

## Comparison of Pain Quality Descriptors in Cancer Patients with Nociceptive and Neuropathic Pain

KYRIAKI MYSTAKIDOU<sup>1</sup>, EFI PARPA<sup>1</sup>, ELENI TSILIKA<sup>1</sup>, MARIA PATHIAKI<sup>1</sup>,  
ANTONIS GALANOS<sup>1</sup> and LAMBROS VLAHOS<sup>2</sup>

<sup>1</sup>*Pain Relief and Palliative Care Unit, Department of Radiology, Areteion Hospital,  
School of Medicine, University of Athens, Korinthias St., Athens;*

<sup>2</sup>*Radiology Department, Areteion Hospital, University of Athens, School of Medicine, Vas. Sofias, Athens, Greece*

**Abstract.** *Background: The aim of this study was to explore the differences in the descriptors for neuropathic and nociceptive pain in cancer patients. Patients and Methods: One hundred and eighty-six cancer patients who participated in the study completed the Greek version of the McGill Pain Questionnaire (G-MPQ) for the assessment of their pain quality. Results: Significant differences were found between type of pain in all G-MPQ classes. Statistically significant associations were found between Present Pain Intensity and type of pain ( $p=0.002$ ). Multivariate logistic regression analyses showed that patients who selected the descriptors "pricking" and "annoying" were 2.64 times and 2.2 times, respectively, more likely to experience nociceptive rather than neuropathic pain ( $p=0.020$  and  $p=0.015$ , respectively). Further analysis showed that sensory seemed to be the most significant indicator for type of pain (95%, CI: 0.911-0.974,  $p<0.001$ ). Conclusion: Sensory quality and some of pain descriptors may differentiate neuropathic from nociceptive pain in cancer patients.*

Cancer-related pain has been estimated to afflict 55-95% of patients at advanced stages (1). Cancer pain is a complex and subjective experience that influences a wide variety of nervous system functions including sensory affective and cognitive components (2, 3). The standard definition for pain is that it is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage", which has been defined by the International Association for the Study

of Pain (IASP) (4). Pain tends to create many other problems, such as chronic fatigue, sleep disturbance, inability to participate in activities, compromised immune function and mood disorder. An awareness of how pain contributes to suffering will enable physicians to prevent it from happening (5, 6). It has also been estimated that undertreatment of cancer pain contributes to a poor quality of life in patients with cancer (7). One explanation of the inadequate management of cancer pain is related to an inadequate pain assessment at the end of life (8). Numerous surveys have observed that the prevalence of unrelieved pain is greater than 50% (9-14).

Description of a pain condition and the patients' reported pain intensity can provide valuable information for diagnosis and for the establishment of a physical therapy program that will improve the patient's condition (15). It is well-known that pain is difficult to describe; patients often do not seem to find the appropriate words to do so. In addition, multiple pain complaints are common among cancer patients and somatic and neuropathic pain frequently coexists (16, 17). For these reasons, pain assessment and control are some of the most important goals of cancer care.

Among the variety of measurements for assessing pain intensity (18, 19), the McGill Pain Questionnaire (MPQ) (20) was chosen for its validity and reliability. It was proven to be a sensitive instrument in evaluating the quality of pain in patients with cancer and other chronic diseases (20-22).

Research studies indicated that patients with certain pain syndromes frequently select certain words to describe their pain (23, 24). It was reported that patients with cancer pain describe their pain as shooting, sharp, gnawing, burning or heavy (25, 26). Several studies have assessed the ability of qualitative descriptors to distinguish cancer pain according to etiological classification (24, 27). Descriptions of pain quality are useful to characterize neuropathic, nociceptive or combined pain. Neuropathic pain is often described as: lancinating, burning, pressure or vice-like, electric, shock-like, pricking and tingling (24, 28). Nociceptive pain is

*Correspondence to:* Kyriaki Mystakidou, Pain Relief and Palliative Care Unit, Department of Radiology, Areteion Hospital, School of Medicine, University of Athens, 27 Korinthias Str., 115 26 Athens, Greece. Tel: +30210 7707669, Fax: +30210 7488437, e-mail: mistakidou@yahoo.com

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usually described in different qualitative terms, such as sharp, aching, throbbing or pressure-like (16). However, the predictive validity of each word in differentiating different cancer types has not been examined adequately.

Recognition of the pathophysiology of pain is essential for clinicians to decide on the appropriate treatment. Thus, differentiating neuropathic from nociceptive pain would be necessary for pain management (25). Therefore, the purpose of this study was: a) to compare cancer pain descriptors as measured from the MPQ in a sample of advanced cancer patients with neuropathic and nociceptive pain; b) to evaluate any significant link between quality of pain and type of pain.

### Patients and Methods

Three hundred and seven cancer patients were referred to the Pain Relief and Palliative Care Unit in Athens, Greece, for pain relief and cancer-related symptoms. Criteria for inclusion in the study were: histologically confirmed malignancy, stages III, IV, age >18, ability to communicate with the health-care professionals and patient informed consent. Patients were excluded if there was a diagnosis of a psychotic illness, or significant cognitive impairment. Although 199 patients satisfied these criteria, 5 (2.5%) patients refused to complete the assessment forms and 8 (4%) did not complete them as they lived too far from Athens. The final sample consisted of 186 cancer patients and their demographic characteristics are shown in Table I. Patients were seen individually either at out-patient clinic or on the wards. A member of the palliative care unit interviewed all patients in order to elicit their medical history including demographic data, prior mental health and current condition. The evaluations were completed in a brief interview. The clinician-rated instrument was that of performance status, measuring the patients' overall physical functioning, as defined by the Eastern Cooperative Oncology Group (ECOG) (0=optimum performance status, 4=worse performance status) (29). Patients with an ECOG performance status score 0-1 were categorized as having "good" performance status, and those with an ECOG performance status score >2 as having "poor" performance status.

The following criteria were used to define the type of pain: A perceived pain with evidence of radiological tissue damage was termed "nociceptive" (30, 31). However, there is also a non-nociceptive pain type which is perceived over an area with identifiable sensory dysfunction without evident tissue damage. This type of pain was termed "neuropathic" pain (30, 32, 33). Finally, "combined pain" is pain in which both nociceptive and neuropathic pain are clearly identifiable (30, 32).

The patients' self-report scale to establish their qualities of pain was the Greek Mc Gill Pain Questionnaire (G-MPQ) (22). If necessary, brief instructions were given on how the questionnaire should be completed while a member of the research team read out the questions when needed. G-MPQ was the standard form of 78 descriptors of pain quality which comprises the second part of the questionnaire (Number of Words Chosen-NWC). It is categorized into 20 groups, representing the four pain rating indices: present rating index-sensory (PRI-S), affective (PRI-A), evaluative (PRI-E), miscellaneous (PRI-M). Four pain rating scores were then added to give the total pain rating index (PRI-T) (21). Pain intensity was measured by a present pain intensity scale (PPI) of the GMPQ, derived from a Likert-type scale ranging from 0 to 5 (0=none, 1=mild, 2=discomforting, 3=distressing,

Table I. Demographic and disease-related patient characteristics.

Characteristics	N	%
Age		
Mean 62.5±11.1 years		Range (25-82)
Years of education		
Mean 11.1±3.6 years		Range (6-16)
Gender		
Male	94	50.5
Female	92	49.5
Diagnosis		
Stomach	22	11.83
Esophageal	14	7.53
Pancreas	17	9.14
Breast	20	10.75
Liver	19	10.22
Colon	17	9.14
Kidney	9	4.84
Lung	12	6.45
Prostate	8	4.30
Bladder	27	14.52
Ovarian	11	5.91
Uterus & Cervix	10	5.38
Family status		
Married	111	59.7
Single	23	12.4
Divorced	33	17.7
Widowed	19	10.2
ECOG score		
0-1	56	30.1
2-3	130	69.9
Metastasis		
No	87	46.8
Yes	99	53.2
Opioids		
Mild	119	64.0
Strong	67	36.0

4=horrible, 5=excruciating). Ethical committee approval and informed consent (from all patients) were obtained.

### Results

*Statistical analysis.* G-MPQ classes were compared between different factors, using the independent samples *t*-test. A multivariate model was used to determine the effect of cancer location, gender, age and ECOG on each PRI class separately. Fisher's exact test was applied to a 2x2 contingency table containing cancer type, gender and age, ECOG and each of the 78 quality word descriptors from the G-MPQ. Logistic regression to assess discriminant ability of the group of all statistically significant words was used. Additional multivariate analysis was used to assess which of the PRI classes are indicators of pain type. The significance level was set at <0.05. Statistical analysis was performed by SPSS v10.00 (Statistical Package for Social Sciences).

Table II. The number of words chosen and the frequency of each selection in patients with nociceptive and neuropathic pain.

Descriptors	Nociceptive (N=79) N (%)	Neuropathic (N=107) N (%)	p-value
<b>Sensory</b>			
Pulsing	11 (13.9)	29 (27.1)	0.047
Pounding	21 (26.6)	15 (14)	0.05
Shooting	29 (36.7)	20 (18.7)	0.001
Pricking	10 (12.7)	30 (28)	0.02
Stabbing	7 (8.9)	1 (0.9)	0.02
Sharp	28 (35.4)	57 (53.3)	0.023
Lacerating	31 (39.2)	19 (17.8)	0.002
Crushing	24 (30.4)	15 (14)	0.011
Wrenching	15 (19)	9 (8.4)	0.05
Stinging	22 (27.8)	12 (11.2)	0.007
Hurting	20 (25.3)	44 (41.1)	0.037
Heavy	33 (41.8)	25 (23.4)	0.012
Splitting	20 (25.3)	8 (7.5)	0.002
<b>Affective</b>			
Tiring	32 (40.5)	60 (56.1)	0.05
Exhausting	34 (43)	22 (20.6)	0.002
Suffocating	24 (30.4)	15 (14)	0.011
Punishing	31 (39.2)	58 (54.2)	0.05
Wretched	39 (49.4)	68 (63.6)	0.05
Blinding	16 (20.3)	6 (5.6)	0.005
<b>Evaluative</b>			
Annoying	24 (30.4)	57 (53.3)	0.003
Unbearable	30 (38)	16 (15)	0.0005
<b>Miscellaneous</b>			
Piercing	32 (40.5)	25 (23.4)	0.019
Tearing	15 (19)	7 (6.5)	0.017
Torturing	27 (34.2)	18 (16.8)	0.01

Table III. Comparison between demographic clinical characteristics, PPI and PRI classes with type of pain.

	Nociceptive N (%)	Neuropathic N (%)	p-value
<b>Gender</b>			
Male	34 (37.0%)	58 (63.0%)	N.S
Female	45 (48.0%)	49 (52.0%)	
<b>ECOG</b>			
0-1	24 (43.0%)	32 (57.0%)	N.S
2-3	55 (42.3%)	49 (57.7%)	
<b>Metastasis</b>			
No	32 (36.8%)	55 (63.2%)	N.S
Yes	47 (47.5%)	52 (52.5%)	
<b>Opioids</b>			
Mild	55 (46.2%)	64 (53.8%)	N.S
Strong	24 (35.8%)	43 (64.2%)	
<b>PPI</b>			
None-Mild-Discomforting	52 (36.4%)	91 (63.6%)	0.002
Distressing-Horrible-Excruciating	27 (64.3%)	15 (35.7%)	
	Mean±SD	Mean±SD	
Age	62.92±11.59	62.20±10.74	N.S
Years of Education	11.19±3.81	11.00±3.44	N.S
<b>PRI</b>			
<b>Classes</b>			
Sensory	22.92±10.3	17.86±7.9	0.0005
Affective	6.39±4.3	4.71±3.4	0.003
Evaluative	2.59±2.1	1.70±1.6	0.001
Miscellaneous	6.99±4.7	5.10±3.6	0.002

Univariate analysis. PPI was reported as none (10%), mild (29%), discomforting (39%), distressing (16%), horrible (3%) and excruciating (3%). None, mild and discomforting were indicated as 0-2 for statistical purpose while distressing, horrible and excruciating were indicated as 3-5.

Out of 186 patients, 69 (37.1%) reported nociceptive pain, 101 (54.3%) neuropathic, while 16 patients (8.6%) reported combined pain. The latter, for the final statistical analyses were reclassified as nociceptive (10 patients, 5.4%) or neuropathic (6 patients, 3.2%).

In the present work, statistically significant differences were found between patients with none-mild-discomforting pain (PPI 0-2) and those with distressing-horrible-excruciating pain (PPI 3-5), in all PRI classes ( $p < 0.0005$ ). Higher scores were found in PRI-sensory in patients with distressing-horrible-excruciating pain than in patients with none-mild-discomforting pain ( $31.69 \pm 7.07$  vs.  $16.68 \pm 6.86$ ,  $p < 0.0005$ ).

Demographic and clinical characteristics were analyzed to determine whether they were associated with neuropathic or nociceptive pain (Table II). There were no differences in type of pain with regard to gender, ECOG, metastasis,

opioids or educational level. Concerning PPI, patients with nociceptive pain revealed more distressing-horrible or excruciating pain than those with neuropathic pain ( $p = 0.002$ ). Similarly, there were statistically significant differences between nociceptive and neuropathic pain in PRI-S ( $p < 0.0005$ ), PRI-A ( $p = 0.003$ ), PRI-E and PRI-M ( $p = 0.001$  and  $p = 0.002$ , respectively).

Additional univariate analyses regarding the NWC revealed that out of 78 descriptors, 24 words differed statistically by pain type (Table III). Statistically significant differences were found for "shooting", which is chosen respectively by 36.7% and 18.7% of the patients with nociceptive and neuropathic pain ( $p = 0.001$ ), for "lacerating" chosen by 39.2% and 17.8% respectively ( $p = 0.002$ ), "heavy" chosen by 41.8% and 23.4% ( $p = 0.012$ ) and for "splitting" which was selected by 25.3% of the patients with nociceptive vs. 7.5% with neuropathic pain ( $p = 0.002$ ). Six affective words were significantly different between the two groups and two descriptors from evaluative class; from the miscellaneous class, "piercing", "tearing" and "torturing" differed statistically by pain type ( $p = 0.019$ ,  $p = 0.017$ ,  $p = 0.01$  respectively).

*Multivariate analyses.* The independent predictors included in the multiple regression (forward method) were those of the preceding univariate analysis in order to examine which of the selected descriptors of the MPQ could predict the type of pain. When 24 significant descriptors was used, logistic regression indicated that only three descriptors were remained in the model ( $\chi^2=23.46, p<0.0005$ ); patients who selected the word "pricking" were 2.6 times more likely to have nociceptive than neuropathic pain (95% CI: 1.166-5.977,  $p=0.020$ ). Similarly, patients who selected the word "annoying" were 2.2 times more likely to have nociceptive than neuropathic pain (95%, CI: 1.167-4.185,  $p=0.015$ ), while those who chose the word "exhausting" were 0.387 times less likely (-1.3%) to have nociceptive than neuropathic pain (95%, CI: 0.197-0.763,  $p=0.008$ ). Further logistic regression analysis was also used in order to examine which of the PRI classes and PPI could predict the type of pain. Therefore, only PRI-Sensory is a significant indicator for type of pain (95%, CI: 0.911-0.974,  $p<0.001$ ).

## Discussion

Several studies revealed that the use of pain assessment tools could improve health care professionals' clinical practice and reduce patient discomfort (9, 34). It is noteworthy that the quality descriptors of pain are most frequently associated with the type of pain or pain syndromes (26). Nevertheless, a limited number of studies compared the association between quality of pain and type of pain (22, 23, 35).

In the current study, statistically significant differences were found between patients with none-mild-discomforting pain (PPI 0-2) and those with distressing-horrible-excruciating pain (PPI 3-5) in all PRI classes ( $p<0.0005$ ) in patients with more intense pain. Higher scores were revealed in PRI-sensory (PPI 3-5), than in patients with less intense pain, consistent with Sella *et al.* (1). No significant associations were observed between type of pain and ECOG, metastasis, opioids or education. Similarly, there were no statistically significant associations between age and gender with type of pain, consistent with Wilkie *et al.* (25). According to PPI, patients with nociceptive pain reported more intense pain (distressing-horrible-excruciating) than those with neuropathic pain ( $p=0.002$ ). Furthermore, significant differences were found between neuropathic and nociceptive pain in all PRI classes. It should be noted that patients with nociceptive pain selected more words from PRI-sensory than those with neuropathic pain ( $p<0.0005$ ).

Some interesting observations arose from the selection of descriptors; 24 out of 78 descriptors differed statistically by pain type. Patients with nociceptive pain selected in a much greater frequency more intense words to describe their pain quality than patients with neuropathic pain. More statistically significant differences were found in descriptors from the

sensory class than in those from the other classes. This may be due to the fact that cancer pain yielded a high value on the sensory dimension and Greek cancer patients may differ from Americans and British in their use of affect to describe pain (1, 21, 22, 36).

Additionally, it was found that descriptors used by cancer patients differ from those chosen by chronic pain patients (7, 37). "Shooting", "crushing", "exhausting", "suffocating" and "piercing" were selected more often from the participants with nociceptive pain whereas "sharp", "hurting" "tiring", "wretched" and "annoying" were selected more often from patients with neuropathic pain. The selection of "pricking" and "punishing" are consistent with previous descriptors of neuropathic pain (23, 26), while "heavy", "lacerating" and "stinging" related to nociceptive pain is supported by previous findings (24, 26). However, descriptors such as "burning", "lancinating", "itching", "cold", "flashing", which are most frequently associated with neuropathic pain in the literature, were not found to be statistically significant in our study, in agreement with findings of Wilkie (16, 26).

In the multiple logistic regression analysis, statistically significant associations were found between only three of the selected words and type of pain. Specifically, patients who selected the descriptor "pricking" were 2.6 times more likely to experience nociceptive than neuropathic pain and those who chose the word "annoying" were 2.2 times more likely to suffer from nociceptive than neuropathic pain. Additionally, patients who described their pain as "exhausting" were 61.3% less likely to have nociceptive than neuropathic pain.

Although univariate analysis revealed significant associations between type of pain with all PRI classes and present pain intensity, further multivariate analysis indicated that only sensory seemed to be a significant indicator for type of pain. More specifically, patients with sensory pain were 5.8% less likely to have nociceptive than neuropathic pain. This might stem from the fact that affective words are less frequently used by neuropathic pain patients as affective disturbance in these patients is less important than in patients with sensory pain (24).

In conclusion, the results of the present study demonstrate that only some pain descriptors and sensory quality might characterize type of pain, supporting the notion that pain assessment through its descriptors and qualities of pain are required in order to determine the most appropriate treatment for cancer pain.

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