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Predictors of high score patient-reported barriers to controlling cancer pain: a preliminary report

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Abstract

Purpose—Pain is one of the most common and devastating symptoms in cancer patients, and misunderstandings on the patient's part can cause major obstacles in pain management.

Method—We evaluated factors associated with patient's high barrier score to managing cancer-associated pain by having 201 patients complete the Korean Barriers Questionnaire II, the Brief Pain Inventory—Korean, the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30, and the Korean Beck Depression Inventory. The Pain Management Index (PMI) was also assessed.

Results—The patients were from nine oncology clinics in university hospitals and a veterans' hospital in South Korea. The median pain score (0–10 scale) was 4, with a median percentage of pain improvement during the last 24 h of 70 %. A total of 150 patients (75 %) received strong opioids, and 177 (88 %) achieved adequate analgesia (positive PMI). Mean scores $\pm$ SD for the Barriers Questionnaire II ranged from 1.5 ± 1 to 2.8 ± 1.1 , with the harmful effects subscale the highest. In the multiple regression model, depression was significantly associated with total barrier score to pain management ($p < 0.0001$). Pain reduction was significantly associated with the fatalism subscale.

Conclusions—Depression was associated with high barrier score in patients with cancer pain. Management of cancer pain should include screening for depression, and management of depression could reduce patient-reported barriers to pain management.

Keywords

Cancer; Depression; Pain management

Introduction

Cancer pain is one of the most devastating symptoms in cancer patients and has negative effects on patients' quality of life. Despite efforts to standardize and establish guidelines for pain treatment, cancer pain has been reported to be undermanaged [1]. In a recent meta-analysis, pain was reported by 33–64 % of cancer patients, 31–45 % of whom reported moderate to severe pain [2]. A national survey about cancer pain management conducted in South Korea in 2006 showed similar results, with 45 % of patients reporting cancer-associated pain. Of this group, 44 % said the pain was moderate to severe, and 42 % said they were satisfied with the management of their pain; 85 % of all of the patients in this survey expressed their desire for complete pain control regardless of cancer treatment method [3].

Numerous patient-related [4–9], systematic [10, 11], and professional [12, 13] barriers are encountered in managing cancer pain. One type of patient-related barrier that may be a major contributor to poor pain control is the patient's perspective about pain medication, which could include concerns about addiction, adverse effects, drug tolerance, the harmful effects of opioids, and distracting physicians from providing cancer treatment [5, 6, 8, 14, 15]. Patients' misbeliefs and concerns about pain management can be detected with the use of the Barriers Questionnaire II (BQ-II), which is a 27-question tool designed to explore patients' misbeliefs about cancer pain and use of analgesics [8, 15]. Patient-related barriers, determined with the use of the BQ-II, were evaluated and validated in many countries and showed that age, education level, emotional status, pain severity, and pain-related symptoms were associated with a high level of patient barriers [6–9, 15, 16].

Because patient-related barriers to pain management have been suggested as an important factor in achieving adequate pain management, numerous interventional studies to attempt to reduce patients' barriers to pain management have been conducted. Among studies to determine the effectiveness of intervention on patients' barriers in long-term follow-up (more than 4 weeks), one study [17] showed significant improvement at the time of follow-up, but others [17–19] did not. Therefore, defining predictors of high barrier score to pain management and modifying this management according to individual situations are keys to improving cancer pain management. To customize the approach to pain management for each patient, identifying the contributing factors for high barrier score and developing an individualized approach in the education of patients are important. To comply with the needs of practice, we conducted this multicenter cross-sectional survey to find predictors of high barrier score to cancer pain management with the use of the BQ-II.

Methods

Participants

This study, conducted in nine oncology clinics in university hospitals and a veterans' hospital in South Korea, was a cross-sectional survey of 201 patients with cancer who had reported cancer-associated pain. Patients who were older than 20 years, had a diagnosis of cancer, and were considered by their physicians to have an alert mental status were included in the study. Patients who had undergone surgery within the previous 3 weeks were excluded because postoperative acute pain might be reflected in the reported pain. Patients with mental disabilities were also excluded. The institutional review boards of the

participating institutions approved this protocol, and written informed consent was obtained from all participants before entry into the study.

Collection of clinical characteristics

Clinical characteristics of patients and treatments they received were recorded by the investigator on the day of the survey. Patients were asked simple questions about marital status, education, employment status, smoking history, and alcohol drinking. Patients were also asked to complete the following questionnaires: Brief Pain Inventory—Korean (BPI-K) [20] (part of which was used to calculate the Pain Management Index [PMI]) [21], Korean Beck Depression Inventory [22], European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) [23], and the Korean Barriers Questionnaire II (KBQ-II).

BPI-K measurement of pain intensity and characteristics

Pain was measured with the BPI-K [20], a validated translation into Korean of the Brief Pain Inventory [24, 25]. The Brief Pain Inventory consists of six parts: (1) presence of pain; (2) site of pain; (3) four-item pain score (from 0 to 10) for the worst, least, and average pain during the last 24 h and right now; (4) type of pain medication; (5) percentage of pain relieved during the last 24 h; and (6) seven-item associated symptom score (from 0 to 10) including interference with general activity, mood, walking ability, normal work, relations with other people, sleep, and enjoyment of life. A pain severity index was calculated using the mean of the four-item pain score and an interfering score was calculated using the mean score of seven-item associated symptoms. The BPI-K has been widely used in Korea.

Adequacy of analgesic use

Adequate use of analgesics was evaluated by using the PMI [21], which was developed to assess the adequacy of opioid use in pain management. The patient-related pain score was the “worst pain” score experienced during the 24 h before the BPI-K survey and categorized according to severity into no (0), mild (1–4), moderate (5–6), or severe (7) pain. Analgesic scores of 0, 1, 2, and 3 were assigned for no pain medication, non-opioid medication, weak opioid use, and strong opioid use, respectively. The PMI, which was calculated by subtracting a patient-related pain score from an analgesic score, could range from –3 (a patient with severe pain receiving no analgesic drugs) to +3 (a patient receiving morphine or equivalent and reporting no pain). Negative scores indicated inadequate use of analgesics, and scores of 0 or higher were considered a conservative indicator of acceptable use of analgesics.

Dosage of analgesics

The total daily doses and types of pain medication were collected from patient medical records on the day of the survey. Dosages of opioids were calculated and recorded as the morphine equivalent daily dose (MEDD) with an opioid conversion ratio in patients who received strong opioids [26]. The MEDD was calculated as the sum of total doses of opioids during 24 h including long-acting opioids and short-acting opioids for breakthrough pain.

Korean Beck Depression Inventory measurement of depression

Depression was measured by using the Korean Beck Depression Inventory, based on a validated translation of the Beck Depression Inventory [27] into Korean [22]. The Beck Depression Inventory is a self-report instrument consisting of 21 questions, with each question scored from 0 to 3. A higher score indicates a more severe degree of symptoms. A score of 21 has been suggested as the optimal cut-off value that classifies depression in Korean version.

EORTC QLQ-C30 measurement of quality of life

Quality of life was measured by using the EORTC QLQ-C30, which consists of 30 questions assessing the patient's global health with symptomatic and functional scales [23]. The EORTC QLQ-C30 has been translated into 82 languages including Korean [28], and a high score indicates a good quality of life. We used the Korean version of EORTC QLQ-C30 and scored per the official manual [29]. We used the global health status and functional scales of the EORTC QLQ-C30 for the evaluation.

Barriers Questionnaire II

The BQ-II [8] is a 27-item instrument that explores patients' beliefs about cancer pain and the use of analgesics and beliefs that can interfere with pain management. The BQ-II is composed of four subscales: (1) physiologic effects (12 items), (2) fatalism (3 items), (3) communication (6 items), and (4) harmful effects of analgesics (6 items). The *physiologic effects* include beliefs that the adverse effects of analgesics will be inevitable and unmanageable, concerns about tolerance, and concerns about not being able to monitor changes in one's body with strong opioid use. *Fatalism* includes fatalistic beliefs about the likelihood of achieving control of cancer-associated pain. *Communication* includes concerns that reporting pain distracts the physician from treating the underlying disease or is not acceptable because of the patient's desire to be a "good" patient. *Harmful effects of analgesics* include the fear of drug addiction and of the harmful effects of pain medicine to the immune system. The level of agreement is measured from 0 (do not agree at all) to 5 (agree very much). Mean scores for subscale and total scale were used for analysis, with a higher score indicating stronger barriers.

The BQ-II has been appropriately validated [8]. We conducted linguistic translation and backward translation process under the permission of the author, S. Gunnarsdottir. Two investigators who fluently speak English translated the English version of the BQ-II into Korean, and a bilingual medical doctor retranslated it into English. The back-translated English questions were compared with those of the version translated by Drs. Kwon and S. Gunnarsdottir. When the back-translated questions were not identical to those of the original version, translation and back-translation process was repeated until the retranslated version was identical to the original version. The established version of back-translation was tested with 15 cancer patients and modification was performed reflecting their understanding.

Statistical consideration

The primary objective of this study was to explore the factors associated with high scores in the BQ-II. Demographic data and clinical characteristics of patients were summarized by using frequencies and percentages for categorical variables and using means and standard deviations for continuous variables. Pain and EORTC QLQ-C30 scores were summarized using medians and interquartile range.

Barrier scores were summarized within categorical patient's and clinical characteristics using means and standard deviations and compared using *t*-tests, while continuous measures such as pain and QOL were described with Pearson correlations and significance of differences from zero correlation were tested using Fisher's *z* transformation at $\alpha = 0.0002$.

We use multiple linear regression analysis to explore the independent effects of factors on barriers. Factor explored included those for which <0.05 in univariate analysis. Candidate factors were demographic characteristics, pain variables, functional scales and symptom items of the EORTC QLQ-C30, and depression. The results are presented as regression coefficients with 95 % confidence intervals.

A p value of 0.0002 was considered statistically significant for all univariate comparisons based on a Bonferroni correction allowing up to 250 comparisons at an overall type I error rate of 5 %. The F test and the final tests for significance for variables remaining in the final multiple regression models were also tested at the 0.0002 level. Statistical analysis was performed with SAS STAT version 9.2 (Cary, NC, USA) and SPSS® statistics software, version 19.0 (SPSS, Inc., Chicago, IL, USA).

Results

A total of 221 patients with cancer who were experiencing pain associated with their disease were eligible for inclusion in this study, and 210 patients were enrolled between August 27, 2009 and October 25, 2010, for an enrollment rate of 95 % (210/221). Of the 210 patients, 9 were excluded from the analysis because they either failed to answer more than two sets of questionnaires or did not return the questionnaires, resulting in 201 patients eligible for analysis (Table 1).

Table 1 describes the characteristics of the 201 patients. The median patient age was 58 years (interquartile range (IQR) 58–64 years); 59 % of patients were men, 53 % reported a religious affiliation, and 82 % were married. The most common cancer was gastrointestinal cancer (39 %), followed by lung cancer (20 %). More than half (58 %) of the patients were receiving active anticancer treatment (chemotherapy or chemoradiation) at the time of the survey.

The pain-related factors are detailed in Table 2. Most of the patients (88 %) were receiving adequate pain medication, based on the PMI, and 150 patients (75 %) were receiving strong opioids. The MEDD was 60 mg among patients who were receiving strong opioids. The median pain intensities were 4, 2, and 6 for average, minimum, and maximum pain scores, respectively. The median (IQR) scores for interference with pain were 5 or less for all categories. The scores for interference with mood and enjoyment of life were the highest with a median number of 5.

In the univariate analysis, all demographic variables, including age, sex, religion, education, marital status, employment status, alcohol intake, and smoking history, were not related to any barriers to cancer pain management (Tables 3 and 4). Pain-related variables, including pain severity, pain improvement, interferences with pain, PMI, and MEDD, were not significantly associated with barriers score (Tables 3 and 4). Depression was moderately associated with barriers in physiologic effects, communication, and total score and weakly associated with harmful effects (Table 4) in a Pearson correlation. Barriers in physiologic effects were positively related to depression and were negatively related to emotional functioning of EORTC QLQ-C30 ($p = 0.0002$; Table 4). Barriers in fatalism were not related to any of the variables. Patients with lower functioning scores in EORTC QLQ-C30 and higher depression score in BDI had high barrier score in communication. Harmful effect was related to depression only (Table 4).

Final models for multiple regression analysis included only those variables for which the univariate p value was <0.05 and then remained in the model through the process of backwards stepwise regression using Bayesian information criteria as the fit statistics. In the multiple regression analysis, high total barrier score was explained by depression with 23 % variance (Table 5, $p < 0.0001$). In the multiple regression model with physiologic barriers as the dependent variable, 14 % variance was explained with the presence of depression as an independent variable. In the multiple regression model of fatalism as dependent variable, fatalism was explained with 18 % variance with employment, ever smoker, less pain control, and MEDD as independent variables. In the multiple regression model of communication as

dependent variable, depression and physiologic functioning of EORTC QLQ-C30 were explained with 23 % variance. Depression was the significant predictor in the models of barriers in physiologic effects, communication, and total score ($p < 0.0001$; Table 5). Barriers in fatalism were related to less pain control.

Discussion

In this study, depression was significantly associated with high total BQ-II score and subscales of physiologic barriers and barriers in communication to pain management in the multiple regression model. Fatalism was related to less pain reduction.

Previous studies with barriers to pain management consistently showed a positive correlation of barriers with adequate pain medication using the PMI [5, 8, 30]. In contrast to those studies, in this study, none of the barriers were related to the PMI in the univariate analysis ($p > 0.2$). This difference between previous trials and our study may be due to a difference in the proportion of patients with relatively low pain intensity and the proportion of those using strong opioids. Unlike in the previous trials, our study group included a high proportion of patients using strong opioids (150/201 or 75 %) with a positive PMI (88 %), and the median average pain score was relatively low.

Although the PMI is used widely as an indicator of adequate pain management, it may not detect inadequate pain control in patients using strong opioids because regardless of pain control, every patient using strong opioids would have a positive PMI. Therefore, we need another indicator to evaluate adequacy of pain management in patients using strong opioids. Among the pain-related variables in this study, reduced percentage of pain during the last 24 h was negatively associated with low scores in fatalism to pain management in the multivariate analysis (Table 4). This result suggests that percentage of pain reduction can be an indicator for pain control, but more studies are needed to validate its role and determine the cut-off point.

In our study, depression was the significant independent predictor for certain BQ-II subscales (physiologic effects, communication, and harmful effects) and for high total barrier scores to cancer pain management in a multiple linear regression model ($p < 0.0001$); patients who were more depressed tended to report high barrier scores to pain management (Table 5). Similarly, several trials have reported a positive correlation between depression and some subscales of the barrier score or the total barrier score [4, 5, 8, 31], and one [5] of these studies suggested that depression was a predictor of high barrier score to pain management. In our study population, we found that patients with depression (25 %) had more severe pain, more interfering symptoms, and poorer quality of life than did those without depression ($p < 0.05$).

The frequency of depression in cancer patients has been reported to be 3–77 % [32], and the co-occurrence of cancer pain and depression has been frequently reported as a cluster of symptoms [33, 34]. Our results suggest that physicians should consider the possibility of depression in patients with cancer pain and manage both symptoms at the same time. A positive correlation of barrier scores with depression was also reported previously [4, 5, 31], suggesting that education about pain management should be combined with the management of depression.

Another study reported the coexistence of severe pain and depression in patients with metastatic breast cancer and suggested that depression plays a role in maladaptive pain behaviors [33]. Our findings suggest that there is frequent association between patient-reported barriers to pain management and depression. This finding suggests that both patient

expression of barrier and depression should be assessed and managed jointly. Barriers should be explored among patients with a high level of depression, and depression should be explored among patients with a high level of barriers.

With regard to demographic variables, the results of our study differ somewhat from those of previous trials [6, 15, 31]. None of the demographic variables except employment status were not remained in the multivariate regression model, nor was employment status not significant in the model. This might be explained by the proportion of our population. The proportion of primary cancer in our study population is slightly different from the other groups; however, there has been no evidence in the literature that the presence of a particular malignancy has an impact on the outcome of cancer pain management. We therefore believe that the results in our population can be accepted as representative cancer pain patients.

Regarding active cancer treatment, it was not associated with high barrier score. However, it might be possible that the time between last chemotherapy and assessment of barriers to pain management influence the barrier's response. Future studies should explore this association.

In our study, we used a Bonferroni correction to control for false positives resulting in multiple comparisons. Although the Bonferroni correction is the most stringent method as well as the most conservative approach, there is a possibility of a higher false negative rate than we expected. There is a need for further confirmation of the factors with multivariate analysis in a larger sample size in the future. Path analysis might be an alternative method to find the related factors to high barrier score to cancer pain management. Until now, there was no study for the level of significance in change of barriers score. Further studies are needed to find the clinically significant changes in the barriers score.

In conclusion, the current findings suggest that a low barrier score in fatalism is associated with a higher 24-h pain control rate, and a high barrier score is associated with depression. In many patients with cancer pain, depression may be a major component of stronger barriers and a lesser response to pain management. Therefore, depression should be assessed in all patients with cancer pain, particularly in patients who fail to respond to pain management or who report high barrier score. Because poorly controlled pain or high barriers to pain management can be an expression of depression, screening for and treatment of depression should be an important component of successful pain management.

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Table 1Clinical characteristics of patients ($n = 201$)

Patient characteristics	Number (%) ^a of patients
Age, median (interquartile range) (years)	58 (58–64)
Sex	
Male	119(59)
Female	82 (41)
Religion	
Christian	44 (22)
Catholic	18(9)
Buddhist	45 (22)
Atheist	92 (46)
Other	2(1)
Education	
Less than high school	86 (43)
High school graduate	76 (38)
College and more	39 (19)
Marital status	
Single	9(5)
Married	165 (82)
Divorced/separated	11(5)
Widowed	16(8)
Employed	60 (30)
Alcohol intake	27 (13)
Smoking history	
Never-smoker/ex-smoker/current smoker	108 (54)/53 (26)/40 (20)
Pack year (mean $\pm$ SD)	13.12 $\pm$ 18.96
Cancer diagnosis	
Gastrointestinal cancer	79 (39)
Lung cancer	40 (20)
Head and neck cancer	31 (15)
Genitourinary/gynecology cancer	14(7)
Breast cancer	12(6)
Other	25 (12)
Active anticancer treatment	117(58)
Depression	51 (25)

^aUnless otherwise specified

Table 2Pain-related factors and EORTC QLQ-C30 functioning scores ($n = 201$)

Characteristics	Median (IQR) ^a
Pain Management Index, number (%) of patients ^b	
0 (adequately managed)	177 (88 %)
<0 (inadequately managed)	23 (12 %)
Brief Pain Inventory	
Pain score during 24 h	
Maximum	6 (3–8)
Minimum	2 (0–3)
Average	4 (2–5)
Current	2(2–4)
Pain severity index	4 (2–5)
% reduction during 24 h	70 % (40–80)
Interference with pain	
Normal activity	3.5 (2–7)
Mood	5 (2–7)
Walking ability	3(1–6)
Normal walk	4 (2–7)
Relation with others	4 (2–7)
Sleep disturbance	3 (1–7)
Enjoyment of life	5 (2–8)
Interference	4(2–6)
Morphine equivalent dose	60 mg/day (15–200 mg/day)
Type of medication, number (%) of patients	
No opioid	26 (13)
Weak opioid	25 (12)
Strong opioid	150(75)
EORTC QLQ-C30	
Global health status	42 (25–67)
Functional scales	
Physical functioning	60 (40–80)
Role functioning	67 (33–78)
Emotional functioning	75 (42–92)
Cognitive functioning	67 (50–83)
Social functioning	67 (33–67)

EORTC QLQ-C30 European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30, *IQR* interquartile range^aUnless otherwise specified^b $n = 200$ (one missing data)

Table 3Differences of barrier score according to the patient's characteristics ($n = 201$, mean $\pm$ SD)

	Physiologic effects	Fatalism	Communication	Harmful effect	Total score
Total patients	2.5 $\pm$ 0.9	1.6 $\pm$ 1.0	1.5 $\pm$ 1.0	2.8 $\pm$ 1.1	2.3 $\pm$ 0.8
Sex					
Female ($n = 82$)	2.5 $\pm$ 1.0	1.5 $\pm$ 1.0	1.5 $\pm$ 0.9	2.7 $\pm$ 1.2	2.2 $\pm$ 0.9
Male ($n = 119$)	2.6 $\pm$ 0.9	1.7 $\pm$ 1.0	1.6 $\pm$ 1.0	2.8 $\pm$ 1.1	2.3 $\pm$ 0.7
Religion					
No religion ($n = 107$)	2.5 $\pm$ 1.0	1.6 $\pm$ 0.9	1.7 $\pm$ 1.0	2.7 $\pm$ 1.1	2.3 $\pm$ 0.8
Religious ($n = 94$)	2.5 $\pm$ 0.9	1.7 $\pm$ 1.0	1.4 $\pm$ 0.9	2.8 $\pm$ 1.1	2.3 $\pm$ 0.8
Education					
<High school graduate ($n = 86$)	2.4 $\pm$ 0.9	1.6 $\pm$ 1.0	1.6 $\pm$ 0.9	2.7 $\pm$ 1.1	2.2 $\pm$ 0.8
High school graduate ($n = 76$)	2.5 $\pm$ 1.0	1.7 $\pm$ 1.1	1.6 $\pm$ 1.0	2.8 $\pm$ 1.1	2.3 $\pm$ 0.8
College and more ($n = 39$)	2.7 $\pm$ 1.0	1.6 $\pm$ 0.7	1.4 $\pm$ 1.1	2.8 $\pm$ 1.1	2.3 $\pm$ 0.8
Marital status					
Married ($n = 165$)	2.5 $\pm$ 1.0	1.7 $\pm$ 1.0	1.6 $\pm$ 1.0	2.8 $\pm$ 1.1	2.3 $\pm$ 0.8
Others ($n = 36$)	2.4 $\pm$ 0.7	1.5 $\pm$ 1.0	1.4 $\pm$ 1.0	2.8 $\pm$ 1.0	2.2 $\pm$ 0.6
Employment					
Employed ($n = 60$)	2.6 $\pm$ 1.0	1.9 $\pm$ 1.1	1.6 $\pm$ 1.0	2.7 $\pm$ 1.0	2.3 $\pm$ 0.8
Unemployed ($n = 141$)	2.5 $\pm$ 1.0	1.5 $\pm$ 1.0	1.5 $\pm$ 1.0	2.8 $\pm$ 1.1	2.2 $\pm$ 0.8
Alcohol intake					
Yes ($n = 27$)	2.6 $\pm$ 1.8	1.7 $\pm$ 0.7	1.6 $\pm$ 1.0	3.0 $\pm$ 1.0	2.4 $\pm$ 0.7
No ($n = 174$)	2.5 $\pm$ 1.0	1.6 $\pm$ 1.0	1.5 $\pm$ 1.0	2.7 $\pm$ 1.1	2.2 $\pm$ 0.8
Ever smoker ($n = 93$)	2.6 $\pm$ 0.9	1.9 $\pm$ 1.0	1.6 $\pm$ 1.0	3.0 $\pm$ 1.1	2.4 $\pm$ 0.8
Never smoker ($n = 108$)	2.4 $\pm$ 1.0	1.4 $\pm$ 0.9	1.5 $\pm$ 0.9	2.6 $\pm$ 1.1	2.2 $\pm$ 0.8
Active anticancer treatment					
Yes($n = 117$)	2.6 $\pm$ 0.9	1.6 $\pm$ 0.9	1.6 $\pm$ 0.9	2.9 $\pm$ 1.0	2.4 $\pm$ 0.7
No ($n = 84$)	2.4 $\pm$ 1.0	1.6 $\pm$ 1.1	1.4 $\pm$ 1.1	2.6 $\pm$ 1.3	2.1 $\pm$ 0.9
Pain Management Index ^a					
0 ($n = 177$)	2.5 $\pm$ 0.9	1.6 $\pm$ 1.0	1.6 $\pm$ 1.0	2.8 $\pm$ 1.1	2.3 $\pm$ 0.8
<0 ($n = 23$)	2.5 $\pm$ 0.9	1.8 $\pm$ 1.1	1.4 $\pm$ 1.0	2.7 $\pm$ 1.3	2.2 $\pm$ 0.8

There were no statistically significant variables in this table

^a $n = 200$ (one missing data)

Table 4

Correlation of barriers to pain management with age, pain, depression, and quality of life (Pearson correlation coefficient with 95 % confidence intervals)

	Physiologic effects	Fatalism	Communication	Harmful effect	Total score
Age	-0.06 (-0.2, 0.07)	-0.07 (-0.21, 0.07)	-0.00 (-0.14, 0.14)	-0.03 (-0.17, 0.11)	-0.06 (-0.19, 0.08)
MEDD	0.03 (-0.11, 0.17)	0.18 (0.04, 0.31)	0.15 (0.01, 0.28)	0.04 (-0.10, 0.18)	0.09 (-0.04, 0.23)
Brief pain inventory					
Pain severity index	0.25 (0.11, 0.38)	0.03 (-0.11, 0.17)	0.25 (0.12, 0.38)	0.14 (0.00, 0.27)	0.25 (0.11, 0.38)
% reduction during 24 h	-0.17 (-0.3, -0.02)	-0.26 (-0.39, -0.12)	-0.16 (-0.30, -0.02)	-0.15 (-0.29, -0.01)	-0.22 (-0.35, -0.08)
Interfering score	0.13 (-0.01, 0.26)	0.01 (-0.13, 0.15)	0.15 (0.01, 0.28)	0.07 (-0.07, 0.21)	0.13 (-0.01, 0.27)
EORTC QLQ-C30					
Global health score	-0.23 (-0.36, -0.10)	-0.14 (-0.27, 0.00)	-0.25 (-0.38, -0.12)	-0.21 (-0.34, -0.08)	-0.28 (-0.40, -0.15)
Functioning score					
Physical function	-0.25 (-0.38, -0.12)	-0.04 (-0.18, 0.10)	-0.38 (-0.49, -0.26)	-0.20 (-0.33, -0.06)	-0.31 (-0.43, -0.17)
Role function	-0.11 (-0.25, 0.03)	-0.04 (-0.17, 0.10)	-0.13 (-0.27, 0.00)	-0.11 (-0.24, 0.03)	-0.13 (-0.27, 0.00)
Emotional function	-0.31 (-0.43, -0.18)	-0.16 (-0.30, -0.03)	-0.38 (-0.50, -0.26)	-0.24 (-0.36, -0.10)	0.37 (0.48, -0.24)
Cognitive function	-0.24 (-0.37, -0.10)	-0.12 (-0.25, 0.02)	-0.30 (-0.42, -0.16)	-0.20 (-0.33, -0.06)	-0.29 (-0.41, -0.15)
Social function	-0.18 (-0.31, -0.04)	0.02 (-0.12, 0.15)	-0.16 (-0.29, -0.02)	-0.17 (-0.30, -0.03)	-0.19 (-0.32, -0.05)
Depression (BDI score)	0.37 (0.25, 0.48)	0.20 (0.06, 0.33)	0.45 (0.33, 0.55)	0.26 (0.13, 0.38)	0.43 (0.31, 0.54)

The variables which were significant at $p = 0.0002$ are in bold

BDI Beck Depression Inventory, MEDD morphine equivalent daily dose (milligram)

Table 5
Multivariate analysis with linear regression (regression coefficient with 95 % confidence interval)

	Physiologic barriers	Fatalism	Communication	Harmful effect	Total score
Intercept	2.07 (1.86, 2.28)	1.82(1.47, 2.17)	1.6(1.15, 2.06)	2.22(1.92, 2.51)	2.15 (1.72, 2.57)
Depression	0.03 (0.02, 0.04)	–	0.03 (0.02, 0.04)	0.03 (0.02, 0.04)	0.02 (0.01, 0.04)
Employed	–	0.4(0.11,0.68)	–	–	–
Smoking history	–	0.33 (0.06, 0.6)	–	0.37 (0.07, 0.66)	0.23 (0.03, 0.42)
% reduction of pain	–	–0.9 (–1.4, –0.45)	–	–	–
MEDD	–	0.0006 (0.0002, 0.001)	–	–	–
Emotional function	–	–	–	–	–0.005 (–0.009, –0.001)
Physical function	–	–	–0.01 (–0.01, –0.003)	–	–
Unadjusted R^2	0.14	0.18	0.23	0.09	0.23
Overall F test significance	<0001	<0.0001	<0.0001	<0.0001	<0.0001

The final variables which were significant at $P \leq 0.0002$ are in bold

MEDD morphine equivalent daily dose (milligram)