interferes with pain response
- Cachectic patients have higher pain scores
- Cachectic patients present pain with neuropathic characteristics

INTRODUCTION

Pain is one of the most common and debilitating symptoms in cancer[1] and is more frequent in advanced stages.[2] It can be classified as nociceptive, neuropathic, or mixed[1] and, in cancer patients, it is usually mixed and may include ischemic, inflammatory, and compressive mechanisms[2,3]. The prevalence and intensity of cancer pain may change according to phenotypic and genotypic heterogeneity of tumors[4], their location, the presence of metastases, the stage of the neoplasia and the aggressiveness of both tumor and its therapy, in addition to patients' intrinsic factors[5].

Radiotherapy is often used with palliative intent in pain treatment, whether pain is caused by destructive tissue damage caused by the tumor or by invasion of nervous structures and soft parts[3-6]. This treatment may achieve complete remission in approximately 30% to 50% of cases and partial remission in more than 80% of cases[7-9], with analgesic equivalence of several dose prescription schemes (30 Gy in 10 fractions, 20 Gy in 5 fractions or 8 Gy single fraction)[10-17]. Considering bone metastases, the most common cause of intractable cancer pain, studies indicate that the analgesic effect of radiation is achieved by stimulating ossification, decreasing the activity of osteoclasts, reducing osteolysis through the death of tumor cells, which results in a reduction of the tumor burden. Pain relief observed in some patients indicates a decrease in inflammatory activity as well as in the concentration of chemical mediators in the irradiated region[7,18].

Several cytokines can be produced in an exacerbated way by the tumor and immune system, affecting pain, its response, exacerbation, and maintenance[2]. If there is a systemic predominance of pro-inflammatory cytokines, there may be worsening of quality of life, pain, fatigue, cognitive changes, resistance to therapy and poor prognosis in cancer patients[2,19]. The study[20] stated that nutrition is a fundamental tool in the treatment of inflammatory and painful conditions. Furthermore, central nervous system (CNS) sensitization, cerebral perception and psychosocial factors play a crucial role in the persistence of the painful experience[21,22]. Furthermore, it is necessary to consider the concept of total pain proposed by Cicely Saunders in 1960, indicating that the basis for the adequate treatment of pain in cancer patients includes, in addition to the various therapeutic modalities, the cultural and psychosocial spheres of these individuals[23,24].

Despite the gap in the literature correlating pain and nutritional status, preclinical studies indicate that poor nutrition can influence the underlying factors of pain in several mechanisms such as: peripheral inflammation, vagal afferent activation, changes in the intestinal microbiota, oxidative stress, and tissue damage[21]. The inflammatory systemic condition present in cachexia may be correlated with pain levels and characteristics, response to opioids, quality of life and psychological aspects in advanced cancer patients[21]. Reference authors[25] emphasize the relevance of the association between pain and nutritional status in those patients precisely because of neuronal function and plasticity, making the analysis of its correlation with pain characteristics extremely interesting and challenging.

Considering cancer and pain management a public health problem, it is necessary to analyze the other components that comprise the therapeutic process, as this knowledge contributes to an effective treatment plan, reduces the financial burden, and increases the quality of life of patients[17,26].

The present study's objective was to analyze the relationship between pain and nutritional status in patients with advanced cancer undergoing antalgic radiotherapy in a public hospital in the Brazilian Amazon.

METHODS

This was a prospective and observational study conducted with patients referred for palliative antalgic treatment in the Radiotherapy Department of the *Hospital Regional do Baixo Amazonas* (HRBA), Santarém, Pará - Brazil. Patients were randomly admitted to the study in accordance with the institutional referral process to the Radiotherapy service. All participants had an indication for radiotherapy for palliative pain relief. Following their initial radiotherapy consultation, those who met the inclusion criteria were invited to participate in the study. Based on this, forty-eight patients were selected and agreed to participate of the study and signed the informed consent form.

The inclusion criteria were age between 18 and 80 years; a painful site that had never been treated with surgery or radiation; no participation in another research project; no cytotoxic chemotherapy or continuous use of anti-inflammatory drugs (because of its potential interference at laboratory tests and cachexia diagnosis); no spinal cord compression, renal or hepatic failure; and no diagnosis of immunodeficiency syndrome or autoimmune disease. During the data collection interval, the following patients were excluded: patients who required a surgical procedure at treated painful site or started using cytotoxic chemotherapy while undergoing radiotherapy, who started participating in another research project or presented disease progression or death in the interval between data collection. Also, patients with incomplete data that precluded classification regarding nutritional status were also excluded.

This study has been approved by the HRBA and the Research Ethics Committee of the University of São Paulo (CAAE 91205118.7.0000.0065), registered at REBEC (Brazilian Registry of Clinical Trials) no. 12632.

Treatment

Patients underwent radiotherapy after clinical evaluation for antalgic therapy. They underwent external beam radiotherapy with three-dimensional radiotherapy planning and photon beam of 6 MV generated by a Linear Electron Accelerator. Dose prescription schemes included 40 Gy in 20 fractions, 30 Gy in 10 fractions, 20 Gy in 5 fractions or 8 Gy single dose.

Data collection

The patients underwent clinical evaluation through questionnaires, also medical records and radiotherapy treatment sheets were reviewed. Data was collected at three different points related to prescribed radiotherapy: before it began (pre), immediately

after it ended (post), and one month after it ended (1 month). Epidemiological analysis, clinical data evaluation, nutritional status and cachexia diagnosis were obtained before radiotherapy treatment. After cachexia diagnosis the patients were divided into cachectic or non-cachectic to analyze pain characteristics and the impact of the treatment received.

For epidemiological analysis, the following variables were analyzed: age, gender, origin, and economic class. Classification of economic class were based on the Brazilian Association of Research Enterprises (ABEP)[27,28]. Current cognitive status was analyzed using the Mini Mental Examination Scale (MMES) and reported premorbid abilities by Premorbid Cognitive Abilities Scale (PCAS)[29-32]. The risk of alcohol abuse was determined using the questionnaire AUDIT[33-35].

For clinical data evaluation, the following were identified: cancer staging, according to the TNM classification of the International Union Against Cancer (UICC); primary site of disease and the treated topographic site regarding International Code of Diseases (ICD); referred comorbidities and clinical status, as the last description of the clinical situation found in electronic medical record.

For nutritional status, anthropometric data of height and weight were recorded to calculate body mass index (BMI). Body composition analysis was performed with dual energy X-ray absorptiometry (DXA) (GE Health Care, Lunar model) using Encore 2010 version 13.40 software. From the data obtained with DXA, the appendicular lean mass index (ALMI) and the fat-free mass index (FFMI) were calculated[36]. To diagnose cachexia, the CASCO questionnaire was used[37-39]. It has 5 domains and the scores of each domain are added to generate final CASCO score, which classifies patients as non-cachectic (if the percentage of weight loss is zero or less than 5% and the questionnaire is negative) and in three levels of cachexia (take 0-25 points, moderate 26-50 points, severe > 51 points)[40,41].

The visual pain scale (VAS) and four multidimensional instruments were used to characterize pain: McGill Questionnaire – short form; *Douleur Neuropatique* 4 (DN4) questionnaire, and Neuropathic Pain Symptoms Inventory (NPSI)[42-44]. The Semmes-Weinstein esthesiometer, also called von Frey filaments, was used to analyze exteroceptive sensitivity and pain threshold at treated site[45].

Regarding the impact of antalgic radiotherapy, the response to treatment was evaluated according to the value found on the VAS; catastrophic thoughts about pain (PCS)[46]; the prevalence of anxiety and depression symptoms (HADS)[47].

Statistical analysis

Pre and Post radiotherapy effects were evaluated using the Wilcoxon test. The Kruskal-Walli's test (unpaired, Dunn's post-test) was used for comparisons between groups. For all analyses, a significance level of $p<0.05$ was adopted, using the GraphpadPrism® version 8.0 (GraphPad Software, Inc.). Data were expressed as mean±standard error of mean (SEM), absolute numbers (n) or percentage (%).

RESULTS

Seventy-five patients were included in this study, but only 48 remained. Of the 48 patients who participated, only 28 (58.3%) had data collected one month after radiotherapy (Figure 1). General analysis showed that 25 of the participants were male and 23 were female, with 60.4% from the city of Santarém. Socioeconomic data showed that 46% had an income of less than 1 minimum wage, 71% performed manual work (with or without qualification), 50% of the population had low education, 47.9% had low cognitive profile, and 93.8% were at low risk for alcoholism (Table 1).

Data were expressed in absolute numbers (n), mean±sem and percentage (%) from the following questionnaires: socioeconomic (ABEP), alcohol abuse (AUDIT), premorbid abilities by Premorbid Cognitive Abilities scale (PCAS) and cognition and schooling (MEEM), occupation and gender. Clinical data regarding primary cancer sites and follow up outcome was also included, based on a heterogeneous sample of 48 patients evaluated in GraphPad prism software 8, n/a: not applicable.

Regarding clinical variables, 73% of the patients denied any concomitant disease, 95.8% had metastatic disease, and 89.5% of the patients were treated for bone metastases. The most common primary sites were prostate (33.3%, n=16) and breast (31.3%, n=15), and the 30 Gray regimen in 10 fractions was the most prescribed schema (91.6%, n=44). Follow-up analysis in January 2022 using data available in the electronic medical record showed that 43.7% of patients underwent some form of therapy, either hormonal therapy (31.2%, n=15) or chemotherapy (12.5%, n=6), and 29.2% (n=14) of patients died (Table 1).

Nutritional status

The stratification by CASCO demonstrated that 24 patients were classified as cachectic, with 12.5% having mild cachexia (n=3), 33.3% moderate cachexia (n=8), and 54.2% having severe cachexia (n=13). Among cachectic patients, mean weight loss was 17.8%. Nevertheless, 62.5% were classified in the normal BMI range. Compartmental analysis revealed 71% patients with low ALMI and 54.2% with low FFMI, highlighting the sarcopenia that occurs in this group of patients and showing that simple analysis of body mass index is not sufficient in this regard. In non-cachectic patients, the mean weight loss was 3.3%. According to BMI, 42% were overweight and 38% were in the normal weight range; 54% had low ALMI and 54% had normal FFMI, once again highlighting the need for individual compartment analysis, as sarcopenic obesity may occur in these patients (Table 2).

ALMI = Appendicular Lean Mass Index; ANO = anorexia; BMI = Body Mass Index; BWC = body weight loss; FFMI = Fat Free Mass Index; IMD = inflammatory, metabolic, and immunological disorders; PHP = physical performance; QoL = quality of life; pts max = maximum of points per domain; n/a = not applicable.

Data were shown in absolute numbers (n) and percentage (%), according to the Nutritional Instrumentalized Assessment and Cachexia Score (CASCO). Calculated with Graphpad prism software 8, based on a heterogeneous sample of 48 patients.

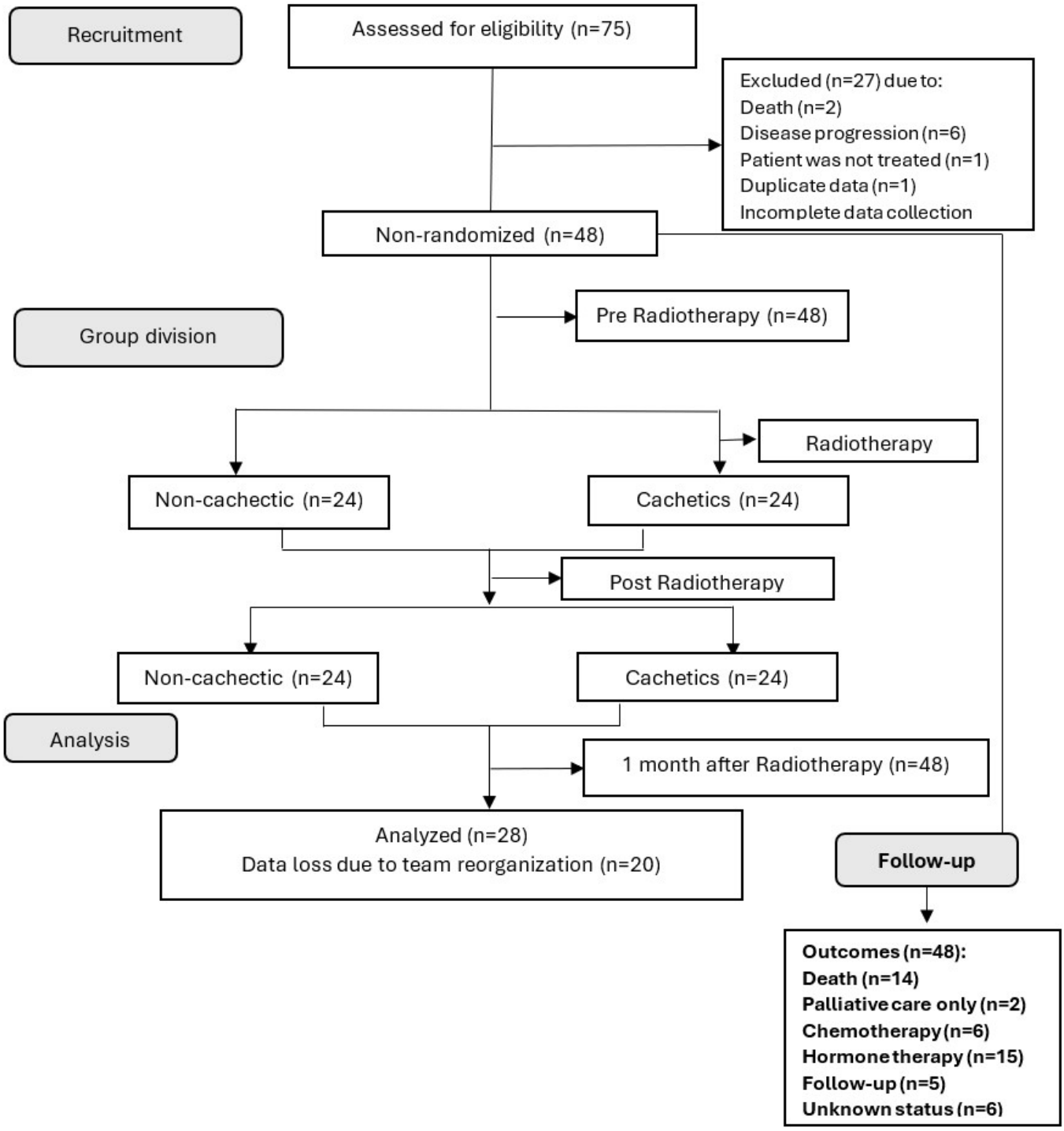

Figure 1. Study Flow Chart. Recruitment, division of groups, analysis and follow-up. Data were expressed in absolute numbers (n).

Regardless of the cachexia stage classification, analysis of the 5 domains of CASCO (Table 2) revealed higher scores in all domains in the cachectic group and an overall mean score of 47.4 versus 20 in non-cachectic group. It is worth noting that the physical performance domain is severely impaired in both groups, with high mean scores, consistent with the clinical characteristics of the population with metastatic neoplasia.

Pain characteristics

Regarding the predominant type of pain, the DN4 questionnaire revealed that the cachectic group had more individuals with neuropathic pain (83.3%) and this amount decreased after irradiation (54.2%), which was not observed in non-cachectic group (41.7% pre and post-RT). Regarding nociceptive pain, the total amount

Table 1. Epidemiological and clinical data.

Epidemiological and clinical history	n	Mean±SEM	%
Women	23	49.1 ± 2.6	48
Men	25	66 ± 1.9	52
Economic Classification (ABEP)			
	n	**Mean±SEM**	**%**
B2	5	25.6 ± 0.7	10
C1	10	20.2 ± 0.4	21
C2	10	15.9 ± 0.3	21
D	22	11.9 ± 0.4	46
E	1	5 ± 0.0	2
Cognition and schooling (MEEM)			
Low schooling/ cognition	24	13.7 ± 0.9	50
Satisfactory schooling/cognition	24	24 ± 0.6	50
Premorbid Cognitive Abilities Scale (PCAS)			
≤15 points (low cognitive profile)	23	6.4 ± 0.98	47.9
≥ 16 points (high cognitive profile)	25	21.4 ± 0.8	52.1
Occupation			
Manual work	34	n/a	71
Services	12	n/a	27
Intelectual	1	n/a	2
Risk of Alcohol abuse(AUDIT)			
Low risk	45	0.11 ± 0.07	93.8
Risk consumption	2	8.0 ± 0.0	4.2
Likely dependency	1	23.0 ± 0.0	2.1

Primary site	Non-cachetics	Cachetics	Follow up outcome	Non-cachetics	Cachetics
	% (n)	% (n)		% (n)	% (n)
Prostate	37.5% (n=9)	29.2% (n=7)	Death	12.5% (n=3)	45.8% (n=11)
Breast	37.5% (n=9)	25% (n=6)			
Lung	8.3% (n=2)	12.5% (n=3)	Palliative care	0	8.3% (n=2)
Uterine cervix	4.17% (n=1)	4.15% (n=1)	Chemotherapy	12.5% (n=3)	12.5% (n=3)
Gastrointestinal	4.17% (n=1)	8.3% (n=2)	Hormone therapy	45.8% (n=11)	16.7% (n=4)
Multiple Myeloma	4.17% (n=1)	4.15% (n=1)	Oncologic follow up	20.8% (n=5)	0
Others	4.17% (n=1)	16.7% (n=4)	Unknown status	8.3% (n=2)	16.7% (n=4)

of non-cachectic patients after RT was reduced by half, however it was observed an increase in the number of cachectic patients who had nociceptive pain, which were maintained at 1 month after RT analysis (Table 3), demonstrating the role of palliative radiation in controlling neuropathic pain.

CASCO = Cachexia Score; Pre = pre-RT; Post = post-RT; 1 month = 1 month post-RT; RT = radiotherapy; MPeT = Mechanical perception thresholds; MPT = mechanical pain threshold; SMPT = supra-mechanical pain threshold; MST = Von Frey filament summation test; ALOD = allodynia at the treated site; WUR = wind up ratio.

Data was shown in absolute numbers (n), percentage (%), according to the Instrumentalized Assessment (DN4 questionnaire, McGill short form and mechanical pain threshold von frey evaluation), based on a heterogeneous sample of 48 patients stratified by CASCO - pre-RT and post-RT patients and 21 patients

Table 2. Nutritional status analysis and cachexia diagnosis

Nutritional status	Non-cachectic		Cachectic	
	n	%	n	%
Body Mass Index (BMI)				
Underweight (<18,5)	2	8	6	25
Healthy weight range (18,6-24,9)	9	38	15	62.5
Overweight (25-29,9)	10	42	3	12.5
Obesity (>30)	3	27	0	0
Appendicular Lean Mass Index (ALMI)				
Low (<7,6 kg/m2 men; < 5,5kg/m2 women)	13	54	17	71
Normal (>7,6 kg/m2 men; >5,5kg/m2 women)	11	46	7	29
Fat Free Mass Index (FFMI)				
Low (<16,7 kg/m2 men; < 14,6 kg/m2 women)	8	33	13	54.2
Normal (16,7 a 19,8 kg/m2 men; 14,6 a 16,8 kg/m2 women)	13	54	8	33.3
High (>19,8 kg/m2 men; >16,8 kg/m2 women)	3	13	3	12.5
CASCO	**Non-cachectic**		**Cachectic**	
Domains	**n**	**%**	**n**	**%**
BWC (40 pts max)	0.1	n/a	21.3	n/a
IMD (20 pts max)	3		4.5	
PHP (15 pts max)	9		10.3	
ANO (15 pts max)	3.6		6.1	
QoL (10 pts max)	4.4		5.2	
Mean Score	20		47.4	

1 month post-RT. Calculated with Graphpad prism software 8 (Kruskal-Wallis test).

The McGill short form questionnaire demonstrated that there was symptomatologic improvement in mean scores in three dimensions (sensory, affective, and evaluative), intensity, and total score in both groups after radiotherapy (Table 3). There was a reduction of 24.2% in the total score in the cachectic group and a reduction of 47.5% in the non-cachectic group comparing pre-RT and 1-month post-RT. Analysis of Mechanical Pain Thresholds revealed no significant difference after stratification by cachexia score at the three time points (Table 3).

Using the Neuropathic Pain Symptoms Inventory (NPSI), a significant decrease in neuropathic symptoms after irradiation (pre-RT: 32.56±3.88/ post-RT: 22.71±3.22; p=0.0004 - Figure 2A) was seen. Non-cachectic patients (post-RT: 12.21±3.08) had a significant reduction in neuropathic pain symptoms compared to the cachectic group (post-RT: 33.21±4.83; p= 0.0176 - Figure 2B), which supported the finding of a worse symptomatic response to irradiation in the cachectic group. The analysis also revealed a longer duration of pain in the cachectic patients (Figure 2C) and a similar paroxysmal pain level between the groups (Figure 2D).

PCS = Pain Catastrophizing Scale; VAS = Visual Analogue Scale; Pre = pre-RT; Post = post-RT; 1 month = 1-month post-RT; RT = radiotherapy; NPSI = Neuropathic Pain Symptoms of 48 pre/ post-RT patients and 21 1- month post-RT patients.

(A) NPSI (***p=0.0004), (B) NPSI (*p=0.0176), (C) VAS (*p=0.0114), (D) PCS (*p=0.0045) and (E) PCS (p>0.9999). Calculated with Graphpad prism software 8, Pre vs. Post-RT – Wilcoxon test or non-cachectic vs Cachectic (pre, post and 1-month post-RT) – Kruskal-Wallis.

Cachectic patients reported higher VAS pain scores (pre-RT: 3,58±0,62/ post-RT: 3,37±0,54/ 1 month post-RT: 2,27±0,61) when compared to non-cachectic (pre-RT: 2,83±0,58/ post-RT: 1,04±0,44/ 1 month post-RT: 2,60±1,10) at all time points examined. Moreover, the non-cachectic group showed significantly lower scores post-RT (Figure 2E), suggesting some influence of nutritional status in the response to pain, more intense and less responsive to antalgic radiotherapy in the cachectic group.

Emotional aspects of pain

Anxiety, Depression, and catastrophic thoughts stratified by CASCO showed higher percentages and scores in cachectic group than non-cachectic (Table 4). Post-RT evaluation between cachectic and non-cachectic were significant (p<0.0001) in catastrophic thoughts of patients (no shown data).

Table 3. Pain profile analysis.

	Non-cachectic			Cachectic			
	Pre-RT	Post-RT	1 month Post-RT	Pre-RT	Post-RT	1 month Post-RT	
Neuropathic pain (DN≥4)	41.7% (n=10)	41.7% (n=10)	30% (n=3)	83.3% (n=20)	54.2% (n=13)	36.4% (n=4)	n/a
Nociceptive pain (DN4<4)	50% (n=12)	25% (n=6)	30% (n=3)	12,5% (n=3)	33.3% (n=8)	36.4% (n=4)	n/a
Painless (DN4=0)	8.3% (n=2)	33.3% (n=8)	40% (n=4)	4,2% (n=1)	27.3% (n=3)	27.3% (n=3)	n/a
Mcgill Dimensions	**Non-cachectic**			**Cachectic**			
	Pre-RT	**Post-RT**	**1 month Post-RT**	**Pre-RT**	**Post-RT**	**1 month Post-RT**	
	mean±sem	**mean±sem**	**mean±sem**	**mean±sem**	**mean±sem**	**mean±sem**	**p-value**
Intensity (0-10)	6.5±0.6	5.3±0.7	4.3±1.3	8.7±0.3	6.2±0.8	4.8±2.1	0.0271*
Sensory (max. 8 pts)	4.4±0.5	3.5±0.6	1.2±0.6	6.4±0.4	4.4±0.7	3±1.7	0.0008*
Affective (max. 5 pts)	3.1±0.4	2.4±0.3	2.0±0.7	3.8±0.3	3.7±0.4	2.4±1.0	0.0982
Evaluative (max. 2 pts)	1.4±0.1	1.0±0.1	0.8±0.3	1.6±0.1	1.4±0.2	0.8±0.4	0.0377*
Total (max. 15 pts)	9.0±0.9	6.9±1.0	4.7±1.8	11.6±0.6	9.3±1.1	6.2±3.0	0.0186*
Mechanical Pain Thresholds	**Non-cachetic**			**Cachetic**			
	Pre-RT	**Post-RT**	**1 month post-RT**	**Pre-RT**	**Post-RT**	**1 month post-RT**	
	mean±sem	**meana±sem**	**mean±sem**	**mean±sem**	**mean±sem**	**mean±sem**	**p-value**
MPeT(g)	0.32±0.09	0.20±0.06	0.09±0.01	0.36±0.09	0.39±0.16	0.15±0.02	>0.9999
MPT (g)	1.24±0.48	0.82±0.34	0.23±0.03	1.54±0.34	1.41±0.48	1.82±0.96	>0.9999
SMPT (VAS)	3.04±0.53	2.79±0.49	2.00±0.42	3.54±0.41	3.70±0.50	2.72±0.76	>0.9999
ALOD (VAS)	5.20±0.84	3.33±0.82	3.30±1.23	4.50±0.77	4.75±0.77	5.63±1.26	>0.9999
WUR	0.73±0.08	0.75±0.07	0.81±0.06	0.70±0.05	0.72±0.05	0.75±0.09	>0.9999

Table 4. Emotional aspects of pain.

Anxiety	**Non-cachectic**			**Cachectic**			**p-value**
	Pre-RT	**Post-RT**	**1 month Post-RT**	**Pre-RT**	**Post-RT**	**1 month Post-RT**	
Likely	12.5% (n=3)	12.5% (n=3)	0%	29.2% (n=7)	29.2% (n=7)	15.4% (n=2)	0.5404
Possible	25% (n=6)	20.8% (n=5)	14.3% (n=2)	25% (n=6)	33.3% (n=8)	38.5% (n=5)	
Unlikely	62.5% (n=15)	66.7% (n=16)	85.7% (n=12)	45.8% (n=11)	37.5% (n=9)	46.2% (n=6)	
Depression	**Pre-RT**	**Post-RT**	**1 month Post-RT**	**Pre-RT**	**Post-RT**	**1 month Post-RT**	**p-value**
Likely	16.7% (n=4)	16.7% (n=4)	14.3% (n=2)	33.3% (n=8)	50% (n=12)	53.8% (n=7)	0.3915
Possible	29.2% (n=7)	33.3% (n = 8)	50% (n=7)	29.2% (n=7)	16.7% (n=4)	15.4% (n=2)	
Unlikely	54.2% (n=13)	50% (n=2)	35.7% (n=5)	37.5% (n=9)	33.3% (n=8)	30.8% (n=4)	
PCS score	**Pre-RT**	**Post-RT**	**1 month Post-RT**	**Pre-RT**	**Post-RT**	**1 month Post-RT**	**p-value**
	mean±sem	mean±sem	mean±sem	mean±sem	mean±sem	mean±sem	>0.9999
	15.75±2.50	11.21±1.48	9.20±3.07	23.79±2.98	20.38±2.77	14.82±4.10	

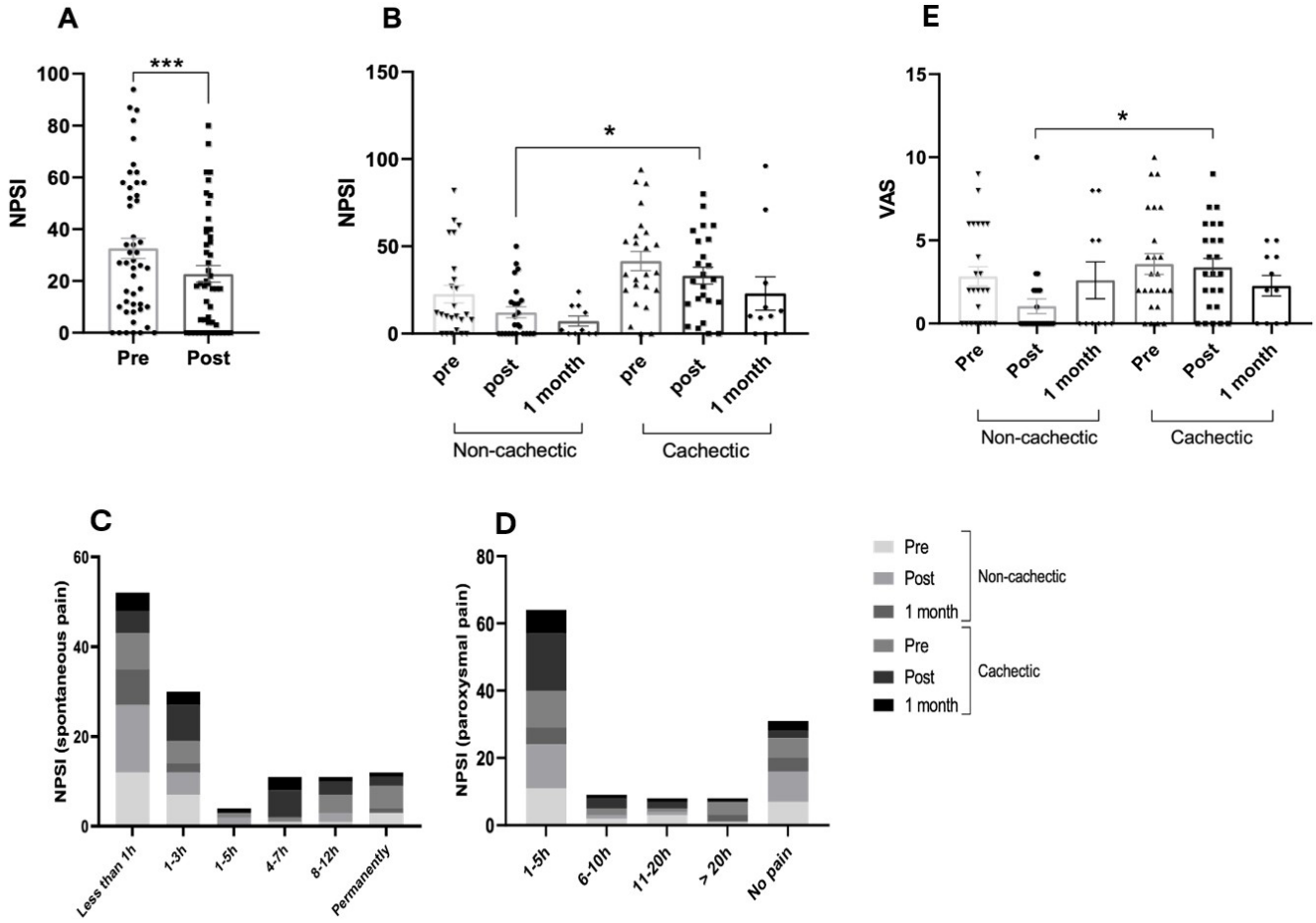

Figure 2. Pain profile. Neuropathic Pain Symptoms (NPSI) of 48 pre/post-RT patients and 21 1- month post-RT patients. (A) NPSI (***p=0.0004), (B) NPSI (*p=0.0176), (C) spontaneous pain on CASCO, (D) paroxysmal pain on CASCO, (E) VAS (*p=0.0114). Calculated with Graphpad prism software 8, Pre vs. Post-RT – Wilcoxon test or Non-Cachectic vs Cachectic (pre, post and 1-month post-RT) – Kruskal-Wallis. Abbreviations: CASCO- Cachexia Score, VAS- Visual Analogue Scale; Pre: pre-RT; Post: post-RT; 1 month: 1 month post-RT; RT: radiotherapy.

Data were shown in absolute numbers (n), percentage (%) and mean±sem according to the Instrumentalized Assessment (Hospital Anxiety and Depression Scale and Pain Catastrophizing Scale), based on a heterogeneous sample of 48 patients stratified by CASCO - pre-RT and post-RT patients and 21 patients 1 month post-RT. Calculations were done using the Graphpad prism software 8 (Kruskal-Wallis test). HADS = Hospital Anxiety and Depression Scale; CASCO = Cachexia Score; Pre: pre-RT; Post: post-RT; 1 month: 1-month post-RT; RT = radiotherapy.

DISCUSSION

In this study, the geographic scope and its peculiarities, with predominantly river access, and with a population mostly of manual workers, is reflected in the characteristics found in the sample. The geographical location is in the Brazilian Amazon, in the state of Pará, which represents 18.6% of this territory. Santarém is the third largest city in the state, where 45.6% of households earn up to half the minimum wage per person and only 38.1% have a sewage system, according to the *Instituto Brasileiro de Geografia e Estatística* (IBGE - Brazilian Institute of Geography and Statistics) data from the last 2020 census[27].

Attention was drawn to the fact that the average age of the studied population was still of working age, in line with the characteristics of low income and precarious health care in the lower Amazon region, requiring centralization of a highly complex healthy network in Santarém. This can certainly have an impact on the economy and maintenance of several families, associated with the psychological stress of the situation, as in addition to having the patient not working, they also need to move a companion to carry out their daily care. The authors report in their study on pain in cancer patients that most patients are men, with a mean age of 50 years and most of them without education or with low education[8,48].

The population studied had an advanced oncological stage and treated primary tumors of the prostate and breast with metastases to the bones. Half of the sample was classified as eutrophic based on BMI, but compartmental analysis showed low lean mass in most patients. About the clinical conditions reported in this study, a similar scenario has been described by several authors in the literature, following natural history of the most prevalent

underlying diseases and their predominantly bone metastasizing route.[7,16,48,49] As it is known, in bones with metastases there is a change in the normal cycle of homeostasis between osteoclasts and osteoblasts, in addition to periosteal and medullary chemical changes, resulting at the perception of acute or chronic pain, associated with neuropathic characteristics, through acidification of the microenvironment, associated with the secretion of cytokines and inflammatory mediators.[7,49]

According to the Brazilian Society of Nutrology (2011)[50], the prevalence of malnutrition in cancer patients ranges from 30 to 80%, depending on the tumor type and stage of the disease. In the present study, according to the CASCO, half of the patients were classified as cachectic, although the majority in this group were eutrophic by BMI.

Oncological cachexia syndrome has an estimated prevalence of 50% to 80% in patients in more advanced stages, causing 20% of deaths in this group[51]. The percentage of patients classified as cachectic in the study could have been different if the sample had considered all patients undergoing Radiotherapy, as some tumor types, such as head and neck, gastrointestinal tract and lung tumors, are more associated with of muscle mass loss than others, such as breast and prostate[52], the most prevalent in this study.

The data also show the importance of compartmental analysis in the construction of the nutritional profile for a better individualized clinical therapeutic plan[53]. The increase in energy consumption due to tumor growth associated with factors that reduce caloric intake, such as those related to the disease itself or resulting from the side effect of antineoplastic therapies, promote weight and lean mass loss in cancer patients[50]. In addition, sarcopenia secondary to aging itself must be considered, as shown by the higher prevalence of low ALMI in men who had a higher mean age than women[54]. The depleted nutritional status also has a negative impact on quality and length of life of the cancer patients, in addition to decreasing tolerance to oncological treatment[50,55]. The need for early investigation of the nutritional status of cancer patients and multidisciplinary intervention becomes increasingly clear when the implications for pain control, reduction of symptoms and quality of life are analysed[55-58].

Cancer pain is extremely complex and involves several neurotransmitters, in addition to being directly related to the tumor biology, type of pain, and inherent patient factors[12]. The prevalence of neuropathic pain in cancer patients can be as high as 40%, and patients with this type of pain report more severe pain and poorer quality of life[59], which correlates with the profile of cachectic patients. In this study, cachectic patients had neuropathic pain, higher pain scores and significantly poorer response to radiotherapy.

The cachectic group had higher rate of worsening of pain after treatment, and greater proportion of partial response, suggesting that the persistent inflammation in cachexia may contribute to the antalgic therapeutic response, also seen in animal studies[60]. The reference authors[61,62] reinforced this hypothesis by noting that cachectic patients require a higher opioid dose for pain control. High baseline pain, young age, absence of visceral metastases, and opioid use are positive predictors of response to radiotherapy.[11]

Regarding the pain response to radiotherapy, a complete response can be achieved in 25% of patients and a partial response in 70%. Pain relief usually occurs within one to two weeks[63]. The study[10] showed a partial response of 49 to 88% in the first month and 60% to 74% three months after treatment. Another study[11] reported that 60% of patients experienced pain improvement with radiotherapy, which is consistent with the data from the present article. As for the preferred dose regimen prescribed in this study (30 Gy in 10 fractions), its equivalence in terms of analgesia is not questioned[10,11].

In this study, patients well responded to antalgic irradiation both immediately and after one month of treatment. They showed significant reduction in pain symptom scores, and reduction in neuropathic pain symptoms. Authors[64] noted that palliative radiotherapy is often used in treatment of painful bone metastases and is effective for improving symptoms and quality of life. Unfortunately, not all patients experience pain relief after radiotherapy. A complete response is observed in approximately 25% of patients, and a partial response in 40 to 60%. The average duration of response is 1 to 4 weeks[65]. Among the patients studied, an immediate complete response was seen in 25% and an immediate partial response in 31.3%, corroborating data from the literature.

Accessing the global reality of cancer pain by proposing a consensus for Latin America, the work of authors[66] shows the influence of pain on the quality of life of patients, associated with the need for training the medical team in the correct management of pain. In the exposition on the data of specialists in Brazil, it was demonstrated that numerous factors interfere in good pain control, from the low socioeconomic conditions of patients, deficiencies in the health system for the policy of drugs and professionals trained in the treatment of cancer pain. It is also considered that public policy does not integrate palliative care and does not coordinate the treatment and returns of patients in the various areas of oncology, as well as the prioritization of tumor treatment, without having clinical protocols for managing cancer pain included in the protocols of cancer treatment in general[66].

The concept of total pain postulated by Saunders is reflected in the population by its impact on patients' characterization and perception of symptoms[23,24]. Moreover, it provides an option and adds an emotional component to the process of palliative care. The indication of radiotherapy, albeit in a palliative manner, brings comfort and a sense of caring. The psychological domain of pain is minimized in this way, as evidenced by analysis of catastrophic thoughts and grading of neuropathic symptoms. In the cachectic group, there was more neuropathic pain with significantly lower response in symptoms and longer pain duration.

There may be a relationship between catastrophism and biological factors such as chronic stress and inflammatory responses[67], which could explain the results in this group. In this study, cachectic patients had more neuropathic pain characteristics and longer pain duration. It was also found that, this group had a higher score for catastrophic thoughts. Still, although more than half of the patients (73%) did not report any comorbidities, symptoms of anxiety and/or depression were noted in 58.3% of them. Depression is usually present in 5% to 30% of cancer patients, and patients with advanced cancer and depression have more symptoms such as pain, this can be bidirectional[11].

The symptoms reported change over time and are usually accompanied by anxiety and depression, which may affect

cognitive functioning, performance in daily life, and psychosocial functioning[68]. Literature reports that worsening pain can heighten psychological distress, including symptoms of depression and anxiety, and this effect is apparent across all stages of cancer[69]. The pain-emotion relationship has been evaluated through functional magnetic resonance imaging (fMRI) of the brain. Images reveal that both cortical and subcortical regions involved in pain perception also play a role in processing emotions, such as insula and cingulate cortices[70]. Anxiety and depression scores, either alone or in combination, were higher in cachectic patients, and although they were not statistically significant, they may suggest that the permanent inflamed state correlates with brain sensitization, as reported in literature[25].

Nutrition and nervous and immune system functioning are also intertwined, and early nutritional interventions may reduce pain in cancer patients[21,22,55]. Therefore, nutritional stratification of cancer patients is urgent because muscle loss can occur even in individuals with normal BMI[71,72]. Performing multidimensional assessment to identify vulnerabilities in the physical, functional, and psychological domains can better guide the treatment and allow early intervention in reversible phases of muscle mass loss, gains in quality of life and tolerability to treatment. The nutritional status of the individual and the extent of systemic inflammation are undeniably related to cancer and pain in general. Because all these mechanisms are complex, it is difficult to analyze them individually[20,60].

CONCLUSION

Considering the results obtained in this study, the negative influence of inadequate nutritional status on the response to antalgic irradiation is clear, and this factor should be considered in the interdisciplinary treatment planning for cancer patients. Further research is necessary, since a significant challenge was the patients' difficulty in returning for follow-up collections one month after treatment. This issue notably reduced the number of patients with analyzable data. Additionally, the research team was unable to remain consistently available for data collection.

REFERENCES

1. Caraceni A, Shkodra M. Cancer pain assessment and classification. Cancers (Basel). 2019;11(4):510. http://doi.org/10.3390/cancers11040510. PMid:30974857.
2. Vendrell I, Macedo D, Alho I, Dionísio MR, Costa L. Treatment of cancer pain by targeting cytokines. Mediators Inflamm. 2015;2015(1):984570. http://doi.org/10.1155/2015/984570. PMid:26538839.
3. Raphael J, Ahmedzai S, Hester J, Urch C, Barrie J, Williams J, Farquhar-Smith P, Fallon M, Hoskin P, Robb K, Bennett MI, Haines R, Johnson M, Bhaskar A, Chong S, Duarte R, Sparkes E. Cancer pain: Part 1: Pathophysiology; oncological, pharmacological, and psychological treatments: a perspective from the British pain society endorsed by the UK association of palliative medicine and the royal college of general practitioners. Pain Med. 2010;11(5):742-64. http://doi.org/10.1111/j.1526-4637.2010.00840.x PMid:20546514.
4. Tepper J. Gunderson and Tepper's Clinical Radiation Oncology. 5th ed. Amsterdam: Elsevier; 2021.
5. Salvajoli JV, Souhami L, Faria SL. Radioterapia em Oncologia. 2nd ed. São Paulo: Atheneu; 2013.
6. Halperin EC, Wazer DE, Perez CA, Brady LW. Perez & Brady's Principles and Practice of Radiation Oncology. 7th ed. Alphen: LLW; 2018.
7. Aielli F, Ponzetti M, Rucci N. Bone metastasis pain, from the bench to the bedside. Int J Mol Sci. 2019;20(2):280. http://doi.org/10.3390/ijms20020280. PMid:30641973.
8. Nomiya T, Teruyama K, Wada H, Nemoto K. Time course of pain relief in patients treated with radiotherapy for cancer pain: a prospective study. Clin J Pain. 2010;26(1):38-42. http://doi.org/10.1097/AJP.0b013e3181b0c82c. PMid:20026951.
9. Milgrom DP, Lad NL, Koniaris LG, Zimmers TA. Bone pain and muscle weakness in cancer patients. Curr Osteoporos Rep. 2017;15(2):76-87. http://doi.org/10.1007/s11914-017-0354-3. PMid:28497213.
10. Pin Y, Paix A, Le Fèvre C, Antoni D, Blondet C, Noël G. A systematic review of palliative bone radiotherapy based on pain relief and retreatment rates. Crit Rev Oncol Hematol. 2017;123:132-7. PMid:29482774.
11. Habberstad R, Frøseth TCS, Aass N, Abramova T, Baas T, Mørkeset ST, Caraceni A, Laird B, Boland JW, Rossi R, Garcia-Alonso E, Stensheim H, Loge JH, Hjermstad MJ, Bjerkeset E, Bye A, Lund J-Å, Solheim TS, Vagnildhaug OM, Brunelli C, Damås JK, Mollnes TE, Kaasa S, Klepstad P. The Palliative Radiotherapy and Inflammation Study (PRAIS) - protocol for a longitudinal observational multicenter study on patients with cancer induced bone pain. BMC Palliat Care. 2018;17(1):110. http://doi.org/10.1186/s12904-018-0362-9 PMid:30266081.
12. Gough N, Miah AB, Linch M. Nonsurgical oncological management of cancer pain. Curr Opin Support Palliat Care. 2014;8(2):102-11. http://doi.org/10.1097/SPC.0000000000000043. PMid:24675403.
13. Fallon M, Giusti R, Aielli F, Hoskin P, Rolke R, Sharma M, Ripamonti CI. Management of cancer pain in adult patients: ESMO Clinical Practice Guidelines. Ann Oncol. 2018;29(Suppl 4):iv166-91. http://doi.org/10.1093/annonc/mdy152 PMid:30052758.
14. Valeriani M, Scaringi C, Blasi L, Carnevale A, De Sanctis V, Bonome P, Bracci S, Marrone G, Minniti G, Enrici RM. Multifraction radiotherapy for palliation of painful bone metastases: 20 Gy versus 30 Gy. Tumori. 2015;101(3):318-22. http://doi.org/10.5301/tj.5000286 PMid:25908049.
15. Sierko E, Hempel D, Zuzda K, Wojtukiewicz M. Personalized radiation therapy in cancer pain management. Cancers (Basel). 2019;11(3):1-23. http://doi.org/10.3390/cancers11030390. PMid:30893954.
16. Bedard G, Wong E. Handbook of bone metastases for healthcare professionals. Toronto: Odette Cancer Centre; 2014.
17. World Health Organization. WHO guidelines for the pharmacological and radiotherapeutic management of cancer pain in adults and adolescents. 2018 [citado 2024 jul 12]. https://www.who.int/publications/i/item/9789241550390
18. Falk S, Bannister K, Dickenson AH. Cancer pain physiology. Br J Pain. 2014;8(4):154-62. http://doi.org/10.1177/2049463714545136. PMid:26516549.
19. Song XJ, Lamotte RH, Xie Z. Regulation of cytokines in cancer Pain. Mediators Inflamm. 2016;2016:2741205. http://doi.org/10.1155/2016/2741205. PMid:27087747.
20. Tick H. Nutrition and Pain. Phys Med Rehabil Clin N Am. 2015;26(2):309-20. http://doi.org/10.1016/j.pmr.2014.12.006. PMid:25952067.
21. Yılmaz ST, Elma Ö, Deliens T, Coppieters I, Clarys P, Nijs J, Malfliet A. Nutrition/dietary supplements and chronic pain in patients with cancer and survivors of cancer: a systematic review and research agenda. Pain Physician. 2021;24(5):335-44. PMid:34323435.
22. Gomez-Pinilla F, Gomez AG. The influence of dietary factors in central nervous system plasticity and injury recovery. PM R. 2011;3(6, Suppl 1):S111-6. http://doi.org/10.1016/j.pmrj.2011.03.001. PMid:21703566.
23. Mehta A, Chan LS. Understanding of the Concept of "Total Pain.". J Hosp Palliat Nurs. 2008;10(1):26-32. http://doi.org/10.1097/01.NJH.0000306714.50539.1a.
24. Wood J. Cicely Saunders,'Total Pain'and emotional evidence at the end of life. Med Humanit. 2022;48(4):411-20. http://doi.org/10.1136/medhum-2020-012107 PMid:33980664.
25. Nijs J, Elma Ö, Yilmaz ST, Mullie P, Vanderweeën L, Clarys P, Deliens T, Coppieters I, Weltens N, Van Oudenhove L, Malfliet A. Nutritional

neurobiology and central nervous system sensitisation: missing link in a comprehensive treatment for chronic pain? Br J Anaesth. 2019;123(5):539-43. http://doi.org/10.1016/j.bja.2019.07.016 PMid:31492528.

26. Raja SN, Carr DB, Cohen M, Finnerup NB, Flor H, Gibson S, Keefe FJ, Mogil JS, Ringkamp M, Sluka KA, Song XJ, Stevens B, Sullivan MD, Tutelman PR, Ushida T, Vader K. The Revised IASP definition of pain: concepts, challenges, and compromises. Pain. 2020;161(9):1976-82. http://doi.org/10.1097/j.pain.0000000000001939 PMid:32694387.
27. Kamakura W, Mazzon JA. Critérios de estratificação e comparação de classificadores socioeconômicos no Brasil. RAE. 2016;56(1):55-70. http://doi.org/10.1590/S0034-759020160106.
28. Associação Brasileira de Empresas de Pesquisa (ABEP). Critério de Classificação Econômica Brasil. 2022 [citado 2024 jul 12]. http://www.abep.org/criterio-brasil.
29. Brucki SMD, Nitrini R, Caramelli P, Bertolucci PHF, Okamoto IH. Suggestions for utilization of the mini-mental state examination in Brazil. Arq Neuropsiquiatr. 2003;61(3B):777-81. http://doi.org/10.1590/S0004-282X2003000500014 PMid:14595482.
30. Bertolucci PHF, Brucki SMD, Campacci SR, Juliano YO. Mini-Exame do Estado Mental em uma população geral: impacto da escolaridade. Arq Neuropsiquiatr. 1994;52(1):1-7. http://doi.org/10.1590/S0004-282X1994000100001. PMid:8002795.
31. Nitrini R, Caramelli P, Bottino CMC, Damasceno BP, Brucki SM, Anghinah R. Diagnóstico de doença de Alzheimer no Brasil: avaliação cognitiva e funcional. Recomendações do Departamento Científico de Neurologia Cognitiva e do Envelhecimento da Academia Brasileira de Neurologia. Arq Neuropsiquiatr. 2005;63(3-A):720-7. http://doi.org/10.1590/S0004-282X2005000400034. PMid:16172733.
32. Apolinario D, Brucki SMD, Ferretti REL, Farfel JM, Magaldi RM, Busse AL, Jacob-Filho W. Estimating premorbid cognitive abilities in low-educated populations. PLoS One. 2013;8(3):e60084. http://doi.org/10.1371/journal.pone.0060084 PMid:23555894.
33. Mendez EB. Uma versão Brasileira do AUDIT (Alcohol Use Disorders Identification Test) [dissertação]. Pelotas: Universidade Federal de Pelotas; 1999 [citado 2024 jul 12]. https://doi.org/10.1590/S0047-208520120003000015.
34. Henrique IF, De Micheli D, Lacerda RB, Lacerda LA, Formigoni ML. Validation of the Brazilian version of alcohol, smoking and substance involvement screening test. Rev Assoc Med Bras. 2004;50(2):199-206. http://doi.org/10.1590/S0104-42302004000200039 PMid:15286871.
35. Jomar RT, Paixão LAR, Abreu ÂMM. Artigo de atualização alcohol use disorders identification test (Audit) e sua aplicabilidade na atenção primária à saúde. Rev APS. 2012;15(1):113-7.
36. Kyle UG, Schutz Y, Dupertuis YM, Pichard C. Body composition interpretation: Contributions of the fat-free mass index and the body fat mass index. Nutrition. 2003;19(7-8):597-604. http://doi.org/10.1016/S0899-9007(03)00061-3. PMid:12831945.
37. Argilés JM, López-Soriano FJ, Toledo M, Betancourt A, Serpe R, Busquets S. The cachexia score (CASCO): A new tool for staging cachectic cancer patients. J Cachexia Sarcopenia Muscle. 2011;2(2):87-93. http://doi.org/10.1007/s13539-011-0027-5. PMid:21766054.
38. Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, Jatoi A, Loprinzi C, MacDonald N, Mantovani G, Davis M, Muscaritoli M, Ottery F, Radbruch L, Ravasco P, Walsh D, Wilcock A, Kaasa S, Baracos VE. Definition and classification of cancer cachexia: an international consensus. Lancet Oncol. 2011;12(5):489-95. http://doi.org/10.1016/S1470-2045(10)70218-7 PMid:21296615.
39. Evans WJ, Morley JE, Argilés J, Bales C, Baracos V, Guttridge D, Jatoi A, Kalantar-Zadeh K, Lochs H, Mantovani G, Marks D, Mitch WE, Muscaritoli M, Najand A, Ponikowski P, Rossi Fanelli F, Schambelan M, Schols A, Schuster M, Thomas D, Wolfe R, Anker SD. Cachexia: a new definition. Clin Nutr. 2008;27(6):793-9. http://doi.org/10.1016/j.clnu.2008.06.013 PMid:18718696.
40. Zukeran MS, Aprahamian I, Vicente BM, Ribeiro SML. Portuguese version of the snaq questionnaire: translation and cultural adaptation. Arq Gastroenterol. 2020;57(2):178-81. http://doi.org/10.1590/s0004-2803.202000000-33. PMid:32609159.
41. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, Haes JCJM, Kaasa S, Klee M, Osoba D, Razavi D, Rofe PB, Schraub S, Sneeuw K, Sullivan M, Takeda F. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst. 1993;85(5):365-76. http://doi.org/10.1093/jnci/85.5.365 PMid:8433390.
42. Ferreira KASL, de Andrade DC, Teixeira MJ. Development and validation of a Brazilian version of the short-form McGill pain questionnaire (SF-MPQ). Pain Manag Nurs. 2013;14(4):210-9. http://doi.org/10.1016/j.pmn.2011.04.006. PMid:24315244.
43. Martinez JE, Grassi DC, Marques LG. Análise da aplicabilidade de três instrumentos de avaliação de dor em distintas unidades de atendimento: ambulatório, enfermaria e urgência. Rev Bras Reumatol. 2011;51(4):299-308. http://doi.org/10.1590/S0482-50042011000400002. PMid:21779706.
44. Eckeli FD, Teixeira RA, Gouvêa ÁL. Neuropathic pain evaluation tools. Rev Dor. 2016;17(Suppl 1):20-2. http://doi.org/10.5935/1806-0013.20160041.
45. Levin S, Pearsall G, Ruderman RJ. Von Frey's method of measuring pressure sensibility in the hand: An engineering analysis of the Weinstein-Semmes pressure aesthesiometer. J Hand Surg Am. 1978;3(3):211-6. http://doi.org/10.1016/S0363-5023(78)80084-7. PMid:659817.
46. Sardá J Jr, Nicholas MK, Pereira IA, Pimenta CAM, Asghari A, Cruz RM. Validação da escala de pensamentos catastróficos sobre dor. Acta Fisiátrica. 2008;15(1):31-6.
47. Botega NJ, Bio MR, Zomignani MA, Garcia C Jr, Pereira WA. Mood disorders among inpatients in ambulatory and validation of the anxiety and depression scale HAD. Rev Saude Publica. 1995;29(5):355-63. PMid:8731275.
48. Tegegn HG, Gebreyohannes EA. Cancer pain management and pain interference with daily functioning among cancer patients in Gondar University Hospital. Pain Res Manag. 2017;2017:5698640. http://doi.org/10.1155/2017/5698640. PMid:28694715.
49. Spencer K, Parrish R, Barton R, Henry A. Palliative radiotherapy. BMJ. 2018;360:k821. http://doi.org/10.1136/bmj.k821. PMid:29572337.
50. Instituto Nacional do Câncer José Alencar Gomes da Silva (INCA). Consenso Nacional de Nutrição Oncológica. Rio de Janeiro: INCA; 2011.
51. Advani SM, Advani PG, Vonville HM, Jafri SH. Pharmacological management of cachexia in adult cancer patients: a systematic review of clinical trials. BMC Cancer. 2018;18(1):1174. http://doi.org/10.1186/s12885-018-5080-4. PMid:30482179.
52. Abbass T, Dolan RD, Laird BJ, McMillan DC. The relationship between imaging-based body composition analysis and the systemic inflammatory response in patients with cancer: a systematic review. Cancers (Basel). 2019;11(9):1-12. http://doi.org/10.3390/cancers11091304. PMid:31487957.
53. Chambard L, Girard N, Ollier E, Rousseau J-C, Duboeuf F, Carlier M-C, Brevet M, Szulc P, Pialat J-B, Wegrzyn J, Clezardin P, Confavreux CB. Bone, muscle, and metabolic parameters predict survival in patients with synchronous bone metastases from lung cancers. Bone. 2018;108:202-9. http://doi.org/10.1016/j.bone.2018.01.004 PMid:29337225.
54. Shaw SC, Dennison EM, Cooper C. Epidemiology of sarcopenia: determinants throughout the lifecourse. Calcif Tissue Int. 2017;101(3):229-47. http://doi.org/10.1007/s00223-017-0277-0. PMid:28421264.
55. Chen Y, Xiang Q, Li C, Zeng Y, Dong J, Zhang P, Li Y, Wang Y, Wang K. Nutritional risk and assessment for patients with cancer pain. Nutr Cancer. 2022;74(1):168-74. http://doi.org/10.1080/01635581.2021.1882510 PMid:33570437.
56. De Waele E, Demol J, Caccialanza R, Cotogni P, Spapen H, Malbrain MLNG, De Grève J, Pen JJ. Unidentified cachexia patients in the oncologic setting: cachexia UFOs do exist. Nutrition. 2019;63-64:200-4. http://doi.org/10.1016/j.nut.2019.02.015 PMid:31029048.
57. Bland KA, Harrison M, Zopf EM, Sousa MS, Currow DC, Ely M, Agar M, Butcher BE, Vaughan V, Dowd A, Martin P. Quality of life and symptom burden improve in patients attending a multidisciplinary clinical service for cancer cachexia: a retrospective observational review. J Pain Symptom Manage. 2021;62(3):e164-76. http://doi.org/10.1016/j.jpainsymman.2021.02.034 PMid:33652095.

58. Vagnildhaug OM, Balstad TR, Almberg SS, Brunelli C, Knudsen AK, Kaasa S, Thronæs M, Laird B, Solheim TS. A cross-sectional study examining the prevalence of cachexia and areas of unmet need in patients with cancer. Support Care Cancer. 2018;26(6):1871-80. http://doi.org/10.1007/s00520-017-4022-z PMid:29274028.

59. Yoon SY, Oh J. Neuropathic cancer pain: prevalence, pathophysiology, and management. Korean J Intern Med (Korean Assoc Intern Med). 2018;33(6):1058-69. http://doi.org/10.3904/kjim.2018.162. PMid:29929349.

60. Laird BJA, Scott AC, Colvin LA, McKeon A-L, Murray GD, Fearon KCH, Fallon MT. Cancer pain and its relationship to systemic inflammation: an exploratory study. Pain. 2011;152(2):460-3. http://doi.org/10.1016/j.pain.2010.10.035 PMid:21159432.

61. Morio K, Yamamoto K, Yano I. Relationship between tramadol response and cancer cachexia: a retrospective cohort study. Am J Hosp Palliat Med. 2021;38(3):276-82. http://doi.org/10.1177/1049909120945570. PMid:32734768.

62. Chiba T, Takahashi H, Tairabune T, Kimura S, Ueda H, Kudo K. Cancer cachexia may hinder pain control when using fentanyl patch. Biol Pharm Bull. 2020;43(5):873-8. http://doi.org/10.1248/bpb.b19-01086. PMid:32378563.

63. Ziętarska M, Krawczyk-Lipiec J, Kraj L, Zaucha R, Małgorzewicz S. Chemotherapy-related toxicity, nutritional status and quality of life in precachectic oncologic patients with, or without, high protein nutritional support. A prospective, randomized study. Nutrients. 2017;9(10):1108. http://doi.org/10.3390/nu9101108. PMid:29019951.

64. Cellini F, Manfrida S, Deodato F, Cilla S, Maranzano E, Pergolizzi S, Arcidiacono F, Di Franco R, Pastore F, Muto M, Borzillo V, Donati CM, Siepe G, Parisi S, Salatino A, D'Agostino A, Montesi G, Santacaterina A, Fusco V, Santarelli M, Gambacorta MA, Corvò R, Morganti AG, Masiello V, Muto P, Valentini V. Pain REduction with bone metastases STereotactic radiotherapy (PREST): A phase III randomized multicentric trial. Trials. 2019;20(1):609. http://doi.org/10.1186/s13063-019-3676-x PMid:31661034.

65. Habberstad R, Frøseth TCS, Aass N, Bjerkeset E, Abramova T, Garcia-Alonso E, Caputo M, Rossi R, Boland JW, Brunelli C, Lund J-Å, Kaasa S, Klepstad P. Clinical predictors for analgesic response to radiotherapy in patients with painful bone metastases. J Pain Symptom Manage. 2021;62(4):681-90. http://doi.org/10.1016/j.jpainsymman.2021.03.022 PMid:33794301.

66. Escobar Alvarez Y, Agamez Insignares C, Ahumada Olea M, Barajas O, Calderillo G, Calvache Guamán JC, Caponero R, Cavenago Salazar BA, Del Giglio A, Pupo Araya AR, Villalobos-Valencia R, Yepes Pérez A, Zumelzu Delgado N. Cancer pain management: recommendations from a Latin-American experts panel. Future Oncol. 2017;13(27):2455-72. http://doi.org/10.2217/fon-2017-0288 PMid:28777006.

67. Sehn FC. Validação da Escala de Pensamentos Catastróficos e associação do catastrofismo com marcadores biológicos. [dissertação]. Porto Alegre: Universidade Federal do Rio Grande do Sul; 2012.

68. Russo MM, Sundaramurthi T. An overview of cancer pain: epidemiology and pathophysiology. Semin Oncol Nurs. 2019;35(3):223-8. http://doi.org/10.1016/j.soncn.2019.04.002. PMid:31085106.

69. Arora A, Saini SK, Nautiyal V, Verma SK, Gupta M, Kalra BP, Ahmad M. Cancer pain, anxiety, and depression in admitted patients at a tertiary care hospital: a prospective observational study. Indian J Palliat Care. 2019;25(4):562-6. http://doi.org/10.4103/IJPC.IJPC_4_19 PMid:31673213.

70. Gilam G, Gross JJ, Wager TD, Keefe FJ, Mackey SC. What Is the Relationship between Pain and Emotion? Bridging Constructs and Communities. Neuron. 2020;107(1):17-21. http://doi.org/10.1016/j.neuron.2020.05.024. PMid:32562660.

71. Tang PL, Wang HH, Lin HS, Liu WS, Chen LM, Chou FH. Body composition early identifies cancer patients with radiotherapy at risk for malnutrition. J Pain Symptom Manage. 2018;55(3):864-71. http://doi.org/10.1016/j.jpainsymman.2017.10.005. PMid:29051113.

72. Bye A, Sjøblom B, Wentzel-Larsen T, Grønberg BH, Baracos VE, Hjermstad MJ, Aass N, Bremnes RM, Fløtten Ø, Jordhøy M. Muscle mass and association to quality of life in non-small cell lung cancer patients. J Cachexia Sarcopenia Muscle. 2017;8(5):759-67. http://doi.org/10.1002/jcsm.12206 PMid:28493418.

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