

# Single Centre Prospective Study of Systematic Pain Evaluation in Portuguese Patients with Metastatic Prostate Cancer



## Estudo Unicêntrico Prospetivo de Avaliação Sistemática da Dor em Doentes Portugueses com Cancro da Próstata Metastizado

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### ABSTRACT

**Introduction:** Pain is one of the most common symptoms reported by cancer patients and is associated with decreased quality of life. Assessment of pain with standardized questionnaires reduces variability in its interpretation and may increase effectiveness of medical interventions. Prostate cancer is the most frequent male neoplasm in Portugal. We designed this study to evaluate the impact of a standardized pain questionnaire on pain management in patients with metastatic prostate cancer.

**Material and Methods:** Single centre prospective observational study of patients with metastatic prostate cancer. The study was designed to evaluate the benefit of systematically evaluating pain with Brief Pain Inventory-Short Form prior to a scheduled medical oncology consult. Patients reporting pain were reassessed one week later by telephone. To assess the benefit two consecutive cohorts were established based on communication of questionnaire results to the treating physician.

**Results:** We recruited 207 patients of which 60% reported pain. Statistically significant decrease in mean pain intensity one week after the scheduled appointment was noted (3.95 vs 3.01;  $p < 0.001$ ). Patients whose Brief Pain Inventory-Short Form was provided to their oncologist experienced greater reduction in pain, which was non-significant ( $p = 0.227$ ). Using Brief Pain Inventory-Short Form assessment resulted in a higher probability of pain control (43.5% vs 30.9%;  $p = 0.193$ ).

**Discussion:** The prevalence of pain founded was higher than described in the literature, probably because our sample was less selected than the published in clinical trials. After the scheduled appointment, there was a statistically significant reduction in mean pain intensity, but the explicit use of this questionnaire was not associated with a statistically significant reduction of pain.

**Conclusion:** Patients with metastatic prostate cancer have a high prevalence of pain. Evaluation and treatment by medical oncologists is associated with a reduction of mean pain intensity. The use of Brief Pain Inventory-Short Form was associated with a non-significant increased reduction of pain.

**Keywords:** Neoplasm Metastasis; Pain; Pain Measurement; Prostatic Neoplasms

### RESUMO

**Introdução:** A dor é o sintoma que mais frequentemente afeta a qualidade de vida de doentes com cancro. A utilização de ferramentas padronizadas para avaliação da dor pode diminuir a variabilidade associada à sua avaliação e aumentar o sucesso das intervenções terapêuticas. Em Portugal, o cancro da próstata é a neoplasia masculina mais frequente. Avaliamos o impacto clínico da aplicação sistemática de um questionário padronizado de avaliação da dor em doentes com cancro da próstata metastizado.

**Material e Métodos:** Coorte prospetiva, unicêntrica, com amostragem consecutiva de doentes com cancro da próstata metastizado que, antes de uma consulta programada, responderam ao questionário *Brief Pain Inventory-Short Form*. Aos doentes que reportaram dor, o questionário foi aplicado, telefonicamente, uma semana depois. Para avaliar o impacto desta ferramenta na prática clínica constituímos dois grupos, sequenciais, em função da disponibilização dos resultados do questionário.

**Resultados:** Nos 207 doentes incluídos, 60% apresentavam dor. A consulta de oncologia médica esteve associada a uma diminuição significativa da intensidade média de dor (3,95 vs 3,01;  $p < 0,001$ ). A redução da dor no grupo de exposição foi superior à verificada no grupo controlo, embora sem significado estatístico ( $p = 0,227$ ). A probabilidade de controlo de dor com a disponibilização do questionário foi de 43,5% vs 30,9% no grupo controlo ( $p = 0,193$ ).

**Discussão:** A prevalência de dor encontrada foi superior à descrita literatura, provavelmente pela nossa amostra ser menos selecionada do que a dos ensaios clínicos publicados. Após a realização da consulta, verificou-se uma redução estatisticamente significativa da intensidade média de dor, mas a utilização explícita do questionário não esteve associada a uma redução estatisticamente significativa.

**Conclusão:** Em doentes com cancro da próstata metastizado a prevalência de dor é elevada. A sua avaliação e tratamento por oncologistas associam-se à redução da intensidade média de dor. A utilização sistemática do *Brief Pain Inventory-Short Form* associou-se a um aumento não significativo do benefício terapêutico.

**Palavras-chave:** Avaliação da Dor; Dor; Metástase Neoplásica; Neoplasias da Próstata

### INTRODUCTION

Pain has been defined as “an unpleasant sensory and emotional experience associated with an actual or potential tissue damage or described in terms of an injury”.<sup>1,2</sup> Pain is

a common symptom in patients with cancer, with a major impact on quality of life of both patients and their families.<sup>3</sup> A systematic review found that 53% of the patients with

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cancer presented with pain and that moderate to severe pain was described by more than one third of these patients.<sup>4</sup> Even though relieved pain may be achieved in 90% of the patients, suboptimal pain management is often unrecognized by healthcare professionals.<sup>5</sup> One of the major causes for this is the discrepancy between the pain described by the patient and the awareness of pain intensity among physicians. Pain self-assessment scales are considered as gold-standard due to the subjective nature of the symptom.<sup>3</sup>

Uni and multidimensional pain assessment scales have been developed, with wide inter-individual variability.<sup>6</sup> Despite these limitations, pain assessment through the application of standardized and validated questionnaires may bring benefits as these are tools allowing for a standard evaluation and for an easier communication between patients and healthcare professionals.<sup>7</sup> The Brief Pain Inventory-Short Form (BPI-SF) scale is a measurement tool for the assessment of chronic pain in terms of severity and location, as well as in terms of the interference with activities of daily living (ADL), relation with others and response to analgesia, which has already been translated and validated for the Portuguese language.<sup>8,9,10</sup> This questionnaire was selected due to its multidimensional, widespread, easy-to-use and user-friendly characteristics.

Prostate carcinoma is the most frequently found cancer disease in Portuguese male patients and, due to a tropism to bone tissue, is frequently associated with bone metastases with a high potential to cause pain.<sup>11</sup> Pain prevalence in patients with advanced prostate carcinoma found in clinical trials ranges between 2 and 46%.<sup>12-17</sup> However, prevalence is probably underestimated due to a patient selection oriented by the inclusion criteria into clinical trials, therefore preventing from obtaining a clear definition of pain prevalence and severity in non-selected patients.<sup>18</sup>

This study aimed at the assessment of the clinical impact of the application of the BPI-SF questionnaire into the clinical approach to patients with advanced prostate cancer, the identification of pain prevalence and its impact on the quality of life of these patients.

## MATERIAL AND METHODS

This was a prospective study involving a consecutive sampling of patients with metastatic prostate cancer attending a scheduled Medical Oncology appointment at the *Instituto Português de Oncologia do Porto (IPO Porto)*. Patients having accepted to participate in the study were asked to complete the BPI-SF survey, with the help of the nursing staff, when necessary. At first, the results of the questionnaire were not shared with the treating physician (control group). Upon the conclusion of the control group recruitment, patients were selected for an interventional group and the questionnaire results were shared with the treating physician before the appointment. No pain management protocol nor any standard therapy recommendation were implemented, leaving pain management entirely to the on-

colologist's own judgement. Patients having described the presence of pain were contacted by phone within one week upon the appointment ( $\pm 2$  days) in order to assess mean pain severity. The study design is shown in Fig. 1.

The study was previously approved by the Ethics Committee of the IPO Porto and authorisation for data collection and electronic data handling was given by the *Comissão Nacional de Proteção de Dados*.

## Inclusion / exclusion criteria

Literate patients, not followed by the first author, with a positive histology consistent with prostate adenocarcinoma, imaging findings of metastatic disease and having accepted to participate were included in the study. Patients who had not described any pain in response to the item 1 of the BPI-SF questionnaire, patients attending a specialist chronic pain clinic and patients having attended a non-scheduled appointment at the IPO Porto on the subsequent week to the Medical Oncology scheduled appointment were excluded from the study in order to allow for the assessment of the impact of the systematic use of the BPI-SF questionnaire in patients with painful disease.

A total of 207 patients with metastatic prostate cancer were selected from March through October 2016, 87 from which were excluded due to noncompliance with the inclusion criteria or to presenting with exclusion criteria (Fig. 2).

## Collected data

The BPI-SF questionnaire allows for the assessment of an experience of pain by using two pain-related constructs, namely pain intensity and interference with ADL as well as response to analgesia.<sup>10</sup> This is a 11-item tool (4 items regarding the assessment of pain intensity and 7 regarding the assessment of the impact on quality of life) with responses obtained by using a numeric scale ranging from 0 to 10, in which the higher the score the higher the pain intensity or the more relevant the interference with ADL. The questionnaire has been applied immediately before the Medical Oncology appointment. The item 5 (mean pain within the week previous to the application of the BPI-SF questionnaire) has been repeated by phone and carried out within 7 days ( $\pm 2$  days) from the date of study inclusion.

Each patient's medical, pathological and therapeutic information has been obtained from medical records by using a standard data collection spreadsheet. The collected information regarding the issue 7 of the questionnaire (pain management) was supplemented by the information obtained from patient's medical record, whenever suitable.

## Outcome measures

The difference between mean pain severity (item 5) obtained before the medical appointment and the one described one week later was the primary outcome measure. In addition, the presence of properly managed pain was established whenever a two-point reduction in mean pain score was obtained one week upon the appointment.

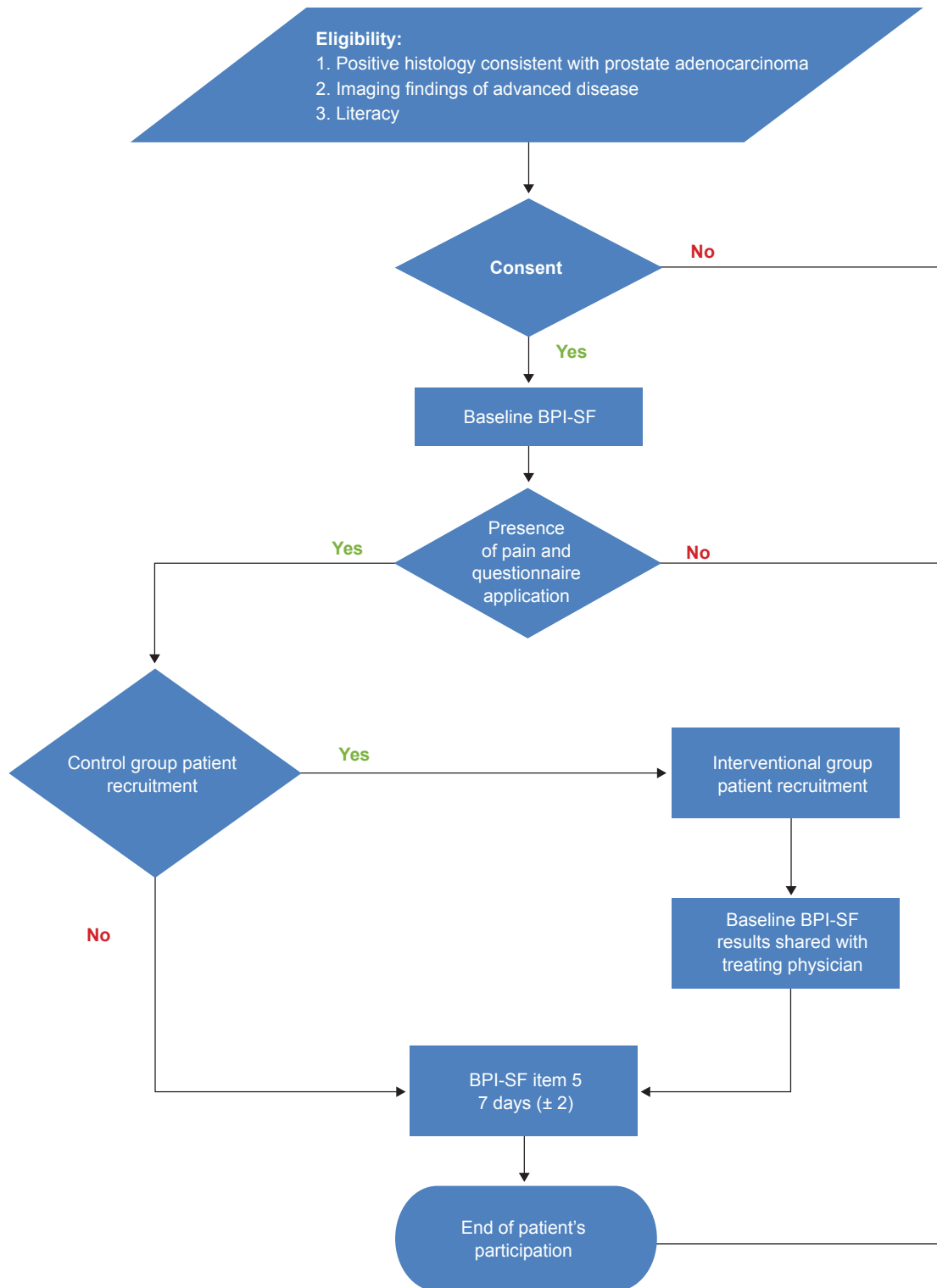


Figure 1 – Study design

**Statistical analysis**

This study was designed so that a mean reduction of at least one point in mean pain severity was identified by the Student's t-test in the interventional vs. control group. A 1.5 standard deviation of the difference has been assumed, as well as a 95% confidence interval and an 80% power; at least 37 participants were required for each group. At least

45 patients were selected for each group in order to compensate for any losses to follow-up.

Descriptive statistics methods were used for the analysis of clinical, pathological and therapeutic variables, according with what is appropriate for each variable. Mean and 95% confidence interval, as well as median and interquartile range were calculated regarding the items that

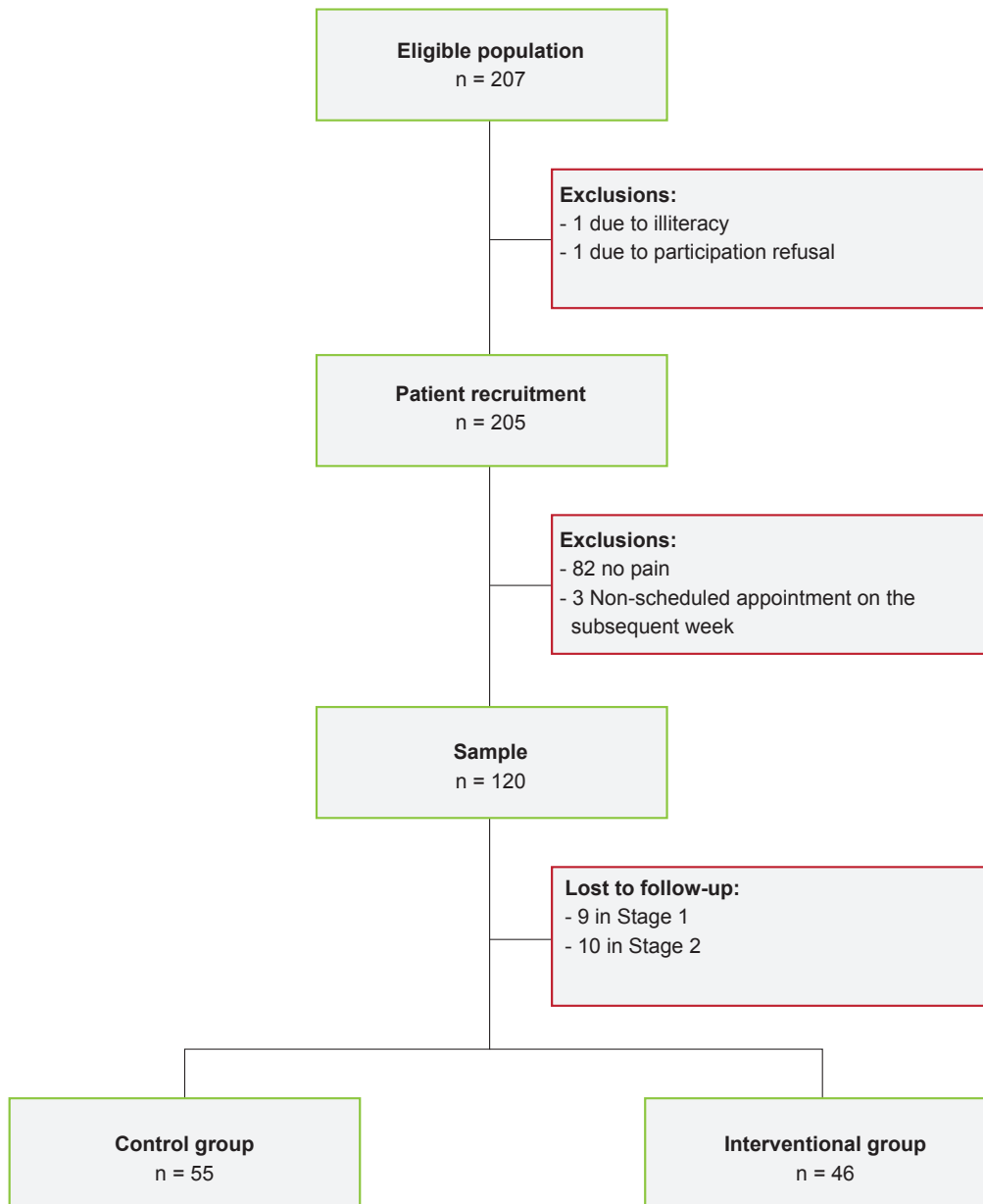


Figure 2 – Flowchart of patient's selection criteria

were assessed by the BPI-SF questionnaire. In addition, pain severity was assessed by a three-point verbal scale [mild (1-3), moderate (4-6) and severe pain ( $\geq 7$ )], which was converted from the numeric scale.<sup>19</sup> Mean scores in the seven items regarding the dimension of pain interference with ADL were calculated whenever valid responses had been given to at least four of these seven items. In addition, the percentage of patients having reached a properly managed pain was estimated in an independent way for both groups, as well as 95% confidence intervals.

All patients having complete the study procedures were considered for the assessment of primary outcome measure. The impact of the Medical Oncology appointment has been assessed by comparing the distribution of mean pain intensity before vs. upon the appointment. The impact on pain intensity of sharing the result of the BPI-SF question-

naire with the treating physician was assessed with an independent group Student's t-test for the mean difference between mean pain score before vs. upon the appointment in each group. The impact of the use of the BPI-SF questionnaire through the application of a chi-square test has been considered for the assessment of properly managed pain variable upon a scheduled Medical Oncology appointment. Multivariate regression models have been used for estimating the impact of potential confounding factors on the measure of the impact of a medical appointment and having shared the results of the questionnaire with the treating physician. A reduction in pain score between the initial and the subsequent assessment (linear regression) and the presence of properly managed pain between the initial vs. the subsequent assessment (logistic regression) were considered as dependent variables. Castration-resistant

disease, previous docetaxel and antalgic radiation therapy, previous bone surgery, presence of pathological fracture, zoledronic acid therapy and history of chronic non-cancer related pain were considered as confounding factors. A 5% type I error has been assumed for all the comparisons. No corrections for multiple comparisons were made, given the exploratory nature of the study.

All the patients having accepted to participate in the study were considered for the assessment of pain prevalence in patients with metastatic prostate cancer.

## RESULTS

Our group of patients, mostly presenting with an ECOG (Eastern Cooperative Oncology Group) performance status of 0 or 1 (83%) had a median age of 71 years and mostly presented with metastatic bone disease (83.7%). The main characteristics of the patients, including those lost to follow-up are shown in Table 1.

### Pain prevalence and characteristics

A 60% pain prevalence (95% CI: 53.3 – 66.7) has been found. A mean pain intensity score of 4.0 on the week previous to the medical appointment was found (95% CI: 3.7 – 4.4; 75<sup>th</sup> percentile: 5.0). As regards maximum and minimum pain on the week previous to the appointment, a mean score of 6.0 (75<sup>th</sup> percentile: 8.0) and 1.9 (75<sup>th</sup> percentile: 3.0) were obtained, respectively (Table 2). Limbs (52%), spine (27.6%) and pelvic girdle (22.8%) were most frequently affected. When pain was analysed in terms of subgroups of intensity, most patients have described moderate or severe pain (60%, n = 73), even though only 5% of these patients have described a severe pain, half from these presented with ECOG status  $\geq 2$  and these were more frequently diagnosed with non-cancer related pain by the treating physician (one in three), caused by non cancer-

related benign pathologies. Lower scores of non-cancer related pain were found in patients with mild and moderate pain (19.1% and 28.8%, respectively) (Table 3).

A mean score of 3.8 was found in this group of patients, regarding pain's interference with ADL (95% CI: 3.3 – 4.3; 75<sup>th</sup> percentile: 5.0). General activity, walking ability and work were the most affected domains (mean 5.0; 4.5; 4.6 respectively, Table 2).

### Characteristics of analgesia

Around one third of the patients (30.8%, n = 37) were not prescribed with any analgesics, despite having described the presence of pain. A total of 22 of these patients (59.5%) presented with moderate pain and only one patient with severe pain (2.7%). A percentage of 46.8% of the patients with mild pain were on nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen and 34% on opioids, while 52.2% of the patients with moderate pain were on NSAIDs and acetaminophen and 43.3% on opioids and, in patients with severe pain, 66.7% were on NSAIDs and acetaminophen and also 66.7% on opioids. Patients in the subgroup with moderate pain were more frequently on strong opioids, even though none of the patients with severe pain was on these previous to the medical appointment (Table 3).

An increase in prescribed NSAIDs and acetaminophen, as well as opioids (mainly weak opioids), has been found in both groups upon the medical appointment. A higher percentage of patients on opioids has been found in the control group vs. interventional group (Table 4). The percentage of patients with severe pain on weak opioids was changed from 66.7 to 83.3% upon the Medical Oncology appointment, even though none of these patients was prescribed with strong opioids.

Table 1 - Characteristics of our group of patients with painful metastatic prostate cancer

	Control group (n = 55)	Interventional group (n = 46)	Lost to follow-up (n = 19)
<b>Patient characteristics</b>			
Median age (years)	71 (range: 52 - 90)	70 (range: 47 - 92)	77 (range: 60 - 83)
ECOG status 0 - 1	87.0%	82.6%	83.3%
ECOG status $\geq 2$	13.0%	17.4%	16.7%
Non-cancer related pain	20.4%	28.3%	31.6%
<b>Disease characteristics</b>			
Gleason $\geq 8$	54.7%	50.0%	56.3%
Gleason 7	35.8%	22.7%	37.5%
Gleason $\leq 6$	9.4%	27.3%	6.3%
Metachronous metastases	65.5%	47.8%	47.4%
Time since spreading (median)	20 months	23.5 months	20 months
Bone spreading	92.7%	80.4%	63.2%
Extra-bone spreading	47.3%	41.3%	57.9%
Castration-resistant disease	78.2%	47.8%	47.4%
Previous docetaxel	52.7%	37.0%	31.6%

Table 2 - Results of the pre-appointment applied BPI-SF

Questionnaire items	Total sample (n = 101)		Control group (n = 55)		Interventional group (n = 46)	
	Median (25 <sup>th</sup> - 75 <sup>th</sup> Q)	Mean (95% CI)	Median (25 <sup>th</sup> - 75 <sup>th</sup> Q)	Mean (95% CI)	Median (25 <sup>th</sup> - 75 <sup>th</sup> Q)	Mean (95% CI)
<b>Pain intensity</b>						
Q3 – worst pain	6 (5 - 8)	6 (5.6 - 6.5)	6 (5 - 8)	6.1 (5.5 - 6.7)	6 (5 - 7)	5.9 (5.2 - 6.7)
Q4 – least pain	2 (1 - 3)	1.9 (1.5 - 2.2)	2 (1 - 3)	2.1 (1.7 - 2.6)	1 (0 - 2)	1.5 (0.9 - 2.1)
Q5 – mean pain	4 (3 - 5)	4 (3.7 - 4.4)	4 (3 - 5)	4.1 (3.7 - 4.7)	4 (3 - 5)	3.8 (3.3 - 4.3)
Q6 – pre-medical appointment pain	3 (0 - 4)	2.8 (2.3 - 3.3)	3 (1 - 5)	3.2 (2.5 - 3.9)	2 (0 - 3)	2.3 (1.5 - 3.1)
<b>Pain-related interference</b>						
Q9 – interference with ADL	4 (2 - 5)	3.8 (3.3 - 4.3)	4 (3 - 5)	4.1 (3.5 - 4.7)	3.3 (1.3 - 4.6)	3.3 (2.5 - 4.1)
Q9A – general activity	5 (2 - 8)	5 (4.3 - 5.7)	5 (3 - 8)	5.4 (4.6 - 6.3)	4 (1 - 7)	4.4 (3.2 - 5.5)
Q9B – mood	4 (2 - 6)	4.4 (3.7 - 5)	5 (3 - 7)	4.6 (3.8 - 5.4)	4 (1 - 6)	4 (3.1 - 5)
Q9C – walking ability	5 (1 - 7)	4.5 (3.8 - 5.2)	5 (1 - 8)	4.9 (4 - 5.8)	3 (0 - 6)	3.9 (2.7 - 5.1)
Q9D – work	4 (1 - 7)	4.6 (3.9 - 5.2)	5 (3 - 8)	5.2 (4.3 - 6.1)	3 (0 - 6)	3.5 (2.5 - 4.6)
Q9E – relation with others	2 (0 - 5)	3 (2.3 - 3.6)	2 (0 - 5)	3 (2.2 - 3.9)	1.5 (0 - 4)	2.9 (1.9 - 3.9)
Q9G – sleep	2 (0 - 5)	3 (2.4 - 3.6)	2 (0 - 5)	3 (2.2 - 3.8)	2 (0 - 5)	2.9 (1.9 - 4)
Q9G – enjoyment of life	1 (0 - 3)	2.3 (2.8 - 3.6)	2 (0 - 5)	2.8 (1.9 - 3.6)	0 (0 - 2)	1.5 (0.7 - 2.3)

### Impact of the medical appointment and the use of the BPI-SF questionnaire

Mean pain score upon the Medical Oncology appointment was reduced from 3.95 to 3.01 in the 101 patients having complete all the study evaluations, with a statistically significant mean difference (0.94;  $p < 0.001$ ). Mean pain score reduction in the interventional group (1.15; 95% CI: 0.71 – 1.60) was higher when compared to the control group (0.76; 95% CI: 0.31 – 1.22) even though with a statistically non-significant difference (0.39; 95% CI: -0.25 – 1.02;  $p = 0.227$ ). The difference was changed to 0.17 (95% CI: -0.55 – 0.88;  $p = 0.646$ ) when adjusted for potential confounding variables by using a multivariate linear regression model.

A 43.5% likelihood of reaching a properly managed pain when sharing the results of the BPI-SF questionnaire with the treating physician was found vs. 30.9% in the control group, even though this benefit was not statistically significant (OR = 1.72;  $p = 0.193$ ). The adjustment for confounding factors in a multivariate logistic regression model was associated with a reduction in the association between the BPI-SF questionnaire and a properly managed pain (OR = 1.51;  $p = 0.368$ ). A severe pain was described by 8.1% ( $n = 3$ ), moderate by 73% ( $n = 27$ ) and mild by 18.9% ( $n = 7$ ) of the 37 patients with properly managed pain (reduction  $\geq 2$  points). A 57.5% likelihood of reaching a properly managed

pain was found in the six patients having described maximum pain  $\geq 7$ , with a statistically significant difference when compared to patients with pain  $< 7$ .

### DISCUSSION

Pain is frequently described by patients with advanced prostate cancer and pain management should be among the top priorities for the oncologist. Our group of patients was selected due to the propensity for the development of pain in metastatic prostate cancer, particularly with bone spreading. A higher pain prevalence was found in our study when compared to a phase-III clinical trial in patients diagnosed with this pathology and in different stages of the disease. This difference is probably due to the fact that a less selective group of patients has been used, when compared to those that were used in the major clinical trials.<sup>12-17</sup> To the best of authors' knowledge, this is the first study allowing for the identification of pain prevalence in patients with metastatic prostate cancer in the Portuguese population. Even though representing a single reference oncological centre, which may have overestimated pain prevalence due to a referral bias, a low risk has been considered, due to the fact that patients presenting at all stages of the disease were admitted and followed at this institution, where approximately 37% of the patients living in the Northern region have been admitted and 13% of the Portuguese patients



Table 3 - Patient characteristics regarding nominal scales

	Mild pain (n = 47)	Moderate pain (n = 67)	Severe pain (n = 6)
<b>Patient characteristics</b>			
Age ≥ 65 years	78.7%	85.1%	100.0%
ECOG status 0-1	93.5%	81.8%	50.0%
Non-cancer related pain	19.1%	28.8%	33.3%
<b>Disease characteristics</b>			
Bone metastases	91.5%	76.1%	100.0%
Castration-resistant disease	63.8%	58.2%	83.3%
Spreading time > 12 months	74.5%	59.7%	100.0%
<b>Analgesia</b>			
Analgesics	70.2%	67.2%	83.3%
Acetaminophen	25.5%	34.3%	50.0%
NSDAIs	21.3%	17.9%	16.7%
Corticosteroids	36.2%	41.8%	50.0%
Adjuvants	12.8%	7.5%	0
Previous opioids	34%	43.3%	66.7%
Weak opioids	25.5%	25.4%	66.7%
Strong opioids	8.5%	17.9%	0
Antalgic radiation therapy	12.8%	9%	0
<b>Cancer treatment</b>			
Zoledronate	40.4%	43.3%	33.3%
Docetaxel	44.7%	41.8%	50.0%

Table 4 - Analgesia medication

Analgesia	Control group (n = 55)		Interventional group (n = 46)	
	Before	After	Before	After
Acetaminophen	35.9%	39.1%	26.8%	32.1%
NSDAIs	18.8%	20.3%	19.6%	19.6%
Strong opioids	15.6%	15.6%	10.7%	10.7%
Weak opioids	34.4%	45.3%	19.6%	26.8%
Adjuvants	12.5%	12.5%	5.4%	8.9%
Corticosteroids	48.4%	48.4%	30.4%	30.4%
Topical therapies	1.6%	1.6%	1.8%	1.8%

were diagnosed with prostate cancer.<sup>20-22</sup>

The use of standardized tools for pain assessment allows for a better knowledge on the subjective experience associated with pain. Most patients presented with pain located to the appendicular skeleton, which is less frequently affected by advanced prostate cancer. This may be explained by the frequency of non-cancer related pain syndromes. Larger number of patients with severe pain were diagnosed with non-cancer related pain by the treating physician, showing how relevant is the contribution of non-cancer related pathologies to pain in our group of patients. A mean pain score of 3.95 was found on the week before the medical appointment and moderate pain was described by most of the patients. Having attended a chronic pain outpatient clinic or a non-scheduled appointment on the following week to the

completion of the questionnaire were considered as exclusion criteria so that nothing except the treating physician's clinical judgement would interfere with therapy; therefore, patients with potentially more severe pain were excluded from the study, which may have underestimated pain intensity in our study. In addition, the performance dimensions associated with mobility were those that were most significantly interfered by pain. This pattern of mobility-associated pain is also frequently associated with non-cancer related pathologies, which should be taken into consideration in view of the median age of our group of patients. The fact that mean score of interference with ADL was higher than mean pain score is worth mentioning, as it raises the issue of a potential patient's poorer self-evaluation.

As regards analgesia, a high use of corticosteroids is

worth mentioning as, even though these are well-known anti-inflammatory drugs used in advanced prostate cancer, this drug class is also used together with cancer treatment, making the assessment of their contribution to properly managed pain more difficult.

None of the patients with severe pain was on opioids and the fact that not only patients assessed in subsequent appointments but also patients assessed for the first time were included in the study is worth mentioning, as second or third-step analgesics drug-naïve patients were included.

This study was aimed at the identification of the clinical benefit of a systematic pain assessment with the BPI-SF questionnaire in patients with metastatic prostate cancer. Even though with a non-experimental design, the clinical characteristics of the patients included in each group were well balanced and typically represented this population of patients. Upon a medical appointment, a statistically significant 0.94-point reduction in mean pain intensity score has been found, even though the explicit use of the BPI-SF questionnaire was not associated with a significant reduction in mean pain intensity (0.39 points;  $p = 0.227$ ). The study has been designed with an 80% power for the identification of a 1-point difference in mean pain intensity score. Considering that a clinically significant difference would correspond to a mean 1.5-2-point reduction and that the correction of the measure of association for potential confounding factors was associated with a reduction, the isolated use of this tool would unlikely correspond to any benefit for the patients, would not other empowering measures for higher clinical efficacy had been used. One of the possible measures would be the systematic use of this tool, particularly upon an adequate medical training in order to value each of the dimensions of the BPI-SF questionnaire. In addition, its routine use would make awareness among patients easier, giving support to the clinical usefulness of the systematic and continuous pain assessment by using the questionnaire when associated with a medical pain management education program.

## CONCLUSION

The use of the BPI-SF questionnaire in medical routine is feasible. A systematic pain assessment provides treating physicians with a better knowledge on pain and therefore on better pain management, even though with a statistically non-significant impact. This tool was useful for pain assessment, due to the associated systematisation and standardisation. The implementation of training programs in chronic pain management and the continuous use of this tool will allow for a better enhancement of each of the dimensions and subsequent improvement in the quality of pain management and quality of life in patients with advanced prostate cancer. This group of patients represented a population with no standard and systematic pain assessment aimed at a tailored analgesia.

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## HUMAN AND ANIMAL PROTECTION

The authors declare that the followed procedures were according to regulations established by the Ethics and Clinical Research Committee of the IPO Porto and according to the Helsinki Declaration of the World Medical Association.

## DATA CONFIDENTIALITY

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

## CONFLICTS OF INTEREST

The authors declare that there were no conflicts of interest in writing this manuscript.

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## REFERENCES

- Swarm RA, Abernethy AP, Angheliescu DL, Benedetti C, Buga S, Cleeland C, et al. National Comprehensive Cancer Network – Adult cancer pain. *J Natl Compr Canc Netw*. 2013;11:992-1022.
- Merskey H, Bogduk N. Classification of chronic pain- Descriptions of chronic pain syndromes and definitions of pain terms. 2<sup>nd</sup> ed. Seattle: International Association of Study of Pain Press; 1994.
- Lesage P, Portenoy RK. Trends in cancer pain management. *Cancer Control*. 1999;6:136-45
- Van den Beuken-van Everdingen MH, de Rijke JM, Kessels AG, Schouten HC, van Kleef M, Patijn J. Prevalence of pain in patients with cancer: a systematic review of the past 40 years. *Ann Oncol*. 2007;18:1437-49.
- Portenoy RK. Epidemiology and syndromes of cancer pain. *Cancer*. 1989;2298-307
- Farrar JT. Advances in clinical research methodology for pain clinical trials. *Nat Med*. 2010;16:1284-93.
- Cleeland CS, Gonin R, Hatfield AK, Edmonson JH, Blum RH, Stewart JA, et al. Pain and its treatment in outpatients with metastatic cancer. *N Engl J Med*. 1994;330:592-6.
- Keller S, Bann CM, Dodd SL, Schein J, Mendoza TR, Cleeland CS. Validity of the brief pain inventory for use in documenting the outcomes of patients with noncancer pain. *Clin J Pain*. 2004;20:309-18.
- De Andrés Ares J, Cruces Prado LM, Canos Verdecho MA, Penide Villanueva L, Del Valle Hoyos M, Herdman M, et al; Validation of the short form of the brief pain inventory (BPI-SF) in Spanish patients with non-cancer-related pain. *Pain Pract*. 2015;15:643-53.
- Azevedo LF, Pereira AC, Dias C, Agualusa L, Lemos L, Romão J, Castro-Lopes JM. Translation, cultural adaptation and multicentric validation study of chronic pain screening and impact assessment instruments. *Dor*. 2007;6-56.
- Autio KA, Bennett AV, Jia X, Fruscione M, Beer TM, George DJ, et al. Prevalence of pain and analgesic use in men with metastatic prostate cancer using a patient-reported outcome measure. *J Oncol Pract*. 2013;9:223-9.



12. De Bono JS, Oudard S, Ozguroglu M, Hansen S, Machiels JP, Kocak I, et al. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. *Lancet*. 2010;376:1147-54.
13. Scher HI, Fizazi K, Saad F, Taplin ME, Sternberg CN, Miller K, et al. Increased survival with enzalutamide in prostate cancer after chemotherapy. *N Engl J Med*. 2012;367:1187-97.
14. Petrylak DP, Tangen CM, Hussain MH, Lara PN Jr, Jones JA, Taplin ME, et al. Docetaxel and estramustine compared with mitoxantrone and prednisone for advanced refractory prostate cancer. *N Engl J Med*. 2004;351:1513-20.
15. Tannock IF, de Wit R, Berry WR, Horti J, Pluzanska A, Chi KN, et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. *N Engl J Med*. 2004;351:1502-12.
16. Ryan CJ, Smith MR, de Bono JS, Molina A, Logothetis CJ, de Souza P, et al. Abiraterone in metastatic prostate cancer without previous chemotherapy. *N Engl J Med*. 2013;368:138-48.
17. Fizazi K, Scher HI, Molina A, Logothetis CJ, Chi KN, Jones RJ, et al. Abiraterone acetate for treatment of metastatic castration-resistant prostate cancer: final overall survival analysis of the COU-AA-301 randomised, double-blind, placebo-controlled phase 3 study. *Lancet Oncol*. 2012;13:983-92.
18. Breivik H, Cherny N, Collett B, de Conno F, Filbet M, Foubert AJ, et al. Cancer-related pain: a pan-European survey of prevalence, treatment, and patient attitudes. *Ann Oncol*. 2009;20:1420-33.
19. Breivik H, Borchgrevink PC, Allen SM, Rosseland LA, Romundstad L, Hals EK, et al. Assessment of pain. *Br J Anaesth*. 2008;101:17-24.
20. RORENO. Registo Oncológico Regional do Norte 2010. Porto: IPO; 2015.
21. RORENO. Registo Oncológico Nacional 2016. Porto: IPO; 2016.
22. Registo Oncológico 2010. Instituto Português de Oncologia do Porto Francisco Gentil. Porto: IPO; 2012.