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Edmonton Classification System for Cancer Pain: Comparison of Pain Classification Features and Pain Intensity across Diverse Palliative Care Settings in Canada

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Abstract

Background: The goal of the Edmonton Classification System for Cancer Pain (ECS-CP) is to create an international classification system for cancer pain. Previous studies reinforce the need for standardized training to ensure consistency across assessors. There is no universally accepted classification for neuropathic pain.
Objectives: Our primary objective was to describe the prevalence of ECS-CP features in a diverse sample of advanced cancer patients, using assessors with standardized training. The secondary objectives were to: (1) determine the prevalence of neuropathic pain using the Neuropathic Pain Special Interest Group (NeuPSIG) criteria and (2) examine the relationship between specific predictors: ECS-CP features, age, Palliative Performance Scale, Morphine Equivalent Daily Dose (MEDD), setting, and pain intensity; and neuropathic pain.
Methods: A total of 1050 adult patients with advanced cancer were recruited from 11 Canadian sites. A clinician completed the ECS-CP and NeuPSIG criteria, and collected additional information including demographics and pain intensity (now). All assessors received standardized training.
Results: Of 1050 evaluable patients, 910 (87%) had cancer pain: nociceptive ($n=626$; 68.8%); neuropathic ($n=227$; 24.9%); incident ($n=329$; 36.2%); psychological distress ($n=209$; 23%); addictive behavior ($n=51$; 5.6%); and normal cognition ($n=639$; 70.2%). The frequencies of ECS-CP features and pain intensity scores varied across sites and settings, with more acute settings having higher frequencies of complex pain features. The overall frequency of neuropathic pain was 24.9%, ranging from 11% (hospices) to 34.2% (palliative outpatient clinic) across settings. Multivariate logistic regression analysis revealed that age <60 years, MEDD ≥19 mg, pain intensity ≥7/10, and incident pain were significant independent predictors of neuropathic pain ($p<0.05$).

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Conclusion: The ECS-CP was able to detect salient pain features across settings. Furthermore, the frequencies of neuropathic pain utilizing the NeuPSIG criteria fits within the lower-end of literature estimates (13%–40%). Further research is warranted to validate the NeuPSIG criteria in cancer pain.

Keywords: cancer pain; Edmonton Classification System for Cancer Pain; NeuPSIG criteria; neuropathic pain; pain assessment; pain intensity

Introduction

STANDARDIZED APPROACHES for assessing and classifying cancer pain, similar to the Tumor–Nodes–Metastases staging system in Oncology are necessary to identify and treat patients with complex pain syndromes.[1] However, the complex, multidimensional nature of cancer pain presents unique challenges for pain classification.

Over the past 30 years, a research program to develop a universally accepted pain classification tool has developed into the Edmonton Classification System for Cancer Pain (ECS-CP).[1–21] The ECS-CP includes five features—pain mechanism, incident pain, psychological distress, addictive behavior, and normal cognition.[1] Although pain intensity is not presently a feature of the ECS-CP, moderate and severe pain intensity at initial assessment has been identified as significant predictors of increased time required to achieve stable pain control and associated with increasing morphine equivalent daily doses (MEDD) and adjuvants.[22]

The European Palliative Care Research Collaborative (EPCRC) agreed that the ECS-CP could effectively evolve into an international classification system for cancer pain; therefore, the ECS-CP was included in a multisite research initiative of the EPCRC.[23] This resulted in a secondary analysis and publication of the prevalence of ECS-CP features and pain intensity in a diverse international sample of advanced cancer patients.[4] Of the 1051 evaluable patients, 1034 underwent ECS-CP assessment, with 670 having cancer pain. The ECS-CP features for all sites were: nociceptive pain ($n=534$, 79.7%); neuropathic pain (Ne) ($n=113$, 16.9%); incident pain ($n=408$, 60.9%); psychological distress ($n=212$, 31.6%); addictive behavior ($n=30$, 4.5%); and normal cognition ($n=616$, 91.9%). The average of pain intensity (now) varied substantially across sites, ranging 1–5 (of 10). Most patients ($n=401$; 69.9%) rated their pain intensity as mild.

Although all sites had detailed written administration guidelines of the ECS-CP, the assessors were not formally trained. Some inconsistency in assessments is inherent in any assessment tool, particularly when involving multiple collaborating sites. Therefore, some of the differences across sites may have been owing to the interpretation of the administration guidelines and definitions. This was a noted area for improvement.

One ECS-CP feature that needs more objective and universal classification is Ne.[24–27] Ne when compared with nociceptive pain is associated with reduced Palliative Performance Scale (PPS), increased MEDD, and pain intensity.[28–30] This suggests that Ne is associated with more complex pain markers than nociceptive pain.

Given that adequate assessments of pain mechanisms are critical to achieving stable pain control,[18,25,31–35] the International Association for the Study of Pain created the Neuropathic Pain Special Interest Group (NeuPSIG) criteria for classifying Ne.[36] This system relies upon clinically apparent criteria: (1) history of relevant neurological lesions or disease; (2) pain distribution neuroanatomically possible; (3) pain is associated with sensory signs in the same neuroanatomically plausible distribution; and (4) diagnostic test confirming a lesion of disease of the somatosensory nervous system explaining the pain. Ne is either ''possible,'' ''probable,'' or ''definite'' if the first two, three, or four criteria are fulfilled, respectively.

This system has been well explored in nonmalignant Ne, largely outperforming screening questionnaires that rely upon qualitative descriptors.[37–41] Given the low inter-rater reliability of these questionnaires, researchers have commented on the ''desperate'' need for a gold standard classification of Ne.[26] Although the NeuPSIG criteria has not been well explored in malignant Ne,[37] it represents a next step toward a systematic, practical, and reproducible classification method.[24,25]

Owing to the limitations of the EPCRC study and need for more objective Ne classification, we designed a similar study to the EPCRC in the Canadian context, with the addition of the NeuPSIG criteria. Our primary objective was to describe the prevalence of ECS-CP features in a diverse sample of advanced cancer patients. We hypothesized that the frequencies of pain classification features and pain intensity scores would vary across sites and settings, with more acute palliative care settings having more complex pain features than less acute settings. We also had two secondary objectives concerning Ne: (1) to examine the prevalence of Ne using the NeuPSIG criteria and (2) to examine the relationship between specific predictors (ECS-CP features, age, PPS, MEDD, settings, and pain intensity) and pain mechanism (Ne vs. non-Ne).

Methods

Study design

We enlisted palliative care specialists from 11 sites across Canada; these sites represented five settings of specialist palliative care services: hospital palliative consult service (acute care) ($n=273$), palliative outpatient clinic (clinic) ($n=374$), hospital palliative care unit (PCU) ($n=174$), hospice PCU (hospice) ($n=82$), and palliative homecare (homecare) ($n=7$) (Table 1). A palliative care specialist completed a standard assessment for each patient with cancer referred to their service. The co-principal investigators (R.F., C.N.) and research project manager (V.M.) conducted an online training session to review the use of the ECS-CP, pain intensity assessments, and the NeuPSIG criteria with each of the site collaborators before data collection. The study was conducted between June 2018 and July 2020, with collaborating sites being phased in overtime, based on ethics approval at each site.

TABLE 1. FREQUENCIES (*n*, %) OF COLLABORATING SITES BY SETTING (*n* = 910)

	Setting					
Location	*Hospice PCU,* n *(%)*	*Hospital PCU,* n *(%)*	*Hospital palliative consult,* n *(%)*	*Palliative outpatient,* n *(%)*	*Palliative homecare,* n *(%)*	*Total,* n *(%)*
Edmonton outpatient	—	—	—	98 (26)	—	98 (11)
Calgary (TBCC)	—	—	—	97 (26)	—	97 (11)
Vancouver PSMPC	—	—	—	92 (25)	—	92 (10)
Edmonton TPCU	—	91 (52)	—	—	—	91 (10)
Kingston CCSEO	—	—	—	85 (23)	—	85 (9)
Edmonton community	—	—	83 (30)	—	—	83 (9)
Kingston Hospital	—	—	83 (30)	—	—	83 (9)
Ottawa Hôpital Élisabeth	—	83 (48)	—	—	—	83 (9)
Edmonton Acute	—	—	82 (30)	—	—	82 (9)
Montreal Site	82 (100)	—	—	—	—	82 (9)
Yukon Hospital	—	—	25 (10)	2 (1)	7 (100)	34 (4)
Total	82 (9)	174 (19)	273 (30)	374 (41)	7 (1)	910

Site details:
(1) CCI Pain & Symptom Clinic (Edmonton) (*n* = 100).
(2) TBCC—Outpatient cancer center pain/symptom management consult service (Calgary) (*n* = 100).
(3) Vancouver Centre of BC Cancer: PSMPC (*n* = 100).
(4) TPCU (Edmonton) (*n* = 100).
(5) CCSEO palliative care clinic (Kingston) (*n* = 100).
(6) Community Consults—hospital only (Edmonton) (*n* = 100).
(7) Kingston General Hospital (Acute Care) (Kingston) (*n* = 100).
(8) Hopital Élisabeth-Bruyere Hospital PCU (Ottawa) (*n* = 100).
(9) Hospital Consults (Acute Care) (Edmonton) (*n* = 100).
(10) Montreal Institute for Palliative Care/Teresa Dellar Palliative Care Residence (*n* = 100).
(11) Yukon Hospital (*n* = 38); Yukon Hospital Outpatient (*n* = 2); Yukon home and LTC (*n* = 10).
CCI, Cross Cancer Institute; CCSEO, Cancer Centre of South Eastern Ontario; LTC, long-term care; PCU, palliative care unit; PSMPC, Pain & Symptom/Palliative Care Clinic; TBCC, Tom Baker Cancer Center; TPCU, Tertiary Palliative Care Unit.

Sample

The primary inclusion criteria were cancer patients older than 17 years, who had been referred to a palliative care service. The collaborators at each site screened 100 consecutive patients using the inclusion criteria. The exception was the Yukon site, which screened 50 patients, owing to recruitment challenges. Only patients with pain directly or indirectly related to the cancer were included in the ECS-CP assessment. In total 1050 patients were screened.

Data collection

Data were documented using REDCap, a secure web application for building and managing online surveys and databases—accessed through a local institutional partner at the University of Alberta. The research project manager and co-principal investigators reviewed each database for data cleaning.

Demographics

Age, gender, cancer diagnosis, and setting were documented.

Edmonton Classification System for Cancer Pain

The ECS-CP has five features: mechanism of pain, and presence/absence of incident pain, psychological distress, addictive behavior, and cognitive function. Detailed descriptions for using the definitions in a clinical context are included in the Quick User Guide and Administration Manual.[3,4]

For each feature, there are several possible options. Only one appropriate response is selected. If the patient does not have any cancer pain, (i.e., ''No'' under mechanism of pain), then no further assessment is required. Otherwise, an in-depth assessment is warranted. A pain classification profile is then assigned to each patient, using the following lettering system: N (mechanism of pain), I (incident pain), P (psychological distress), A (addictive behavior), C (cognitive function).

NeuPSIG criteria

The NeuPSIG criteria rely upon four clinically apparent criteria. As they are increasingly satisfied, the clinician increases their diagnostic confidence by classifying the patient as having possible, probable, or definite Ne, respectively (as defined in the Introduction section). The NeuPSIG criteria will be used to denote Ne here.

Pain intensity

Patients rated their pain intensity (now) using the Pain Numerical Rating Scale; this consists of an 11-item scale, ranging from 0 (no pain) to 10 (worst possible pain). Pain assessments are routine clinical practice in the collaborating sites. If patients were unable to rate pain owing to cognitive impairment, then this information was completed with assistance (e.g., clinician and/or family) and recorded as proxy data.

Data analysis

Data were analyzed using descriptive statistics (frequencies and proportions for categorical variables; mean and standard

deviations were reported for continuous variables) to determine the prevalence of ECS-CP features, PI, and Ne (using NeuPSIG criteria) in the total sample, collaborating sites, and setting. The prevalence rates of ECS-CP features across sites and settings were compared using chi-square test. The continuous PI ratings were combined to generate three classically defined categories: mild (0–3), moderate (4–6), and severe (7–10).[16,42]

Binary logistic regression analyses determined the factors associated with the outcome variable, pain mechanism (Ne vs. non-Ne). Univariate logistic regression analysis was performed and factors significant at $p < 0.10$ level were included in the multivariate models. A series of multivariate analyses were conducted. The final model was chosen using variables significant at $p < 0.05$ and clinically relevant variables. The model providing best prediction probability was chosen, in which Ne was categorized as either ''possible/probable/definite'' or ''probable/definite.'' The independent variables were ECS-CP features (yes vs. no), age (<60 vs. ≥60), PPS (>40% vs. ≤40%), MEDD (≥19 vs. <19 mg), setting (hospice, acute care, home care, clinic, vs. PCU), and pain intensity (score 4–6, 7–10 vs. 0–3). The cutpoint of MEDD was determined using receiver operating curve method, and the cutpoint with high sensitivity and specificity value was chosen for dichotomizing MEDD value. The odds ratio and corresponding 95% confidence intervals (CIs) were reported, using a p-value <0.05. SPSS version 25 was used to perform all statistical analysis.

Ethical considerations

Ethical approval was obtained from the appropriate health research ethics and scientific boards at each site. Informed consent was not obtained from patients, as we were collecting clinical data that were routinely documented in all services. In addition, to ensure generalizability of this pain classification system, it was important to include all who met the eligibility criteria. Many eligible patients were cognitively impaired and not able to provide consent. The local ethics boards in Alberta and internationally have previously approved a more complicated international validation study protocol, for which patient consent was not required.[1]

Training

A series of investigator meetings and training sessions were held with the collaborating sites. An initial videoconference explained the purpose of the study and specific instructions on completing the ECS-CP and other variables. Regular communication via e-mail updates of study progress and clarification of uncertainties were managed from the organizing center in Edmonton. Site collaborators were provided with study documents, including the ECS-CP manual and Quick User Guide.[3,4]

Results

Participant characteristics

A total of 1050 cases were included in the description of participant characteristics where 910 (87%) had cancer pain. Table 2 provides a summary of participant characteristics ($n = 1050$). Most patients were older than 60 years (median age, 68 years; with range, 20–102), and with a median PPS of 50% (range, 10–100).

Table 2. Patient Characteristics ($n = 1050$)

Characteristic	*Median*	*Mean*	*SD*	*Range*
Age	68.0	67.2	13.7	20–102
Performance status (PPS)	50.0	50.5	17.3	10–100
	Freq., n *(%)*			
Gender—Female	505 (48)			
Primary cancer diagnosis				
Gastrointestinal	277 (26.4)			
Respiratory system	229 (21.8)			
Female genital organs	84 (8.0)			
Breast	78 (7.4)			
Hematopoietic	75 (7.1)			
Male genital organs	59 (5.6)			
Head and neck	57 (5.4)			
Urinary tract	52 (5.0)			
Bones and connective tissue	29 (2.8)			
Eye, brain, and other	25 (2.4)			
Other	85 (8.1)			
Type of patient				
Inpatient	638 (60.8)			
Outpatient	412 (39.2)			
Setting				
Palliative outpatient	402 (38.3)			
Hospice palliative consult	338 (32.3)			
Hospital palliative care unit	200 (19.0)			
Hospice palliative care unit	100 (9.5)			
Palliative homecare	10 (1.0)			
Mechanism of pain				
Pain syndrome (Ne, Nc, or Nx)	910 (87.0)			
No pain syndrome (No.)	140 (13.0)			

PPS, Palliative Performance Scale; SD, standard deviation.

Frequencies of ECS-CP features

Table 3 summarizes the frequencies of ECS-CP features across all settings (910): nociceptive pain ($n = 626$; 68.8%); Ne ($n = 227$; 24.9%); incident pain ($n = 329$; 36.2%); psychological distress ($n = 209$; 23.0%); addictive behavior ($n = 51$; 5.6%); and normal cognition ($n = 639$; 70.2%). There was considerable variability in frequencies of ECS-CP features across settings. The most consistent scores (i.e., smallest range) were for addictive behavior (0%–14.4%). In contrast, the widest range was for normal cognition (50.0%–87.2%) and incident pain (29.3%–71.4%). These differences across settings were statistically significant for each feature, as detailed in Table 3.

Pain intensity

Figures 1 and 2 illustrate the variability of pain intensity (now) across sites and settings, respectively, using box plots. For Figure 1, median pain intensity ranged from 3 (Montreal site hospice and Ottawa's Hôpital Élisabeth PCU) to 6 (Calgary's TBCC and Edmonton's Outpatient clinics). The 95% CI varied for each site, with the smallest interval for Edmonton's Community acute care (2–5), and the largest interval for Ottawa's Hôpital Élisabeth PCU (0–6).

TABLE 3. FREQUENCY DISTRIBUTION (*n*, %) OF PAIN CLASSIFICATION FEATURES ACROSS FIVE SETTINGS (*n* = 910)

Pain feature	*Classification code*	*Hospice PCU,* n *(%)*	*Hospital PCU,* n *(%)*	*Hospital palliative consult,* n *(%)*	*Palliative outpatient,* n *(%)*	*Palliative homecare,* n *(%)*	*All sites,* n *(%)*	p
Nociceptive pain	Nc	67 (81.7)	90 (51.7)	223 (81.7)	240 (64.2)	6 (85.7)	626 (68.8)	0.000
Neuropathic pain	Ne	9 (11.0)	53 (30.5)	36 (13.2)	128 (34.2)	1 (14.3)	227 (24.9)	0.000
Incident pain	Ii	30 (36.6)	55 (31.6)	80 (29.3)	159 (42.5)	5 (71.4)	329 (36.2)	0.000
Psychological distress	Pp	24 (29.3)	41 (23.6)	60 (22.0)	84 (22.5)	0 (0)	209 (23.0)	0.025
Addictive behavior	Aa	0 (0)	25 (14.4)	8 (2.9)	18 (4.8)	0 (0)	51 (5.6)	0.000
Cognition (normal)	Co	43 (52.4)	87 (50.0)	178 (65.2)	326 (87.2)	5 (71.4)	639 (70.2)	0.000

Range in frequencies across all five settings. Patient able to provide accurate present and past pain history unimpaired.

Aa, addictive behavior present; Co, no impairment; Nc, any nociceptive combination of visceral and/or bone or soft tissue pain; Ne, neuropathic pain syndrome with or without any combination of nociceptive pain; Ii, incident pain present; Pp, psychological distress present.

As illustrated in Figure 2, there is considerable variability in median pain intensity, with overlapping interquartile range and 95% CIs. The median pain intensity ranged from 3 with homecare and hospice, 4 with acute care and PCU, and 5 with clinics.

When examining the pain intensity categories across sites, the frequency of mild, moderate, and severe were 348 (38.2%), 315 (34.6%), and 247 (27.1%) respectively.

Neuropathic pain

Of the 910 patients with cancer pain, the frequency for Ne across all sites was 227 (24.9%). This frequency also varied by site ranging from 11% for Montreal site hospice to 43.5% for Vancouver's Pain & Symptom/Palliative Care Clinic (PSMPC) (Table 4).

Figure 3 illustrates the frequencies of pain mechanisms across settings. The frequencies of Ne were highest in clinic (34.2%) and PCUs (30.5%). Conversely, the lowest frequencies were in hospice (11%) and acute care (13.2%). Among the 227/910 cases with Ne, the frequency of possible, probable, and definite Ne, as classified by the NeuPSIG criteria was 30%, 31%, and 39%, respectively.

The final multivariate logistic regression analysis included variables that were significant ($p < 0.05$) to predict Ne (Table 5). Younger age, higher MEDD, severe pain intensity, and incident pain were predictors of Ne. The frequency of cases for which Ne was predicted using these four variables was higher when only probable/definite Ne were included in the categorization of Ne compared with a less conservative categorization of possible/probable/definite Ne (i.e., 81.9% vs. 74.5%).

Discussion

Main findings

Most patients (86.6%) in this study had cancer pain, with relatively even frequencies of pain intensity: mild (38.2%), moderate (34.6%), and severe (27.1%). The predominant pain mechanism was nociceptive (68.8%). Nearly one-third had incident pain (36.2%), and one-quarter had psychological distress (23.0%). Most had normal cognition (70.2%), and the least frequent feature was addictive behavior (5.6%). These frequencies largely differ from the last multicenter study analyzing the frequency of ECS-CP features in an international sample

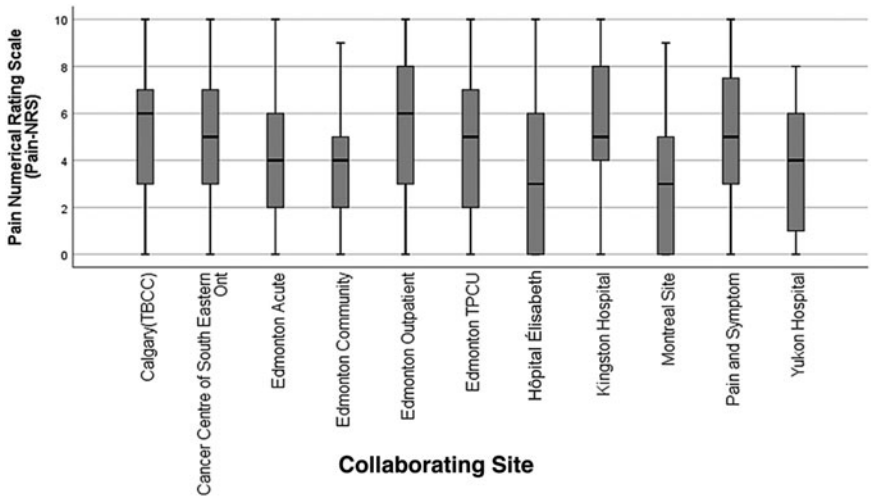

FIG. 1. Box plots of pain intensity (rated right now) by collaborating site (*n* = 910).

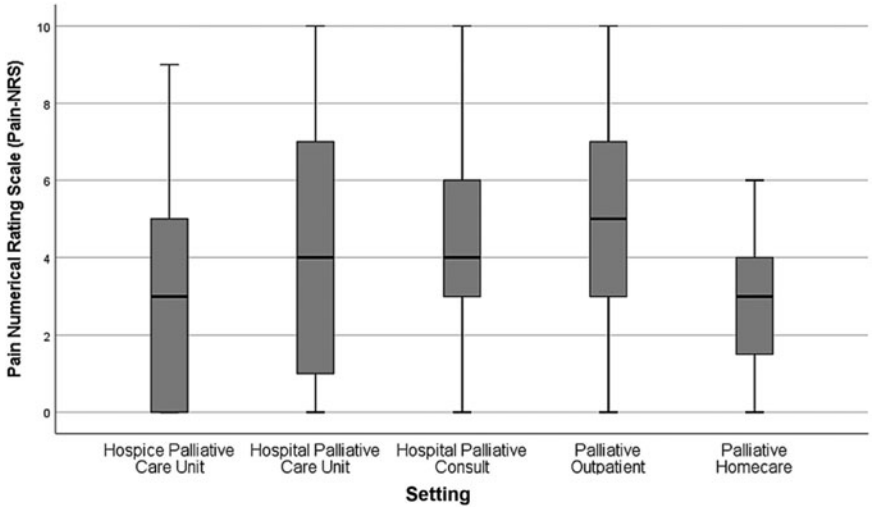

FIG. 2. Box plots of pain intensity (rated right now) by setting ($n=910$).

(Canada, Australia, Europe, and Norway) of advanced cancer patients conducted by the EPCRC.[4] There, only two-thirds of patients had cancer pain and the majority had mild pain intensity (69.9%).

Meanwhile, there were higher frequencies of psychological distress (31.6%), incident pain (60.9%), nociceptive pain (79.7%), and normal cognition (91.9%). Addictive behavior however had a similar frequency (4.5%). These variations may reflect the differences in referral criteria between sites. Canadian centers may refer to palliative care later in the disease trajectory where more frequent, intense, and Ne may be prevalent, whereas earlier referrals that may also be centered in psychosocial support could explain the higher psychological distress frequency. The higher incident pain frequency is intriguing. The EPCRC study had a higher proportion of clinic patients than our study (57% vs. 41%), which is the setting with the highest incident pain frequency (42.5%). However, even that frequency of 42.5% is below the 60.9% recorded in the EPCRC study. The normal cognition variation is best explained by the requirement for patient consent to collect data in the EPCRC study, therefore, necessitating intact cognition. Of course, these variations may also be explained by cultural and socioeconomic differences between sites, and the lack of formal standardized training in the EPCRC study.

Table 4. Frequency Distribution (*n*, %) of Pain Mechanism by Site for Patients with a Pain Syndrome ($n=910$)

	Non-neuropathic pain (Nc/Nx) (n = *683*)		*Neuropathic pain (Ne)* (n = *227*)	
Site	N	%	n	%
Vancouver PSMPC	52	56.5	40	43.5
Calgary TBCC	61	62.9	36	37.1
Edmonton TPCU	63	69.2	28	30.8
Kingston CCSEO	59	69.4	26	30.6
Ottawa Hôpital Élisabeth	58	69.9	25	30.1
Edmonton Outpatient	72	73.5	26	26.5
Yukon Hospital	29	85.3	5	14.7
Edmonton Community	72	86.7	11	13.3
Kingston Hospital	72	86.7	11	13.3
Edmonton Acute	72	87.8	10	12.2
Montreal Site	73	89.0	9	11.0
Total	683	75.1	227	24.9

Nc, nociceptive pain; Nx, insufficient information to classify.

In addition, the ECS-CP detects salient differences of pain features across settings. Our study showed that Ne (denoted using the NeuPSIG criteria) and incident pain were most frequent in clinic with a prevalence of 34.2% and 42.5%, respectively. The highest frequency of incident pain was in homecare (71.4%); however, this is challenging to interpret with only five patients in this category. Furthermore, psychological distress (29.3%), addictive behavior (14.4%), and normal cognition (87.2%) were most frequent in hospice, PCU, and clinic, respectively.

Pain intensity also varied between sites, and clinics had the highest median pain intensity (5/10), followed by the PCUs and acute care (4/10). Homecare and hospice had the lowest median value (3/10).

These measures of variability in pain classification features across sites may be related to the types of patients admitted to these sites and variation in interpretation of the ECS-CP definitions and guidelines. Of note, patients with more complex pain syndromes, such as having Ne and higher pain intensity, may be more likely referred to clinic and PCU, respectively. Furthermore, the higher rate of psychological distress and impaired cognition in hospice and PCU, and addictive behavior in PCU detected, may justify their requirement for well-resourced interdisciplinary support and adjuvants.[12,43]

In addition, the NeuPSIG criteria detected differences in Ne prevalence between sites. Clinic and PCU programs had higher Ne prevalence at 34.2% and 30.5%, respectively. The overall prevalence of 17%–25% (definite/probable vs. definite/probable/possible, respectively) fits within the lower

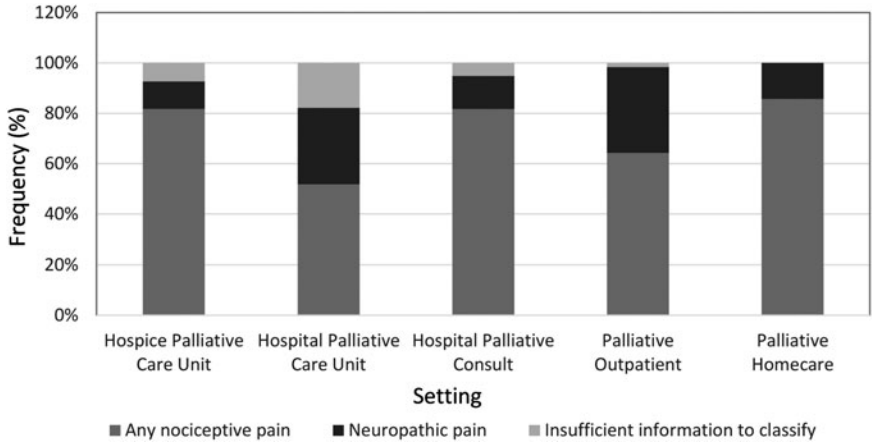

FIG. 3. Frequency distribution (%) of pain mechanism by setting for patients with a pain syndrome ($n = 910$).

TABLE 5. MULTIVARIATE LOGISTIC REGRESSION ANALYSIS OF PREDICTORS OF NEUROPATHIC PAIN (POSSIBLE, PROBABLE, AND DEFINITE[a]; PROBABLE AND DEFINITE ONLY[b])—($n = 910$)

	Possible/probable/definite[a]		*Probable/definite*[b]	
Variables	*Odds ratio*	p	*Odds ratio*	p
Age, years				
≥60	1		1	
<60	1.804	0.001	1.908	0.001
PPS, %				
≤40	1		1	
>40	1.023	0.923	0.997	0.991
MEDD, mg				
<19	1		1	
≥19	1.564	0.009	1.449	0.051
Incident pain				
Io or Ix	1		1	
Ii (present)	1.744	0.001	1.635	0.009
Psych distress				
Po or Px	1		1	
Pp	1.286	0.196	1.133	0.564
Addictive behavior				
Ao or Ax	1		1	
Aa (present)	1.449	0.258	1.341	0.407
Cognition				
Ci or Cu	1		1	
Co (normal)	1.353	0.165	1.302	0.286
Setting				
Hospice	1		1	
PCU	2.592	0.021	1.690	0.258
Acute care	0.962	0.925	0.883	0.788
Clinic	2.758	0.013	2.076	0.107
Homecare	1.268	0.838	1.653	0.669
Pain intensity				
0–3	1		1	
4–6	1.523	0.043	1.440	0.128
7–10	1.917	0.003	2.095	0.003

All variables significant at univariate analysis ($p < 0.10$) included for multivariate analysis.

[a]Overall percentage of possible/probable/definite = 74.5%.

[b]Overall percentage of probable/definite = 81.9%

Ao or Ax, addictive behavior absent or insufficient information to classify; Ci or Cu, partial or complete cognitive impairment; Co, normal cognition; Io or Ix, incident pain absent or insufficient information to classify; MEDD, morphine equivalent daily doses.

end of literature estimates of 13%–40%,[25,26,30,44,45] suggesting that these criteria provide a more conservative estimate of Ne.

Using multivariate analysis, Ne was associated with other features of complex pain syndromes such as younger age, higher MEDD, severe pain intensity, and incident pain. About 81.8%–82.5% of patients meeting the probable/definite Ne criteria had these four features, compared with 74.5%–75.2% when possible Ne was included. Therefore, the probable/definite Ne categorization resulted in a model that reflects clinical characteristics associated with Ne.

Limitations of the study

Most patients were recruited primarily from hospital and clinic. Smaller numbers were recruited in other settings, especially homecare, which made interpretation of their results challenging. Furthermore, although clinicians underwent formal training on applying the ECS-CP, its effect on inter-rater reliability was not measured. Therefore, any inconsistency in the interpretation of these assessment tools is unknown; this can be compounded with multiple data collection sites in diverse health systems.

Moreover, although the NeuPSIG criteria may be the most systematic, practical, and reproducible method for classifying malignant Ne, they have yet to be formally validated. Furthermore, its requirement for history of a neurological lesion precludes diagnosis for those without access to these investigations. Finally, another feature of the ECS-CP that may benefit from review is addiction, which was first accepted and defined in the validation study in 2005.[5] This is arguably becoming outdated with the increasing use of the term ''Substance Use Disorder.''[46]

What this study adds

This is the first multicenter study assessing the ECS-CP features across multiple settings, where each assessor received standardized training. This additional training may enhance inter-rater reliability to promote high-quality data.[47] Furthermore, this is the first study wherein the NeuPSIG criteria were used to classify Ne within the ECS-CP. The

simplicity and utility in classifying Ne shown here justifies its use within the ECS-CP and as a tool in general.

Conclusion

The ECS-CP detects salient differences of pain features across different settings. These differences help clarify the unique patient characteristics and needs of each site. Furthermore, the diverse range of features and pain intensity likely reflects differences in patient complexity, referral criteria, and disease trajectory. A standard cancer pain classification system such as the ECS-CP could eventually enable clinicians to better assess and manage cancer pain, compare research results, and allocate resources.

The NeuPSIG criteria provide a feasible classification of Ne and detects prevalence estimates that are similar to other studies. Moreover, relying on the classification of definite or probable Ne may provide a more conservative diagnosis of Ne. Furthermore, this classification appears to be associated with other features of complex pain syndromes such as a higher MEDD, younger age, incident pain, and severe pain intensity. Therefore, the NeuPSIG criteria may be considered for the diagnosis of Ne within the ECS-CP; however, further research is warranted to validate the accuracy of the NeuPSIG criteria applied to cancer pain.

Authors' Contributions

The authors confirm contribution to the article as follows: study conception and design: R.F. and C.N.; data collection: S.B., J.D., L.G., P.H., L.H., A.K., and P.L.; analysis and interpretation of results: M.B., R.F., C.N., V.M., S.G.; draft article preparation: M.B., C.N., R.F., V.M., S.G. All authors reviewed the results and approved the final version of the article.

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