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Chronic Pain, Functionality and Quality of Life in Cancer Survivors

João Pedro do Poço Castro Gonçalves

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Chronic Pain, Functionality and Quality of Life in Cancer Survivors

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João Pedro do Poço Castro Gonçalves

Aluno do 6º ano profissionalizante de Mestrado Integrado em Medicina

Afiliação: Instituto de Ciências Biomédicas Abel Salazar – Universidade do Porto

Endereço: Rua de Jorge Viterbo Ferreira, n.º 228, 4050-313 Porto

Endereço eletrónico: jpocogoncalves@gmail.com

Orientador: Professora Doutora Dalila Maria Rodrigues Gonçalves Veiga Mora

Assistente hospitalar de Anestesiologia do Centro Hospitalar Universitário do Porto, EPE – Hospital Geral Santo António

Afiliação: Serviço de Anestesiologia do Centro Hospitalar Universitário do Porto

Endereço: Largo Prof. Abel Salazar, 4099-001 Porto

Coorientador: Professor Doutor António Manuel Ferreira Araújo

Assistente hospitalar graduado sénior de Oncologia do Centro Hospitalar Universitário do Porto, EPE – Hospital Geral Santo António

Professor Catedrático Convidado do Instituto de Ciências Biomédicas Abel Salazar - Universidade do Porto

Afiliação: Serviço de Oncologia do Centro Hospitalar Universitário do Porto e Instituto de Ciências Biomédicas Abel Salazar – Universidade do Porto

Endereço: Largo Prof. Abel Salazar, 4099-001 Porto

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Epígrafo

*“De médico, poeta e louco,
todos temos um pouco”*

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Abstract

The increasing number of cancer survivors associated to a longer average life-span after diagnosis of an oncological disease facilitates the observation of deleterious long-term effects of both oncological disease and its treatment. Among these effects, chronic pain emerges as one of the most prevalent and, with its onset, there is a decrease in these patients' functionality and quality of life. The main focus in oncological disease treatment has been tumour eradication and average life expectancy extension after diagnosis, neglecting these deleterious long-term effects.

This study aims at assessing the prevalence and characteristics of chronic pain in cancer survivors, as well as pain interference in their quality of life and functionality.

The study selected cancer survivors (n=85) after dismissal from oncology service to assess the presence and characteristics of chronic pain, their health-related quality of life and pain related disability through a combination of different questionnaires.

Chronic pain prevalence was 23.5%. 85% of patients reported neuropathic pain descriptors and 45% presented diagnostic criteria for neuropathic pain. Of these patients, 45% were followed-up for pain surveillance and 35% underwent analgesic medication. There was a median Pain Disability Index of 20.50 (14.50-35.00) and an average HRQoL of 0.5338 in chronic pain patients and 0.8872 in patients without pain. We found that chronic pain was the main negative predictor of HRQoL and was associated to decreased functionality. This study also concluded that these patients often were not offered the appropriate long-term medical follow-up.

These findings entail a need to raise awareness among health professionals to the importance of timely diagnosis and treatment of pain and its impact on HRQoL and functionality of long-term cancer survivors, as well as the need to change clinical practice in order to improve healthcare provided to these patients.

Keywords (MeSH Terms): Cancer Survivor; Chronic Pain; Disability; Functionality; Quality of Life.

Resumo

O número crescente de sobreviventes de cancro associado ao maior tempo médio de vida após diagnóstico de doença oncológica permitem observar efeitos deletérios a longo prazo, quer da doença oncológica, quer do tratamento efetuado. De entre esses efeitos, a dor crónica emerge como um dos mais prevalentes e, associado ao surgimento desta, verifica-se uma diminuição da funcionalidade e da qualidade de vida destes doentes. O grande foco perante a doença oncológica tem sido a erradicação do tumor e o prolongamento da esperança média de vida após o diagnóstico, descurando estes efeitos deletérios a longo prazo.

Este estudo tem como objetivo avaliar a prevalência e as características da dor crónica em sobreviventes de cancro, bem como a interferência da dor na qualidade de vida e funcionalidade.

Para o estudo, foram selecionados sobreviventes de cancro (n = 85) com alta do serviço de oncologia, de forma a avaliar a presença e características de dor crónica, a qualidade de vida relacionada com a saúde e a incapacidade relacionada com a dor, através de um conjunto de diferentes questionários.

A prevalência de dor crónica foi de 23,5%. 85% dos doentes referiam descritores de dor neuropática e 45% apresentavam critérios de diagnóstico para dor neuropática. Destes doentes, 45% eram seguidos para vigilância da dor e 35% realizavam medicação analgésica. Verificou-se um índice de incapacidade relacionado com a dor mediano de 20,50 (14,50-35,00) e uma QdVRS média de 0,5338, nos doentes com dor crónica, e de 0,8872 nos doentes sem dor. Com este estudo, verificou-se que a dor crónica era o principal preditor negativo da QdVRS e estava associada a pior funcionalidade dos sobreviventes de cancro e que estes doentes frequentemente não obtinham o devido seguimento a longo prazo.

Estes achados representam uma necessidade de consciencializar os profissionais de saúde sobre a importância do diagnóstico e tratamento atempados da dor bem como o seu impacto na QdVRS e na funcionalidade dos sobreviventes de cancro, além da necessidade de adaptar a prática clínica para melhorar os cuidados de saúde prestados a esses doentes.

Palavras-chave (Termos MeSH): Dor crónica; Funcionalidade; Incapacidade; Qualidade de Vida; Sobrevivente de Cancro.

Lista de Abreviaturas

BPI – Brief Pain Inventory

CHUP – Centro Hospitalar Universitário do Porto

DN4 – *Douleur Neuropathique en 4 Questions*

EQ-5D-3L – EuroQol Questionnaire, 5 dimensions, 3 levels

HRQoL – Health-Related Quality of Life

ICD-11 – International Classification of Diseases, 11th edition

PDI – Pain Disability Index

QdVRS – Qualidade de Vida Relacionada com a Saúde

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Introduction

Medical technological breakthroughs and, more specifically, in the Oncology area have provided tools for an earlier diagnosis of oncological disease and treatment options with a higher success rate.¹⁻⁴ As a result, and in association with an increase in average life expectancy, the number of survivors and the number of life years after diagnosis of an oncological disease has increased over the years,^{1-3,5,6} with an estimated 43.8 million survivors in 2018, up to 5 years after diagnosis.⁷ In Portugal, the estimated number of survivors is 719.2 per 100.000 inhabitants.⁷ Presently, it is estimated that globally more than 40% of patients diagnosed with cancer live more than 10 years after their diagnosis.⁸

Consequently, an increase in the incidence of medium/long term side effects has been seen, whose presentation depends on the location and extent of the disease, the presence of metastases, as well as, the type of treatments, such as chemotherapy, radiotherapy, hormone therapy, immunotherapy or surgery.^{6,9-12} Of the registered side effects, pain is one of the most prevalent^{4,10} and presents one of the biggest impacts on patients' quality of life. The estimated prevalence of chronic pain in cancer survivors can be as high as 40%,^{1,6,8,12,13} depending on the primary tumour location and performed treatment. Everdingen *et al* establish the prevalence of chronic pain after curative treatment as 39.3% (CI 95% 33.3 to 45.3),^{9,14} of which 27.6% report moderate to severe pain.^{14,15} Other studies suggest that chronic pain can reach 50% in breast cancer survivors,^{6,11,14,16} 40% in head and neck cancer survivors,^{13,17} and 27% in colorectal cancer survivors.^{2,17,18}

The aetiology of pain may be related to the tumour itself, the presence of metastases or as a secondary effect of treatment. However, the presence of pain may also be unrelated to cancer or its treatment.^{4,10} According to the World Health Organization's International Classification of Diseases, 11th Edition (ICD-11),¹⁹ chronic cancer-related pain can be caused by primary tumour or by metastases, referred as chronic cancer pain, or by its treatment, the latter referred as chronic post-cancer treatment pain. This pain persists or recurs for at least 3 months and presents no other better explanation from another mechanism.^{19,20}

Chronic cancer pain results from tissue damage caused by tumour expansion or metastases' development, activating inflammatory mechanisms and from neuropathic mechanisms, such as compression and destruction of sensory nerve terminals and denervation of the area affected by the primary tumour and/or metastases.²⁰ Pain may persist even after tumour eradication,¹⁵ through peripheral and central sensitization mechanisms.

Mechanisms associated with peripheral and central sensitization reduce the threshold of nociceptor activation for noxious and non-noxious stimuli, being equally associated to central wind-up mechanisms and activation of NMDA receptors.²¹

Exposure to inflammatory mediators and tissue damage of primary sensory neurons (peripheral nociceptors) result in peripheral sensitization, which translates into a threshold reduction and, consequently, an increase of these neurons' responsiveness. This response is limited to the injury site. Thus, it represents a form of pain due to nociceptor activation requiring the presence of an active aggression (inflammatory mediators, tissue, or neuronal injury).²¹⁻²³

Prolonged exposure to an intense peripheral noxious stimulus, tissue injury or neuronal injury cause changes that include lowering the sensitive terminals' threshold leading to an excitatory synaptic response increase (central hyperexcitability) associated with an inhibitory response and pain modulation decrease, as well as pain spreading to unaffected areas characterizing central sensitization. Hence, both noxious and non-noxious stimuli will cause a disproportional pain hypersensitivity as to the nature and extent of the lesion which translates into allodynia or secondary hyperalgesia.²¹⁻²⁴

Post-surgical pain has an enormous prevalence in surgeries such as thoracotomy or mastectomy: 30 to 50% of patients who underwent thoracotomy¹⁵ and in more than 50% of patients after breast surgery.²⁵ 31% of rectal cancer patients undergoing surgery report chronic pain in the pelvic area or lower limbs, 41% of whom report daily pain.²⁶ The neuropathic pain component in chronic post-surgical pain is extremely prevalent, although not always identified by patients as pain. At least 6 months after chemotherapy treatment, 30% of patients report neuropathic pain, with the most reported descriptors being tingling, numbness and burning.^{8,9,27} Radiotherapy wise, 20% of breast cancer patients experience clinically significant pain (EN> 3/10 using the Brief Pain Inventory (BPI) questionnaire)²⁸ and in patients who received curative radiotherapy for head or neck tumour at 5 years, 53% report chronic orofacial pain.²⁹

Chronic cancer-related pain presents a high negative impact, sometimes even superior to cancer itself, on patients' quality of life, affecting their daily life activities, their relationships, mood, sleep, and several other health aspects, in general.^{1,9,18,30-32} 10 to 20% of survivors report experiencing severe chronic pain that affects their daily life and normal functioning, a number that reaches 40% in the initial period after treatment, and studies have shown that these limitations can persist up to 20 years after treatment.^{8,33,34}

Most of cancer-related pain (chronic cancer-related pain) can be treated using multimodal pharmacological and non-pharmacological therapies.^{30,35,36} The impact of untreated

or inadequately treated pain can be devastating to a patients' quality of life, affecting one's physical and psychological well-being as well as one's social interactions.³⁵

Historically, the major treatment focus for cancer disease approach was tumour eradication and increasing average life expectancy after diagnosis, neglecting the medium- and long-term impact of the disease and prevention of chronic pain development.^{1,6,13,14,35} Currently, oncological diseases' higher cure rate and the larger number of studies on the prevalence of chronic pain in this population have been an important vehicle to promote health professionals' awareness, conducting studies in the context of the impact of chronic pain on patients' health-related quality of life, as well as the development of therapeutic guidelines for the adequate treatment of these patients.

The objective of this study is to assess patient population discharged from the medical oncology appointment at Centro Hospitalar Universitário do Porto (CHUP) between March 2016 and June 2019, assessing the prevalence and characteristics of chronic pain in cancer survivors, as well as the interference of pain in their quality of life and functionality. Pain's medical follow-up and analgesic medication intake were equally investigated.

Methods

We analysed retrospectively 334 patients discharged from the Medical Oncology consultation between March 2016 and June 2019. Of these, 42 patients were excluded as they were discharged to another hospital for follow-up, 68 due to death, 39 for not presenting malignant disease, 36 for not having follow-up appointments, 34 for still being followed-up, 13 for incomplete clinical information and 17 who did not respond/refused to respond to the study. Therefore, 85 patients (25.45%) were included in the study, having responded to a telephone interview.

The study took place in two phases, involving, in the first phase, consultation of clinical files (n = 334) and selection of participants (n = 102) and, in the second phase, a telephone interview (n = 85).

The consultation of electronic clinical files allowed to collect information on:

- i. the patient, including variables such as age, gender, marital status, education, employment status;

- ii. the oncological disease, such as location of the primary tumour, months since diagnosis, presence of metastasis;
- iii. the cancer treatment performed: chemotherapy, radiotherapy, hormone therapy, immunotherapy and/or surgery.

The telephone survey included the following variables:

- iv. presence or absence of chronic pain;
- v. health-related quality of life, through the application of the Portuguese version of “EuroQoL EQ-5D-3L”;

In patients who reported pain, the following were also evaluated:

- vi. factors related to chronic pain, such as anatomical location, type of medical follow-up and analgesic medication intake;
- vii. evaluation and characterization of pain, through the application of the following questionnaires “Brief Pain Inventory (BPI)” (adapted), “Pain Disability (PDI)” and “Specific questionnaire for screening of pain Neuropathic Pain - *Douleur Neuropathique en 4 Questions (DN4)*” (adapted), validated for the Portuguese language.

Table I presents the description of the categories considered for the analysis of the variables under study.

Pain

Pain was assessed using a set of questionnaires: BPI, PDI and DN4.

From the Brief Pain Inventory (BPI) questionnaire, the first four items were applied, namely the dichotomous item for verification of the existence of pain, an item for the location of pain, indicating pain areas in a human body representative diagram (converted into coding for anatomical pain localization), a 2 items pain intensity scale (maximum and minimum), featuring numerical rating scales (from 0 to 10). This questionnaire also includes medium and at the moment intensity items, as well as a set of questions on medication and pain interference that were not applied.³⁷

The Pain Disability Index (PDI) questionnaire aims to evaluate important dimensions of disability and functional pain interference, regardless of the location and the diagnosis of chronic pain. It consists of seven dimensions, with a numerical scale of 11 points, where 0 represents the total absence of disability and 10 represents total disability (≥ 2 - mild; ≥ 5 - moderate; ≥ 8 -

severe), assessing the pain related disability in family and home responsibilities, recreational activities, social activities, at work/occupation, sexual behaviour, self-care and life-support activities. The results obtained for each dimension can be added up to obtain a value of the pain-related disability index, measured on an increasing disability scale from 0 to 70 points, reflecting the interference associated with pain in daily life activities.³⁷

The DN4 questionnaire was developed by the French Group of Neuropathic Pain to differentiate neuropathic pain from nociceptive pain. It consists of 10 items grouped into 4 sections. The first seven, applied in this study, are related to the quality of pain (burning sensation, painful cold sensation, electric shocks sensation) and its association with abnormal sensations (tingling, pricking, numbness, itching). The other 3 items (not applied in this study) are related to neurological examination in the painful area (touch hypoesthesia, prick hypoesthesia, touch allodynia). A positive item receives a value of 1 and a negative item receives a value of 0.³⁷

Quality of Life

Health-related quality of life was assessed based on the application of the EuroQoL 5 dimensions questionnaire (EQ-5D-3L), which comprises the following five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has three levels (no problems, some problems, and extreme problems). The HRQoL value can be calculated based on results obtained and a predetermined value set, with values expressed on a scale of 1 corresponding to total health to 0 corresponding to death. Negative values are also considered for quality of life states considered worse than death. Greiner *et al*, established the questionnaire's value set for the European population.^{31,38-40}

Quality of Life Predictors

In order to understand which variables best predict Health-Related Quality of Life, we performed a linear regression analysis, having predictors organized in three blocks:

- (a) variables related to the patient, including gender (female), age and marital status (married);
- (b) variables related to the disease, such as the number of months since diagnosis and the number of treatments (3 or more treatments);
- (c) variables related to chronic pain.

The studied variables were obtained through Electronic Clinical Processes and telephone interviews, with the authorization and approval by the Ethics Committee for Health, the

Department of Education, Training and Research, and the Responsible for Clinical Information Access of Centro Hospitalar Universitário do Porto.

Statistical analysis was performed using the IBM SPSS Statistics®, version 26.0.

Results

Individuals had an average age of 65.33 years, 50.6% (n = 43) being female and 49.4% (n = 42) male. 72.9% (n = 62) were 60 or older, 70.6% (n = 60) were married, 50.6% (n = 43) attended between the 1st and 4th grade of education and 68.2 % (n = 58) were retired (Table II).

Primary tumour's most prevalent locations were: Digestive (50.6% n = 43), Head and Neck (15.3%, n = 13) and Breast (14.1%, n = 12). 69.4% (n = 59) of the patients were in the period between 5 and 10 years after diagnosis. 87.1% (n = 74) of the patients did not present metastasis (Table III).

95.3% (n = 81) of the patients underwent chemotherapy, 49.4% (n = 42) underwent radiotherapy, 10.6% (n = 9) underwent hormone therapy, 2.4% (n = 2) underwent immunotherapy and 88.2% (n = 75) underwent surgery. 62.4% (n = 53) of patients underwent up to two types of treatment (Table IV).

Of the patients surveyed, 23.5% (n = 20) present chronic pain. The most referred sources of pain locations were: Lumbar Area (25%, n = 5), Abdomen (20%, n = 4) and Left Upper Limb (15%, n = 3). 45% (n = 9) of these patients, were followed by their Assistant Physician / Family Physician and 35% (n = 7) took analgesic medication (Table V).

In the week prior to the telephone survey, 85% (n = 17) of patients with chronic pain experienced pain. The median of this pain minimum intensity was 4 (2.5 - 4.5) and the median of this pain maximum intensity was 7 (5.5 - 8.5), on a 0 to 10 scale. The most referred as the source of pain were: Lumbar Area (29.4%, n = 5) and abdomen (17.6%, n = 3) (Table VI).

Patients with chronic pain demonstrated a total median pain disability of 20.50 (14.50 to 35.00). As to the different evaluated dimensions, medians were as follows: family / home responsibilities - 5.50 (1.25 to 7.00); Recreation - 3.00 (1.00 to 9.25); Social Activities - 0.50 (0.00 to 4.25); Occupation - 2.50 (0.00 to 7.00); Sexual Behaviour - 0.00 (0.00 to 2.00); Self Care - 2.50 (1.00 to 5.75); Life-Support Activities - 2.50 (1.00 to 7.00) (Table VII).

As to characteristics of neuropathic pain, 30% (n = 6) refer a burning sensation, 15% (n = 3) refer a painful cold sensation, 40% (n = 8) refer an electric shock sensation, 70% (n = 14) report a tingling sensation, 45% (n = 9) report a sting sensation, 60% (n = 12) report numbness

and 35% (n = 7) report itching. 45% (n = 9) of patients report 4 or more characteristics of neuropathic pain at the chronic pain location (Table VIII).

Predictors of quality of life between patients with and without pain (Table IX), comparison:

- Mobility (level 2 or 3): 50% (n = 10) of patients with pain vs. 27.7% (n = 18) patients without pain;
- Personal care (level 2 or 3): 55% (n = 11) of patients with pain vs. 13.8% (n = 9) patients without pain;
- Usual activities (level 2 or 3): 75% (n = 15) of patients with pain vs. 16.9% (n = 11) patients without pain;
- Pain / discomfort (level 2 or 3): 95% (n = 19) of patients with pain vs. 0% (n = 0) patients without pain;
- Anxiety / depression (level 2 or 3): 75% (n = 15) of patients with pain vs. 13.8% (n = 9) patients without pain.

Results (Table X) reveal that the different predictors present a high explanatory power for HRQoL (adjusted $R^2 = 0,449$). The contribution of variables related to patients and to the disease seems to be residual, with only significant changes when chronic pain is introduced in the model.

The different predictors are only significant in the third model, highlighting age and, with greater intensity, pain, both negatively. This means that the older the patients, the lower the HRQoL and, when patients present pain, they present lower HRQoL. It is interesting, in any case, to underline that age only emerges as a significant predictor when pain is introduced into the model (Table XI).

Discussion

The aim of this study was assessment of chronic pain prevalence and its impact on the quality of life of cancer survivors discharged from the Medical Oncology consultation at Centro Hospitalar Universitário do Porto. We demonstrated that close to a quarter of patients presented chronic pain (23.5%, n = 20). Of these, 85% reported the presence of at least one neuropathic pain descriptor, with 45% presenting diagnostic criteria for neuropathic pain (DN4 ≥ 4). Less than half of the patients with chronic pain underwent medical follow-up, and only

slightly more than a third of the patients were taking analgesic medication. There was a median pain-related disability index of 20.50 (14.50 to 35.00).

Previous studies have established that chronic pain could be present in up to 40% of cancer survivors, depending on several factors such as location of the primary tumour, type of treatment or time since diagnosis. In most of the studies carried out, prevalence of pain was assessed in patients still being followed-up in Oncology. Thanks to innovation in medicine, more patients have been surviving and for a longer period after diagnosis, making chronic pain a reality increasingly present in their lives. In this study, we estimated the prevalence of chronic pain in almost a quarter (23.5%) of cancer survivors after curative treatment and discharge from oncology services.

The development of chronic pain after curative treatment raises questions about the therapeutic approach to be taken with these patients, and untreated or incorrectly treated pain can have quite deleterious effects on patients' quality of life and functionality, as well as it may persist up to 20 years after treatment conclusion.^{8,33,34} Thus, we found that less than half the patients had medical follow-up on pain, all of which was done by their assistant physician, and only 35% of these patients underwent analgesic medication to control chronic pain. These results may reflect the historical perspective on the oncological disease that focuses, essentially, on eradicating the tumour and prolonging average life expectancy after diagnosis, neglecting the medium- and long-term impact of oncological disease and its treatment.^{1,6,13,14,35}

In order to proceed with the correct therapeutic approach, it will also be necessary to understand pain characteristics, namely to understand the presence of pain mechanisms: nociceptive, neuropathic, or mixed. It is also fundamental to emphasize the importance of acute pain effective treatment, which often follows treatments applied to these patients, in order to prevent the peripheral and central sensitization mechanisms that underlie chronic pain. On the other hand, the correct and timely identification of a neuropathic pain component often present, presents a relevant impact on the outcome and therapeutic adjustment of these patients. Accordingly, within chronic pain patients in this study, the vast majority (85%) reported the presence of at least one neuropathic pain descriptor, with 45% of these patients having diagnostic criteria for neuropathic pain based on DN4 ($DN4 \geq 4$), even though the physical examination components of this questionnaire were not performed.^{8,9,27}

Several studies have been demonstrating the negative impact of chronic pain presence on functionality and quality of life of cancer survivors, an impact that may even be superior to the impact caused by the diagnosis of cancer disease.^{1,9,18,30-32} Several studies have shown that

the most affected dimensions were work activity,⁴¹⁻⁴⁵ as well as domestic and leisure activities and sexual behaviour.^{42,44,46} Azevedo *et al* described, for the Portuguese population, that the main dimensions affected by chronic pain were family and home responsibilities, leisure time, work and sleep.⁴⁷ In order to assess the impact of pain on this population study, we assessed the pain disability index, the result of which shows that the main dimensions affected by pain were family and home responsibilities (5.50; 1.25-7.00) and recreational activities (3.00; 1.00-9.25). It should be noted that the advanced average age and the employment situation of most members of this population (unemployed or retired - 77.6%) have played a significant role in reducing the level of disability related to some of the tasks surveyed, namely at the occupational level (2.50; 0.00-7.00) and sexual behaviour (0.00; 0.00-2.00). Finally, social activities' dimension tends to be one of the most affected by pain, accounting for the frequent association between chronic pain and depression, which often leads to these patients' greater social isolation. In this study, this association was not verified, probably because we are facing a population of cancer survivors who may show greater resilience from the onset.

We also assessed Health-Related Quality of Life (HRQoL) based on a five-dimensional questionnaire, with a lower absolute HRQoL value in chronic pain patients compared to patients without pain, as well as a higher score in each of the evaluated dimensions. We also found that chronic pain is the main negative predictor of HRQoL, therefore demonstrating its negative impact on the quality of life of cancer survivors.

Conclusion

This study has some limitations, such as the small number of sampled patients and the sole inclusion of patients who were followed up by oncology service, leaving out patients not followed by this service, being translated into a distribution by type of tumour different from the cancer patients' population. Exclusion criteria also included the absence of informed consent or still being under some type of treatment, namely continued care, palliative care, or end-of-life comfort care. Considering these limitations, these results cannot be extrapolated to the general population of cancer patients.

However, the demonstration of a significant prevalence of chronic pain in these cancer survivors as well as its negative impact on functionality and quality of life of these patients represent a strong indication for the need to raise awareness among health professionals who treat these patients to the importance of timely diagnosis and treatment of pain, the necessity to carry out additional and more comprehensive studies on pain, functionality and quality of life

in cancer surviving patients, as well as the need to change clinical practice in order to provide better long-term healthcare for this group of patients.

Attachments

Table I. Characterization of Variables

Variable	Codification
Age	Under 30 years Between 30 and 39 years Between 40 and 49 years Between 50 and 59 years Between 60 and 69 years Between 70 and 79 years 80 or more years
Primary tumour location	Head and Neck (Pharynx, Larynx, Tongue, Thymus, Thyroid) Digestive (Colon, Small Bowel, Stomach, Pancreas, Rectum and Bile Ducts) Genito-Urinary (Bladder, Ovary, Testis) Breast Bone Hidden Primary Central Nervous System (CNS) Synchronous (when there is more than one primary tumour location simultaneously)
Months since diagnosis	60 months or less between 61 and 72 months between 73 and 84 months between 85 and 96 months between 97 and 108 months 109 or more months
Pain Anatomical Location	Head Neck Thorax Abdomen Lumbar Area Left Upper Limb Right Upper Limb Left Lower Limb Right Lower Limb
Chronic Pain Medical Follow-up	Assistant Physician / Family Physician Oncologist Pain Unit None

Table II. Sociodemographic Characterization

Variable	Total N (%)	Pain N (%)	No Pain N (%)	P value
Gender				p = 0.003
Feminine	43 (50.6)	16 (80.0)	27 (41.5)	
Masculine	42 (49.4)	4 (20.0)	38 (58.5)	
Age				p = 0.066
< 30 years	0 (0)	0 (0.0)	0 (0.0)	
30 to 39 years	3 (3.5)	0 (0.0)	3 (4.6)	
40 to 49 years	6 (7.1)	2 (10.0)	4 (6.2)	
50 to 59 years	14 (16.5)	4 (20.0)	10 (15.4)	
60 to 69 years	25 (29.4)	4 (20.0)	21 (32.3)	
70 to 79 years	30 (35.3)	9 (45.0)	21 (32.3)	
80 or more	7 (8.2)	1 (20.0)	6 (9.2)	
Marital Status				p = 0.558
Single	3 (3.5)	0 (0.0)	3 (4.6)	
Married	60 (70.6)	17 (85.0)	43 (66.2)	
Widower	7 (8.2)	1 (5.0)	6 (9.29)	
Partnership	1 (1.2)	0 (0.0)	1 (1.5)	
Divorced	14 (16.5)	2 (10.0)	12 (18.5)	
Schooling				p = 0.759
No formal education	2 (2.4)	1 (5.0)	1 (1.5)	
1 st to 4 th grade	43 (50.6)	11 (55.0)	32 (49.2)	
5 th to 9 th grade	20 (23.5)	4 (20.0)	16 (24.6)	
10 th to 12 th grade	11 (12.9)	3 (15.0)	8 (12.3)	
University education	9 (10.6)	1 (5.0)	8 (12.3)	
Employment Status				p = 0.427
Employed	19 (22.4)	3 (15.0)	16 (24.6)	
Unemployed	8 (9.4)	1 (5.0)	7 (10.8)	
Retired	58 (68.2)	16 (80.0)	42 (64.6)	

(a) X² Test, p<0.05

Table III. Oncological Characterization

Variable	Total N (%)	Pain N (%)	No Pain N (%)	P value
Primary Tumour Location				p = 0.070
Head and Neck	13 (15.3)	1 (5.0)	12 (18.5)	
Digestive	43 (50.6)	11 (55.0)	32 (49.2)	
Genitourinary	5 (5.9)	0 (0.0)	5 (7.7)	
Breast	12 (14.1)	6 (30.0)	6 (9.2)	
Bone	2 (2.4)	0 (0.0)	2 (3.1)	
Hidden Primary	1 (1.2)	1 (5.0)	0 (0.0)	
CNS	3 (3.5)	0 (0.0)	3 (4.6)	
Synchronous	6 (7.1)	1 (5.0)	5 (7.7)	
Months since diagnosis				p = 0.079
60 months or less	3 (3.5)	2 (10.0)	1 (1.5)	
61 to 72 months	1 (1.2)	0 (0.0)	1 (1.5)	
73 to 84 months	12 (14.1)	3 (15.0)	9 (13.8)	
85 to 96 months	12 (14.1)	1 (5.0)	11 (16.9)	
97 to 108 months	16 (18.8)	4 (20.0)	12 (18.6)	
109 to 120 months	18 (21.2)	1 (5.0)	17 (26.5)	
121 or more months	23 (27.1)	9 (45.0)	14 (21.5)	
Metastization				p = 0.754
No	74 (87.1)	17 (85.0)	57 (87.7)	
Yes	11 (12.9)	3 (15.0)	8 (12.3)	

(a) χ^2 Test, $p < 0.05$

Table IV. Treatment Characterization

Variable	Total N (%)	Pain N (%)	No Pain N (%)	P value
Chemotherapy				p = 0.201
No	4 (4.7)	2 (10.0)	2 (3.1)	
Yes	81 (95.3)	18 (90.0)	63 (96.9)	
Radiotherapy				p = 0.279
No	43 (50.6)	8 (40.0)	35 (53.8)	
Yes	42 (49.4)	12 (60.0)	30 (46.2)	
Hormone therapy				p = 0.118
No	76 (89.4)	16 (80.0)	60 (92.3)	
Yes	9 (10.6)	4 (20.0)	5 (7.7)	
Immunotherapy				p = 0.372
No	83 (97.6)	19 (95.0)	64 (98.5)	
Yes	2 (2.4)	1 (5.0)	1 (1.5)	
Surgery				p = 0.779
No	10 (11.8)	2 (10.0)	8 (12.3)	
Yes	75 (88.2)	18 (90.0)	57 (87.7)	
Number of Treatments				p = 0.238
1	2 (2.4)	0 (0.0)	2 (3.1)	
2	51 (60.0)	11 (55.0)	40 (61.5)	
3	24 (28.2)	5 (25.0)	19 (29.2)	
4	7 (8.2)	4 (20.0)	3 (4.6)	
5	1 (1.2)	0 (0.0)	1 (1.5)	

(a) X² test, p<0.05

Table V. Chronic Pain Characteristics

Variable	N (%)
Chronic Pain	
No	65 (76.5)
Yes	20 (23.5)
Location	
Thorax	2 (10.0)
Abdomen	4 (20.0)
Lumbar Area	5 (25.0)
Upper Left Limb	3 (15.0)
Upper Right Limb	2 (10.0)
Lower Left Limb	1 (5.0)
Lower Right Limb	1 (5.0)
Lower Limbs	2 (10.0)
Medical Follow-up	
Assistant Physician / Family Physician	9 (45.0)
None	11 (55.0)
Medication	
No	13 (65.0)
Yes	7 (35.0)

Table VI. Brief Pain Inventory (Last Week)

Variable	N (%)	
Pain		
No	3 (15.0)	
Yes	17 (85.0)	
Location		
Thorax	2 (11.8)	
Abdomen	3 (17.6)	
Lumbar Area	5 (29.4)	
Upper Left Limb	2 (11.8)	
Upper Right Limb	2 (11.8)	
Lower Right Limb	1 (5.9)	
Lower Limbs	2 (11.8)	
Pain Intensity	Maximum (%)	Minimum (%)
0	0 (0.0)	0 (0.0)
1	0 (0.0)	0 (0.0)
2	0 (0.0)	4 (23.5)
3	1 (5.9)	4 (23.5)
4	0 (0.0)	5 (29.4)
5	3 (17.6)	4 (23.5)
6	1 (5.9)	0 (0.0)
7	5 (29.4)	0 (0.0)
8	3 (17.6)	0 (0.0)
9	1 (5.9)	0 (0.0)
10	3 (17.6)	0 (0.0)
Median (P25-P75)	7 (5.5 – 8.5)	4 (2.5 – 4.5)
Average ± Standard Deviation	7.18±1.976	3.53±1.125

Table VII. Pain Disability Index

Variable	Average ± Standard Deviation	Median (P25-P75)
Family / Home Responsibilities	4.50 ±3.220	5.50 (1.25-7.00)
Recreation	4.35 ±3.870	3.00 (1.00-9.25)
Social activity	2.50 ±3.332	0.50 (0.00-4.75)
Occupation	3.45 ± 3.300	2.50 (0.00-7.00)
Sexual behaviour	1.40 ± 2.437	0.00 (0.00-2.00)
Self-Care	3.15 ± 2.834	2.50 (1.00-5.75)
Life-support activity	3.55 ± 3.316	2.50 (1.00-7.00)
Total PDI	23.35 ± 12.470	20.50 (14.50-35.00)

Table VIII. DN4

Variable		N (%)	DN4 Result	N (%)
Burning Sensation	No	14 (70.0)	0	3 (15.0)
	Yes	6 (30.0)		
Painful Cold Sensation	No	15 (75.0)	1	1 (5.0)
	Yes	5 (15.0)		
Electric Shock Sensation	No	12 (60.0)	2	4 (20.0)
	Yes	8 (40.0)		
Tingling	No	6 (30.0)	3	3 (15.0)
	Yes	14 (70.0)		
Pricking	No	11 (55.0)	4	4 (20.0)
	Yes	9 (45.0)		
Numbness	No	8 (40.0)	5	3 (15.0)
	Yes	12 (60.0)		
Itching	No	13 (65.0)	6	2 (10.0)
	Yes	7 (35.0)		

Table IX. EuroQoL EQ-5D-3L

Variable	Total N (%)	Pain N (%)	No Pain N (%)	P value
MOBILITY				
I have no problems in walking about	57 (67.1)	10 (50.0)	47 (72.3)	p = 0.124
I have some problems in walking about	27 (31.8)	10 (50.0)	17 (26.2)	
I am confined to bed	1 (1.2)	0 (0.0)	1 (1.5)	
SELF-CARE				
I have no problems with self-care	65 (76.5)	9 (45.0)	56 (86.2)	p < 0.001
I have some problems washing or dressing myself	20 (23.5)	11 (55.0)	9 (13.8)	
I am unable to wash or dress myself	0 (0.0)	0 (0.0)	0 (0.0)	
USUAL ACTIVITIES				
I have no problems with performing my usual activities	59 (69.4)	5 (25.0)	54 (83.1)	p < 0.001
I have some problems with performing my usual activities	25 (29.4)	15 (75.0)	10 (15.4)	
I am unable to perform my usual activities	1 (1.2)	0 (0.0)	1 (1.5)	
PAIN/DISCOMFORT				
I have no pain or discomfort	66 (77.6)	1 (5.0)	65 (100.0)	p < 0.001
I have moderate pain or discomfort	17 (20.0)	17 (85.0)	0 (0.0)	
I have extreme pain or discomfort	2 (2.4)	2 (10.0)	0 (0.0)	
Anxiety/Depression				
I am not anxious or depressed	61 (71.8)	5 (25.0)	56 (86.2)	p < 0.001
I am moderately anxious or depressed	19 (22.4)	11 (55.0)	8 (12.3)	
I am extremely anxious or depressed	5 (5.9)	4 (20.0)	1 (1.5)	
HRQoL	Average ± Standard Deviation		Median (P25-P75)	
Total	0.8040 ± 0.2317		0.8475 (0.6625 – 1.0000)	
Pain	0.5338 ± 0.2077		0.5463 (0.4106 – 0.6735)	
No Pain	0.8872 ± 0.1668		1.0000 (0.8062 - 1.0000)	

(a) X² test, p<0.05

Table X. HRQoL Predictors

Model	R	R ²	Adjusted R ²	Estimate standard error	Change Statistics				
					R ² Change	F Change	df 1	df 2	Sig, F Change
1	0.199 ^a	0.040	0.004	0.2312510	0.040	1.113	3	81	0.349
2	0.258 ^b	0.067	0.008	0.2308367	0.027	1.145	2	79	0.323
3	0.699 ^c	0.488	0.449	0.1720641	0.421	64.186	1	78	0.000

(a) Predictors: (Constant), married, age, gender (feminine);

(b) Predictors: (Constant), married, age, gender (feminine), number of treatments (3 or more), number of months since diagnosis;

(c) Predictors: (Constant), married, age, gender (feminine), number of treatments (3 or more), number of months since diagnosis, Pain.

Table XI. Coefficients

Model	Nonstandard coefficients		Standard coefficients	t	Sig	Collinearity statistics		
	B	Error	Beta			Tolerance	VIF	
1	(Constant)	1.053	0.146		7.222	0.000		
	Gender (feminine)	0.015	0.051	0.033	0.304	0.762	0.981	1.019
	Age	-0.004	0.002	-0.194	-1.772	0.080	0.989	1.011
	Marital Status (married)	-0.010	0.056	-0.020	-0.177	0.860	0.971	1.030
2	(Constant)	1.008	0.169		5.974	0.000		
	Gender (feminine)	0.006	0.051	0.012	0.110	0.913	0.965	1.036
	Age	-0.004	0.002	-0.189	-1.729	0.088	0.987	1.013
	Marital Status (married)	0.004	0.057	0.007	0.063	0.950	0.941	1.063
	Number of months since diagnosis	0.001	0.001	0.090	0.815	0.418	0.971	1.030
	Number of treatments (3 or more)	-0.066	0.052	-0.139	-1.262	0.210	0.980	1.020
3	(Constant)	1.080	0.126		8.564	0.000		
	Gender (feminine)	0.017	0.038	0.036	0.440	0.661	0.964	1.038
	Age	-0.004	0.002	-0.207	-2.537	0.013	0.986	1.014
	Marital Status (married)	0.058	0.043	0.114	1.348	0.182	0.917	1.090
	Number of months since diagnosis	0.000	0.000	0.063	0.771	0.443	0.970	1.031
	Number of treatments (3 or more)	-0.042	0.039	-0.089	-1.085	0.281	0.975	1.026
	Pain	-0.360	0.045	-0.662	-8.012	0.000	0.961	1.041

(a) Dependent Variable: Health-related Quality of Life (HRQoL)

Appendix

Questionários Aplicados

Inventário Resumido da dor (última semana) - BPI

1. Ao longo da vida, a maior parte de nós teve dor de vez em quando (tais como dores de cabeça de pequena importância, entorses e dores de dentes). Durante a última semana teve alguma dor diferente destas dores comuns?

Sim Não

2. Identifique a zona onde sente dor. (possível seleção múltipla)

1. Cabeça
2. Pescoço
3. Tórax
4. Abdómen
5. Lombar
6. Membro Superior Esquerdo
7. Membro Superior Direito
8. Membro Inferior Esquerdo
9. Membro Inferior Direito

3. Por favor, classifique a sua dor assinalando com um círculo o número que melhor descreve a sua dor no seu máximo durante a última semana.

0 1 2 3 4 5 6 7 8 9 10

4. Por favor, classifique a sua dor assinalando com um círculo o número que melhor descreve a sua dor no seu mínimo durante a última semana.

0 1 2 3 4 5 6 7 8 9 10

Índice de Incapacidade Relacionada com a Dor - PDI

As escalas de classificação apresentadas em baixo medem o impacto da dor na sua vida diária: Queremos saber até que ponto a sua dor o/a impede de realizar as suas atividades normais: Para cada um dos 7 tipos de atividades diárias representadas, assinale com um círculo o número que melhor reflete o nível de incapacidade com que habitualmente se defronta. Uma classificação de 0 significa nenhuma incapacidade, e uma pontuação de 10 significa que a dor o impede de realizar quase todas as suas atividades diárias. A sua classificação deve refletir o impacto global que a dor tem na sua vida, e não apenas quando a dor atinge o seu ponto máximo. Assinale com um círculo um número em todas as atividades apresentadas. Se achar que um determinado tipo de atividade não se aplica a si, assinale com "0".

1. **Responsabilidades familiares/domésticas.** Refere-se a atividades relacionadas com a casa e família. Inclui tarefas e ocupações relacionadas com a casa (ex.: trabalho no quintal) e atividades e obrigações relacionadas com outros membros da família (ex.: levar as crianças à escola)

0 1 2 3 4 5 6 7 8 9 10

2. **Tempos de Lazer.** Incluem-se passatempos, desportos e outras atividades de lazer.

0 1 2 3 4 5 6 7 8 9 10

3. **Atividades Sociais.** Incluem-se festas, teatro, concertos, ir comer fora e outras atividades sociais onde participem familiares e amigos.

0 1 2 3 4 5 6 7 8 9 10

4. **Ocupação.** Refere-se a atividades diretamente relacionadas com o seu trabalho. Inclui-se igualmente trabalho não remunerado, tal como trabalho doméstico ou trabalho voluntário.

0 1 2 3 4 5 6 7 8 9 10

5. **Comportamento Sexual.** Refere-se à frequência e à qualidade da sua vida sexual.

0 1 2 3 4 5 6 7 8 9 10

6. **Cuidados Pessoais.** Incluem-se cuidados pessoais e atividades independentes da vida diária (ex.: tomar um duche, conduzir, vestir-se, etc.)

0 1 2 3 4 5 6 7 8 9 10

7. **Atividades Vitais.** Refere-se a necessidades vitais básicas como comer, dormir ou respirar.

0 1 2 3 4 5 6 7 8 9 10

Questionário Específico para o rastreio de Dor Neuropática - DN4

Por favor, responda às seguintes questões, assinalando uma única resposta para cada alínea

1. A dor apresenta uma, ou mais, das características seguintes?

	Sim	Não
1 - Queimadura		
2 - Sensação de frio doloroso		
3 - Choques elétricos		

2. Na mesma região da dor, sente também um ou mais dos seguintes sintomas?

	Sim	Não
4 - Formigueiro		
5 - Picadas		
6 - Dormência		
7 - Comichão		

Questionário De Qualidade De Vida Do Grupo EuroQol - EQ-5D-3L

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Assinale com uma cruz, um quadrado de cada um dos seguintes grupos, indicando qual das afirmações melhor descreve o seu estado de saúde hoje.

1. Mobilidade

- Não tenho problemas em andar
- Tenho alguns problemas em andar
- Tenho de estar na cama

(NS NR NA)

2. Cuidados Pessoais

- Não tenho problemas com os meus cuidados pessoais
- Tenho alguns problemas com os meus cuidados pessoais
- Sou incapaz de me lavar ou vestir sozinho(a)

(NS NR NA)

3. Atividades Habituais (ex.: trabalho, estudos, atividades domésticas, atividades em família ou de lazer)

- Não tenho problemas em desempenhar as minhas atividades habituais
- Tenho alguns problemas em desempenhar as minhas atividades habituais
- Sou incapaz de desempenhar as minhas atividades habituais

(NS NR NA)

4. Dor/Mal-Estar

- Não tenho dores ou mal-estar
- Tenho dores ou mal-estar moderados
- Tenho dores ou mal-estar extremos

(NS NR NA)

5. Ansiedade/Depressão

- Não estou ansioso(a) ou deprimido(a)
- Estou moderadamente ansioso(a) ou deprimido(a)
- Estou extremamente ansioso(a) ou deprimido(a)

(NS NR NA)

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