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ORIGINAL ARTICLE

Improvement of pain management in a comprehensive cancer center: a comparison of two cross-sectional studies 8 years apart

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Abstract

Context In 2011, a multidisciplinary palliative team (MPT) was established at Rigshospitalet (DK) and a cross-sectional study in inpatients was carried out at the Departments of Oncology and Hematology. High symptom burden, high prevalence of pain (64%), and insufficient analgesic treatment were demonstrated. In 2019, a similar study was carried out.

Objectives This study compares prevalence of symptoms including pain and analyzes analgesic treatment of adult in-patients in a comprehensive cancer center.

Methods Two cross-sectional studies (May–Jun 2011; Feb–Sep 2019). Inclusion criteria: malignant diseases, age ≥ 18 y, able to understand Danish. EORTC QLQ-C30 and Brief Pain Inventory (BPI) were applied.

Results A total of 134 and 183 inpatients were included in 2011 and 2019, respectively. Differences in the two populations were seen; in 2019 more patients had advanced disease (P = 0.0096), lower performance status (P = 0.0028), and a palliative treatment plan (P = 0.0034). The prevalence of impairments and symptoms was high and similar in the 2 years with exception of severe pain (P = 0.0143) and neuropathic pain (P < 0.0001) which increased in 2019. Moreover, pain relief significantly improved, and significantly fewer patients with pain were left untreated. Significant increase in opioid and adjuvant analgesic prescription in 2019.

Conclusion An overall unchanged high symptom burden was observed. However, improvement of pain management was observed in 2019. The establishment of a MPT may possibly have contributed to improved pain management.

Keywords Cancer · Pain · Neuropathic pain · Symptom assessment · Quality of life · Palliative care

Introduction

To ensure comfort and conserve functional capacity in the earlier phases of the cancer disease trajectory management of pain and other symptoms has become an important target for palliative care interventions in order to decrease patients' suffering and improve quality of life [1–3]. Therefore, integration of specialized palliative care (SPC) and oncology early in cancer disease trajectories is internationally

Key message This study provides information on development of symptoms and treatment of adult cancer inpatients eight years after the establishment of a specialized palliative care (SPC) service in a comprehensive cancer center. The prevalence of symptoms during the period remained high; however, significant improvement on pain management and relief was found.

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recognized as a prerequisite for better outcomes [4, 5]. Indicators for this integration and triggers for referral to SPC have been investigated and published [6]. However, consensus has not yet been reached.

In 2011, a cross-sectional study was carried out at the hematological and oncological wards at Centre for Cancer and Organ Diseases at Rigshospitalet, Copenhagen University Hospital, in Denmark. The study which combined the use of Patient-reported Outcome Measures (PROMs) assessing symptoms with a particular focus on pain and clinician reported outcomes (ClinROs) focusing on disease, pain assessment and management, revealed a pronounced symptom burden including high prevalence and severity of pain associated with inadequate pain management [7, 8]. Contemporarily with the 2011 study a SPC team was established at Rigshospitalet Copenhagen University Hospital. Besides offering multidisciplinary palliative care to outpatients and their families including home care, the team was dedicated to offer inpatient palliative consultations by physician and nurse, to engage in local educational programs to strengthen basic palliative care skills, and to initiate and develop palliative care research.

Eight years after, the cross-sectional study was repeated to analyze the current prevalence and severity of impaired functions and symptoms, including pain management. During this period, it was hypothesized that an improvement in pain and symptom control would be observed. Therefore, the aim of this study was to compare the outcomes of the two cross-sectional studies. The purpose of repeating the cross-sectional study on inpatients was to obtain information about the development of symptoms and treatment of hospitalized patients, which may represent a strong indicator for the local capability of symptom management.

Methods

Design, settings, and samples

A comparative study, which comprises historical [7, 8] and recent data (Feb–Sep 2019) from adult inpatients with malignancies at the Departments of Hematology and Oncology, Rigshospitalet Copenhagen University Hospital, Denmark. The historical data derives from two publications performed with the same sample of patients and in this study, they will be referred to as data 2011.

Sample size for the 2019 study was calculated based on a formula proposed for prevalence studies, which included an expected prevalence of moderate to severe pain in the last 24 h = 22% (based on data from the 2011 study [7]), level of confidence = 95%, precision = 0.05 and a finite population correction [9–12]. Considering an expected inclusion rate of approximately 70%, the sample size was estimated to be 179 inpatients for a study period of 3 months.

Inclusion criteria

Inpatients with malignant diseases and age ≥ 18 years.

Exclusion criteria

Patients who were unable to understand the questionnaires, did not understand the Danish language, were not present in the departments for all assessments, and/or were unable to give informed consent. Patients who already had participated in one study round did not participate in the next.

Assessments

The two cross-sectional studies were carried out in the same way. At 9 am on each study day, the leading ward nurse drew up the list of admitted patients and eligible patients were informed verbally and in written form about the study by trained nurses at the wards or by trained physicians and nurses from the Section of Palliative Medicine. In 2011, PROMs were obtained in paper forms that later were typed into a database. In 2019, data was typed directly on a tablet and transferred automatically to a Redcap database (software and workflow methodology for research databases) for statistical processing [13]. Sociodemographic (age and sex) and analgesic consumption data were collected from the electronic patient records.

Disease specific data

Stage (for solid tumors), reasons for hospitalization, antineoplastic treatment, and intention of treatment (curative/adjuvant or palliative), which were collected by a clinical oncologist or hematologist, respectively.

Analgesic consumption

(1) No opioid/adjuvant analgesics (AA), (2) opioids only, (3) opioids and AA. AA was defined as gabapentin, pregabalin, tricyclic antidepressants (TCA), duloxetine and/or prednisolone given on a specific pain indication. Use of paracetamol was also registered.

Trained staff (physicians and nurses) from the Section of Palliative Medicine, assessed the inpatients as follows:

Performance status (PS)

Five-grade Eastern Cooperative Oncology Group (ECOG)/WHO scale [14]. For the non-participating patients, PS was obtained from the electronic patient records when available.

Pain causes and mechanisms for the last 24 h

Multisource screening based on (1) patient-reported outcomes, (2) pain history and pain descriptors via semi structured interview, (3) information from the patients' records regarding radiological verified tumor infiltration/pressure and treatments and/or other causes not related to cancer. Based on this information, pain mechanism was classified as nociceptive (somatic and visceral) and/or neuropathic pain (NP).

Patient Reported Outcomes Measures (PROMs)

Pain intensity (worst, least, average, now and pain relief) was recorded according to the short-form of the BPI [15], which consists of self-assessment numerical scales with numbers from 0 to 10, where 0 is 'no pain' and 10 is 'worst pain imaginable'. The BPI measures specifically for pain the last 24 h. As in the 2011 data, mild pain was defined as 1–4, moderate pain as 5–6, and severe pain as 7–10. Pain relief was registered from 0 to 100%, where 0 is no relief and 100 is total relief [7, 8]. A question regarding the number of daily breakthrough pain episodes was added.

Symptoms and functionality were assessed by the Danish version of the EORTC QLQ-C30 (version 3.0) instrument, which is composed by five function scales (physical, role, cognitive, emotional and social), three symptom scales (fatigue, pain and nausea/vomiting), six single items and additional symptoms (dyspnea, loss of appetite, insomnia, constipation, diarrhea and financial difficulties) and a global health status scale [16]. Responses were converted to 0–100 scales. For the function scales, a high score reflects a good functioning, whereas a high score on a symptom scale reflects a high level of the symptom. Cut-off points > 34 and > 67 were used as thresholds of "symptom" and "severe symptom", respectively, for the symptom scales, corresponding to more than "a little" (33.3) and more than "quite a bit" (66.7) [17]. For the function scales, the thresholds for impairment were < 66 and severe impairment < 33, equivalent to average scores of more than "a little" and "quite a bit" impairment [18]. Prevalence rates for each symptom were estimated using these cut points. Overall, quality of life was not considered a single symptom, and "symptom" percentages were therefore not estimated. The EORTC measures specifically for impairments and symptoms within the last week.

Ethics

All patients received oral and written information, and informed consent was obtained from all patients prior to inclusion. Collecting data from consenting inpatients was approved by the Danish Data Protection Agency (VD-2019–68).

Non-interventional studies do not require approval from Ethic Committee in Denmark. The principles of the Declaration of Helsinki were followed. The investigators (physicians and nurses) were obliged to report if any deficiencies in pain and symptom management were observed.

Statistical analyses

All analyses were carried out using SAS Enterprise Guide v. 7.15 (SAS Institute Inc., Cary, NC, USA). Comparisons were analyzed using Chi-square, Wilcoxon two-sample test. A significance level of 0.05 was generally applied.

Results

In 2011, the Department of Hematology consisted of three wards and the Department of Oncology five wards. In 2019, the total inpatient capacity had been reduced to two and four wards, respectively. To reach the sample size of 179 inpatients, a total of five study rounds at each hospital ward was completed.

Sociodemographic and disease characteristics

Patients' characteristics are outlined in Table 1. Inclusion percentage of eligible inpatient were 76.5% and 67.3% in 2011 and 2019, respectively**.** Mean age was significantly lower in 2011 (P = 0.0003). Lung cancer and chronic leukemia (14.2%), acute leukemia and lymphoma (13.4%) were the most frequent diagnoses in 2011, whereas multiple myeloma (14.8%), acute leukemia (14.2%) and gastrointestinal cancers (12.0%) were the most frequent in 2019. Patients had less advanced cancer disease in 2011 compared to 2019. Prevalence of stage IV cancer was 46.4% in 2011 and 65.4% in 2019 (P = 0.0096), respectively.

Higher percentage of patients with good performance status (PS 0–1) was found in 2011 compared to 2019 (P = 0.0028). More patients were on a curative treatment plan and fewer on a palliative treatment plan in 2011 compared to 2019 (P = 0.0034).

Table 1 Sample characteristics of included participants in the 2011 and 2019 studies, respectively

Variables	Included participants 2011	Included participants 2019	P-values¤
N	134	183	
Inclusion rate of eligible patient (%)	76.5	67.3	
Age (years)			**0.0003**
Mean (SD)	59.2 (13.4)	64.5 (12.7)	
Min–Max	21–88	22–89	
Sex			0.3693
Male, n (%)	80 (59.7)	100 (54.6)	
Female, n (%)	54 (40.3)	83 (45.4)	
Days hospitalization			0.8105
Mean (SD)	9.9 (19.2)	7.8 (14.9)	
Min–Max	0–156	0–135	
Oncologic, n (% of all)	69 (51.5)	81 (44.3)	0.2028*
Lung	19 (14.2)	9 (4.9)	**0.0041**
Urologic	12 (9.0)	15 (8.2)	0.8111
Gastrointestinal	9 (6.7)	22 (12.0)	0.1162
Head neck	13 (9.7)	12 (6.6)	0.3117
Gynecologic	10 (7.5)	12 (6.6)	0.7540
Other oncological	6 (4.5)	11 (6.0)	0.5270
Hematologic, n (% of all)	65 (48.5)	102 (55.7)	0.2028*
Chronic leukemia	19 (14.2)	9 (4.9)	**0.0041**
Acute Leukemia	18 (13.4)	26 (14.2)	0.8437
Lymphoma	18 (13.4)	23 (12.6)	0.8207
Multiple myeloma	6 (4.5)	27 (14.8)	**0.0031**
Other hematologic	4 (3.0%)	17 (9.3)	**0.0242**
Cancer stage, n (%)	69 (100)	81 (100)	**0.0096**
1	6 (8.7)	4 (4.9)	
2	12 (17.4)	7 (8.6)	
3	14 (20.3)	9 (11.1)	
4	32 (46.4)	53 (65.4)	
Not specified	5 (7.2)	8 (9.9)	
PS, n (% of all)	134 (100)	183 (100)	**0.0028**
0	14 (10.4)	5 (2.7)	
1	33 (24.6)	34 (18.6)	
2	33 (24.6)	62 (33.9)	
3	20 (14.9)	63 (34.4)	
4	13 (9.7)	12 (6.6)	
Missing	21 (15.7)	7 (3.8)	
Treatment intend, N (%)	134 (100)	183 (100)	
Curative	72 (53.7)	87 (47.5)	0.4838
Adjuvant	3 (12.2)	2 (1.1)	0.4492
Palliative	40 (29.9)	81 (44.3)	**0.0034**
Other/not specified	19 (14.2)	13 (7.1)	**0.0389**

* Test of the proportion of oncologic and hematologic patients in the two samples; ¤ Bold font indicates statistical significance

Chi-square test for categorical variables and Wilcoxon two-sample test for continuous and ordinal variables

PS, Performance Status

Figure legend: [Patients' characteristics are outlined in Table 1.]

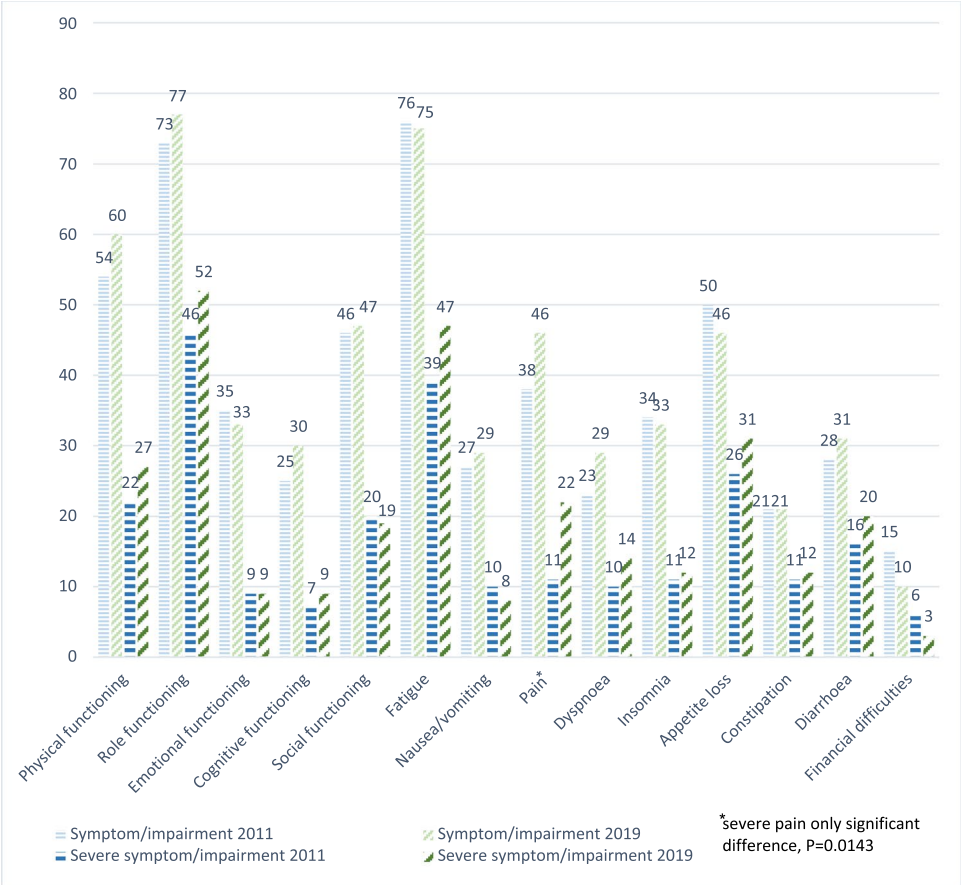

Fig. 1 Proportions of patients who presented impairments and symptoms. Figure legend: [which was 11% in 2011 and 22% in 2019 (P = 0.0143) (Fig. 1).]. Note to figure: color should be used to distinct the different years

Functions and symptoms

A total of 92.5% (n = 124) and 98.4% (n = 180) patients answered the EORTC QLQ-C30 in 2011 and in 2019, respectively.

The severity of functional impairments and symptoms were similar in 2011 and 2019. Both years, the highest level of impairment and severe impairment was seen for role function and the highest prevalences of symptoms were observed for fatigue, appetite loss and pain. Fatigue and appetite loss were also most frequently rated as severe in both assessments. Only in the EORTC symptom scale for pain a significant difference was observed. Here 11% reported severe pain in 2011 and 22% reported severe pain in 2019 (P = 0.0143) (Fig. 1).

Pain causes and prevalence

In 2011 and 2019, pain causes due to tumor pressure/infiltration were found in 42% and 36%, other reasons related to cancer in 19% and 25%, pain caused by antineoplastic treatment in 37% and 18%, and reasons not related to cancer or cancer treatment in 18% and 22%, respectively. The main findings on pain and analgesic treatment are outlined in Fig. 2.

When comparing patient-reported data from the BPI, prevalence of average pain > 0 in the last 24 h, did not differ significantly comparing 2011 and 2019. Further, no significant difference was seen regarding patients reporting moderate/severe pain and presence of breakthrough pain. However, in 2019 pain relief was 22 pp higher (P = 0.0010) and the prevalence of patients left with untreated pain was 35 pp lower (P < 0.0001).

Opioid and paracetamol

The use of opioids, regardless of pain or pain mechanisms almost doubled during the time period with an increase of 24 pp (P < 0.0001). Furthermore, a 38 pp increase in the number of patients having pain and receiving an opioid prescription was seen (P < 0.0001). Also, an increase of

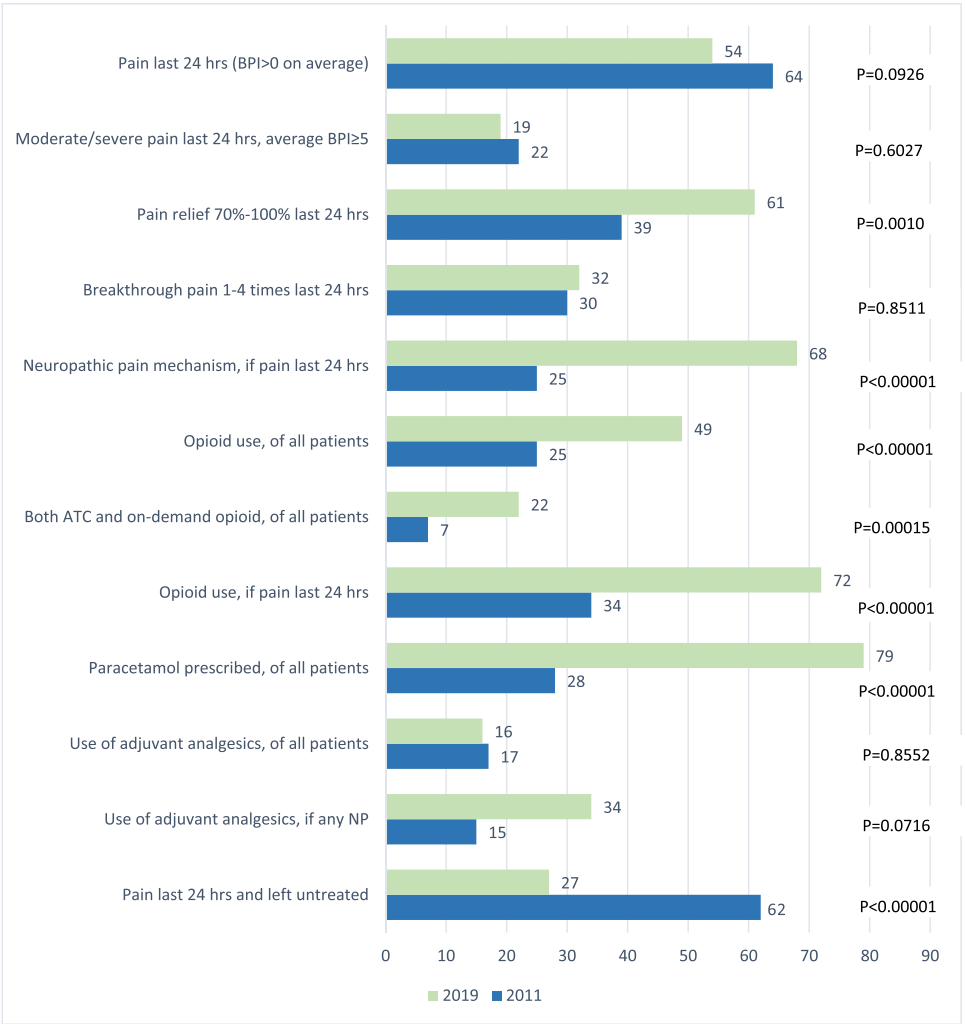

Fig. 2 Pain and analgesic treatment (%). Figure legend: [2011 and 34% in 2019 received an AA prescription, which constituted an increase of 19 pp (P = 0.0716).]. Note to figure: color may be used to distinct the different years, alternatively two tones of grey

15 pp in those with prescriptions of both around-the-clock and on-demand opioids (P = 0.00015), and 51 pp increase in the number of patients with a paracetamol prescription (P < 0.0001).

NP prevalence and AA prescriptions

In 2011, 25% of the patients were found to have NP elements. In 2019, 67% were screened and found to have NP elements, which constituted an increase of 43 pp (P < 0.0001). In patients, who were screened and found with NP pain mechanism, 15% in 2011 and 34% in 2019 received an AA prescription, which constituted an increase of 19 pp (P = 0.0716).

Discussion

Comparison of the two cross-sectional studies using identical methodologies with 8 years apart demonstrated an overall high and generally unchanged degree of impaired functions and symptoms for inpatients with malignant diseases.

When looking at the sociodemographic outcomes of the two cross-sectional samples, it is clearly demonstrated, that although the research methodology was unchanged, the populations and settings have changed. The 2019 population differed statistically in terms of having higher mean age, lower performance status, higher cancer stage and was more frequently on a palliative care treatment plan.

Nevertheless, our strong focus on pain assessment and management of inpatients rendered us with some very interesting and encouraging findings. Despite high pain prevalence in both assessments, a significant higher number of patients reported improved pain relief, and significantly fewer patients with pain were left untreated. Besides this, the

use of opioids increased, and the use of adjuvant analgesics increased in patients with NP components.

Seeking an explanation for these findings, several circumstances must be considered. First, a specialized palliative care unit was established in the Department of Oncology in 2011. The establishment gave rise to clinical research, new treatment modalities, development of guidelines, education and focus on research implementation in palliative care and to some extent involved integration with oncology. The establishment motivated the first cross-sectional study [7, 8]. Second, during the study period substantial changes have also taken place in oncology and hematology and according to the international developments and standards more ambulatory activity has been launched at the expense of number of beds. Thus, a stronger selection on the inpatient capacity, new antineoplastic treatment modalities and toxicity profiles, higher number of inpatients with advanced disease, lower performance status, and more patients with a palliative scope of treatment may all have affected the reported symptom burden. Despite these environment- and patient-related issues concerning the inpatient population, pain assessment and management has improved substantially. Although, other factors may have influenced the favorable outcomes, including the increasing efficacy of antineoplastic treatments on disease as well as symptoms, we will take the liberty to praise the outcomes in this comprehensive cancer center as a result of improved staff behavior concerning pain management. A Norwegian study in a comparable healthcare system, designed in the same way as ours, apart from also including outpatients, did not achieve the same favorable results concerning pain management during a 5-year observation period [19]. However, the significant pain relief found in many of the inpatients of the present study may be associated with the steep rise in the use of opioids and paracetamol. Further, the proportion of inpatients with prescriptions of both around-the-clock and on-demand opioids had increased significantly, indicating a more rational use of opioids in accordance with major guidelines of opioid management of patients with cancer [20, 21]. Although, the EORTC symptom scale for pain showed an increase in severe pain from 11 to 22% in the period, BPI data demonstrated that a significantly higher number of inpatients was reporting improved pain relief in 2019 (Fig. 2). Increased severe pain may be associated with the well-known fact that more severe cases of difficult management exist in more advanced malignancies [22]. The seeming discrepancy between more severe pain and improved pain relief may also arise from the different psychometric properties and designs of the two PROMs EORTC and BPI, where the same patients are asked about pain in different ways and asked to recall the last week vs. last 24 h, respectively. Important to note is also that experienced severe pain and pain relief can coexist, and both may involve social and existential dimensions.

Finally, and most noteworthy was the increased findings and analgesic treatment attempts of NP. Neuropathic cancer pain is associated with worse treatment responses and specific therapy indications, but a standardized clinical diagnosis is still lacking [23]. To address this, the International Study for the Study of Pain has defined three assessment criteria to stratify NP into possible, probable, and definite neuropathic pain [24, 25]. Satisfying these criteria in turn raises the likelihood of NP from possible to probable to definite. Thus, the prevalence of NP in cancer has been found to differ according to the context of care and knowledge of the treating physicians. A higher prevalence was seen in cancer inpatients admitted to specialized pain or palliative care services, where NP prevalence ranged from 49.5% to 57.5%, compared with outpatients attending basic palliative care or oncology services where NP prevalence ranged from 11.8% to 39.7% [26]. The prevalence of NP in the 2019 study was high, although only patient-reported outcomes, history and descriptors of pain, possible tumor infiltration/pressure and side effects of the treatment were used as screening criteria. Thus, NP in cancer is considered highly complex to diagnose and treat, and more likely to be undertreated than nociceptive pain [25]. Therefore, the observed higher prevalence of NP in the present study plausibly reflects more complex inpatient cases, but some detection bias in the assessment of NP done by the two palliative staff groups in 2011 and 2019 may also have influenced the findings. Regarding the observed improved pain treatment including use of adjuvant analgesics, it is noteworthy that SSRI in the 2011 study was defined as an AA and it constituted the majority of the registered AA use. This contrast to the 2019 study, where only use of gabapentin, pregabalin, tricyclic antidepressants (TCA), duloxetine and/or prednisolone given on a specific pain indication were included in the analysis. Thus, the positive findings regarding treatment of NP may be diluted. However, the overall improvements in treatment of pain seem to be substantial and reflect improved skills of the healthcare team regarding identification and treatment of pain including NP.

Strengths and limitations

The PROMs combined with ClinROs in this study seems to be a strong indicator of the staff capability of delivering improved pharmacological pain management. However, the results of the present study with an observational design may be limited because of residual confounding and non-response bias, and therefore cannot prove causality. Another limitation might be the high percentage of patients with hematological malignancies. In other hospitals, the corresponding numbers may be much lower than the about 50%

encountered in this study. This may be a limitation for the external validity of the study.

Conclusion

A significantly higher number of inpatients reported pain relief in 2019 than in 2011. Moreover, the number of inpatients with untreated pain conditions has dropped significantly during the period. The use of opioids and paracetamol has increased dramatically and the diagnosing and AA treatment of patients with NP have improved considerably. Although, the inpatients of the recent study were generally older and more fragile than in 2011, the prevalence regarding impaired physical and role functioning, fatigue and appetite loss were just as pronounced as in 2011. Therefore, in the future, the staff needs to be upskilled to a higher-level concerning assessment and treatment of debilitating non-pain symptoms as well as a research agenda in these symptoms is urgently needed. Upcoming studies should consider the use of similar baseline and follow-up studies when introducing an SPC service at the hospital. This would be valuable in an implementation design, in which hospitals without palliative care services could be comparators.

Author contribution Jonas Sørensen, Per Sjøgren and Geana Paula Kurita were involved in the conception and design of the study. Jonas Sørensen, Per Sjøgren and Geana Paula Kurita made the analysis plan. Jonas Sørensen, Stine Novrup Clemmensen, Tanja Vibeke Sørensen, and Katja Heinecke collected data. Jonas Sørensen and Geana Paula Kurita made the data analysis. Jonas Sørensen, Per Sjøgren, Stine Novrup Clemmensen, Tanja Vibeke Sørensen, Katja Heinecke and Geana Paula Kurita were involved in the interpretation of the data. Jonas Sørensen, Per Sjøgren and Geana Paula Kurita made the draft manuscript, which was revised and approved by all co-authors.

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Data Availability Data is available upon request and can be given within the approval from the Danish Data Protection Agency (VD-2019–68).

Code availability N/A.

Declarations

Ethics approval and consent to participate Collecting data from consenting inpatients was approved by the Danish Data Protection Agency (VD-2019–68). Non-interventional studies do not require approval from Ethic Committee in Denmark. All patients received oral and written information, and informed consent was obtained from all patients prior to inclusion.

Consent for publication N/A

Conflict of interest The authors declare no competing interests.

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