


Prevalence of pain and its association with symptoms of post-traumatic stress disorder, depression, anxiety and distress in 846 cancer patients: A cross sectional study

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Abstract

Objective: Pain depicts a severe physical symptom but its relationship to mental health problems is not well studied in cancer patients. The aim of this study was to investigate the prevalence of pain and its correlation with symptoms of post-traumatic stress disorder (PTSD), depression, anxiety and psychological distress in a large sample of cancer patients.

Methods: From 2010 to 2019, cancer patients who received outpatient treatment at the Medical University of Vienna were assessed with the Post-Traumatic Symptom Scale (PTSS-10) and the Hospital Anxiety and Depression Scales. A visual analogue scale was used to assess pain perception. For statistical analysis, linear regression models were applied to log-transformed data.

Results: Of the 846 cancer patients included in the study, 63.5% experienced pain (mild 43.5%, moderate 13.6%, severe 6.4%). About a third (31.2%) of the total sample presented with significant PTSD symptoms. Significant symptoms of depression, anxiety and distress were present in 13.9%, 15.1% and 25.3%, respectively. Women more often reported symptoms of PTSD, anxiety and distress. Pain scores were significantly related to symptoms of PTSD, depression and psychological distress (all with $p < .001$), but not to anxiety.

Conclusions: Results show a high prevalence of experienced pain and indicate a clear association of elevated pain levels with psychiatric symptoms in oncological patients in a large Austrian sample. In order to decrease experienced pain and to enable better treatment of mental health problems in cancer patients, diagnostic procedures and interventions based on a biopsychosocial model need to be intensified.

KEYWORDS

anxiety, cancer, clinical oncology, depression, mental disorders, outpatients, pain, post-traumatic stress disorder, psycho-oncology, symptom assessment

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1 | BACKGROUND

Cancer pain is a multidimensional experience far beyond a nociceptive biochemical signal and is experienced constantly in up to half of all cancer patients.¹ Due to its complex aetiology, pain presents as nociceptive, neuropathic, nociplastic and psychogenic. Pain has a significant impact on the overall quality of life of cancer patients by influencing physical, psychological and spiritual aspects.^{2,3}

In addition to the high prevalence of pain, psychiatric disorders are common in cancer patients and greatly influence adherence to treatment and quality of life.² It is estimated, that 30%–50% of oncological patients suffer from psychiatric comorbidities.^{4,5} Post-traumatic stress disorder (PTSD) and clinically relevant post-traumatic stress symptoms (PTSS) often go undiagnosed in cancer patients.⁶ The core symptoms of PTSD are experiencing intrusion, showing avoidance behaviour, negative alterations in cognitions and mood, and alterations in arousal and reactivity. While studies assessing full-syndrome PTSD using the criteria of the Diagnostic and Statistical Manual, Fourth Edition (DSM-IV) reported a prevalence of lifetime cancer-related PTSD of 5%–36%, those assessing PTSS showed rates ranging up to 80%.^{6,7} Factors contributing to this rather wide range include the methods of assessing PTSS or PTSD, type and stage of cancer and its form of treatment, former traumatic experiences, the personality and social support systems.^{6–8}

Depression and anxiety are more frequent in cancer patients than in persons without a chronic health condition, but prevalence rates vary widely between studies. In cancer patients, estimated prevalence rates range between 11% and 57% for depression, and between 6.5% and 23% for anxiety.^{9–11} Anxiety disorders often present in association with depression.¹² Furthermore, a recent study in a large sample of cancer patients reported significant correlations of PTSD symptoms with both, depression and anxiety.¹¹

Research suggests that pain is related to mental health problems in cancer patients,^{13–15} but the possible causation and direction of these associations are not clear.^{15,16} Studies indicate that depression may be more frequently linked to pain than anxiety,^{13,14} but results are controversial.^{17–19} Existing studies on the relationship between pain and psychiatric symptoms in cancer patients often work with small sample sizes with limited explanatory power.

In the present study, we investigated the prevalence of PTSD, anxiety, depression and psychological distress in a large sample of cancer patients. We analysed how perceived pain varies with these psychiatric symptoms, which might be helpful for clinicians when they need to integrate respective treatment approaches in clinical oncology.

2 | METHODS

2.1 | Participants

A total of 846 patients participated in the study. In this sample, 428 (50.6%) patients were male, 418 (49.4%) female. Mean age was 57.4

TABLE 1 Cancer types of patients

Solid tumours		
Breast	123	(14.5%)
Lung	99	(11.7%)
Colon	66	(7.8%)
Head/neck	50	(5.9%)
Pancreas	42	(5%)
Kidney	39	(4.6%)
Stomach/oesoph.	37	(4.5%)
Brain	29	(3.4%)
Soft tissue	29	(3.4%)
Other solid	76	(9%)
Haematological		
NHL	20	(2.3%)
MM	14	(1.7%)
AML	12	(1.4%)
CLL	8	(1%)
CML	4	(0.5%)
Other haematology	30	(3.5%)
Other unspecified	88	(10.4%)
(Missing)	80	(9.5%)

Abbreviations: AML, acute myeloid leukemia; CLL, chronic lymphocytic leukemia; CML, chronic myeloid leukemia; MM, multiple myeloma; NHL, non hodgkin lymphom.

years (SD = 15.1). Breast cancer was the most frequently diagnosed solid tumour ($n = 123$, 14.5%), followed by lung cancer ($n = 99$, 11.7%), colon/rectum cancer ($n = 66$, 7.8%), and head and neck cancer ($n = 50$, 5.9%). A total of 88 patients (10.4%) suffered from haematological cancer (Table 1).

2.2 | Materials

Standardised assessment instruments used for this study included a visual analogue scale (VAS) to assess pain levels,¹⁸ the PTSS-10¹⁹ and the Hospital Anxiety and Depression Scales (HADS).²⁰

2.2.1 | Visual analogue scale

The VAS for pain assessment has a range from zero to ten. A score of zero is classified as no pain, scores of up to three (excluding zero) are classified as mild pain, scores of more than three and up to six as moderate pain and scores of more than six as severe pain. The VAS is more sensitive in assessing pain than verbal categorical ratings.¹⁸

2.2.2 | Post-Traumatic Symptom Scale

The PTSS-10 is a self-report screening tool for PTSD symptoms. Each of the ten items of the scale is rated from zero to three. A total score up to 12 implies no significant symptoms of PTSD, a score of 13–30 implies significant PTSD symptoms. Evaluations of the PTSS-10 show high internal consistency (Cronbach $\alpha = 0.93$) and test-retest reliability (ICC = 0.89).¹⁹ Internal consistency in the present study sample was high, with Cronbach $\alpha = 0.85$. As this study was launched in 2010, we assessed the prevalence of PTSD based on DSM-IV criteria.

2.2.3 | Hospital anxiety and depression scale

The HADS is a short self-report screening tool for anxiety and depressive symptoms. It has been in use for over 30 years without losing applicability or validity.^{20–22} It comprises 14 items, each with a scale ranging from zero to three. Three scores can be calculated: the depressive symptoms score (HADS-D) with seven items, the anxiety symptoms score (HADS-A) with seven items, and a total psychological distress score (HADS-T) with all 14 items. Higher scores represent more symptoms. For HADS-D and HADS-A three groups can be formed: scores from 0 to 7 imply no depression/anxiety, 8 to 10 are indicative of a possible anxiety/depressive disorder and 11 to 21 imply significant depressive/anxiety symptoms.²³ For the HADS-T, a total score of or above 16 defines a patient with a significant amount of distress.^{20,24} Internal consistencies (Cronbach α) in the present study sample were high, with $\alpha = .87$ for the HADS-D, $\alpha = .83$ for the HADS-A and $\alpha = .90$ for the HADS-T.

2.3 | Procedure

This study was part of a larger research project performed at the outpatient clinic of the Medical University of Vienna, Department of Medicine I, Divisions of Hematology and Oncology from March 2010 to November 2019. Upon written informed consent, all adult patients who were treated at the outpatient clinic and had a confirmed diagnosis of cancer were invited to participate in the study upon first admission. Questionnaires were available in German language only. Between the years 2013 and 2016, the questionnaires for this study (VAS, HADS and PTSS-10) were administered as part of the larger research project. During this time, 846 patients completed the questionnaires. A response rate cannot be reported, since the total number of questionnaires handed out was not recorded.

The study was conducted in accordance with the International Conference on Harmonization E6 requirements for Good Clinical Practice outlined in the Declaration of Helsinki and approved by the institutional ethics committee of the Medical University of Vienna (EC Nr: 2255/2016).

2.4 | Statistical methods

For analysing HADS and PTSS-10 scales, raw scores were used. To deal with missing values in the two instruments, the half-rule was applied: missing items were imputed with the participant's subscale mean of the non-missing items, if at least half of the items were answered. This method was shown to yield lowest imprecision and bias for scores on individual level in a simulation study.²⁵ In our sample, there were 90 persons with one or more missing values in the PTSS-10, and 55 persons with one or more missing value in the HADS.

To investigate the relation of experiencing pain with HADS scores, PTSS-10 scores, and demographic variables, linear regression models were used. Because of the high skewness in pain scores, a log ($x+1$) transformation was applied. Statistical analysis was carried out in R.²⁶

3 | RESULTS

3.1 | Prevalence of pain and psychiatric symptoms

In total, 537 (63.5%) patients reported experiencing pain. This included 368 (43.5%) patients with mild pain, 115 patients (13.6%) with moderate pain, and 54 patients (6.4%) with severe pain. A group of 309 patients (36.5%) did not report any pain at all. The distribution across the four pain-subcategories was roughly equal among males and females, and among patients with solid tumours and haematological cancer (Table 2).

While roughly a third of the total sample (31.2%, $n = 264$) presented with significant post-traumatic stress symptoms (PTSS-10 scores of 13 or more), approximately a quarter (25.3%, $n = 214$) showed significant psychological distress (HADS-T scores of 16 or more). Significant symptoms for depression or anxiety (HADS-D or HADS-A scores of 11 or more) were present in 13.9% ($n = 118$) and 15.1% ($n = 128$), respectively. A total of 7.2% ($n = 61$) of patients presented with both, depressive and anxiety symptoms above the cut-off scores. Compared to men, women more often reported symptoms of post-traumatic stress ($\chi^2(1) = 18.60, p < .001$), anxiety ($\chi^2(1) = 18.24, p < .001$) and distress ($\chi^2(1) = 4.08, p = 0.043$). Depressive symptoms were reported almost equally often by men and women ($\chi^2(1) = 0.03, p = 0.873$).

3.2 | Relation of pain with psychiatric symptoms

In a first analysis of bivariate correlations, post-traumatic stress, depression, anxiety and distress were all significantly associated with experiencing pain (correlations ranging from 0.293 to 0.349, all $ps < .001$; Table 3).

A subsequent analysis with a linear regression model including post-traumatic stress and distress as predictors, along with the demographic variables age and sex, revealed a significant (statistical,

TABLE 2 Extent of pain across gender and cancer type

Pain category	Gender				Cancer type			
	Men	%	Women	%	Solid tumour	%	Haematological	%
None	158	36.9	151	36.1	211	35.8	41	47.1
Mild	181	42.3	187	44.7	261	44.2	31	35.6
Moderate	58	13.6	57	13.6	80	13.6	11	12.6
Severe	31	7.2	23	5.5	38	6.4	4	4.6

Note: Distribution of pain categories is similar across gender ($\chi^2(3, N = 846) = 1.33, p = .72$), as well as across cancer type ($\chi^2(3, N = 677) = 4.39, p = .22$).

TABLE 3 Correlations of pain with distress, anxiety, depression and post-traumatic stress symptoms

	Pain	Post-traumatic stress	Depression	Anxiety	Distress
Pain	-	0.346***	0.344***	0.293***	0.349***
Post-traumatic stress	0.346***	-	0.654***	0.709***	0.755***
Depression	-	0.654***	-	0.632***	0.905***
Anxiety	-	0.709***	0.632***	-	0.893***

*** $p < .001$.

TABLE 4 Linear regression models investigating statistical predictors of perceived pain

Predictor	Distress			Depression/Anxiety		
	Estimate	CI	p	Estimate	CI	p
(Intercept)	0.27	0.07–0.46	0.008	0.30	0.10–0.50	0.004
Post-traumatic stress	0.02	0.01–0.03	<0.001	0.02	0.01–0.03	<0.001
Distress	0.02	0.01–0.03	<0.001	-	-	-
Depression	-	-	-	0.03	0.02–0.04	<0.001
Anxiety	-	-	-	0.01	-0.00–0.03	0.135
Sex: Female	-0.11	-0.20–-0.01	0.026	-0.10	-0.19–-0.00	0.049
Age	0.00	-0.00–0.00	0.346	0.00	-0.00–0.00	0.480
Observations	829			829		
R^2/R^2 adjusted	0.155/0.151			0.157/0.151		

Note: Values of the pain scale were $\log(x+1)$ transformed due to the high skewness in pain scores.

not causal) influence of post-traumatic stress and distress. More symptoms in these scales were associated with more pain (Table 4, Distress model). A more detailed linear regression model, splitting up distress into separate depression and anxiety predictors, revealed that only depression, but not anxiety had a significant association with experiencing pain (Table 4, Depression/Anxiety model). Each additional point on the HADS-D depression scale was associated with an increase of 0.03 in the log-transformed pain scale. As an example, the difference of experiencing no depressive symptoms (HADS-D score of 0) to experiencing somewhat significant depressive symptoms (HADS-D score of 11) was associated with a very significant increase from 5 to 7.29 points in the middle range of the pain scale.

The association of post-traumatic stress with pain was found to be similar. Each additional point on the PTSS-10 scale was associated with an increase of 0.02 in the log-transformed pain scale. Using a similar example as above, the difference between having no PTSS (zero points on the PTSS-10 scale) and having significant symptoms

(13 points) was associated with a significant increase from 5 to 6.89 in the middle range of the pain scale.

Both of these models showed moderate explanatory power (adjusted $R^2 = .151$ for both models), which, according to Cohen's guidelines,²³ represents a medium effect ($f^2 = .178$).

4 | DISCUSSION

The present study revealed that pain was significantly related to symptoms of PTSD, depression and psychological distress, but not to anxiety. While approximately two-thirds of all patients experienced pain in varying intensities, a third suffered from PTSD, a quarter from general psychological distress and one-eighth each suffered from significant symptoms of depression or anxiety.

Prevalence rates of pain and mental health problems found in this study are generally reflected in the current literature. The

prevalence of pain in our sample of cancer outpatients is in line with a meta-analysis describing that 39.3%–66.4% of cancer patients experience pain.¹ Rates of significant PTSS in the present study sample, with a prevalence of 31.2%, were clearly increased compared to the prevalence rates of full-syndrome PTSD, which were shown to be 6.4% for current and 12.6% for lifetime cancer-related PTSD in clinical assessments.⁸ Due to the fact that no structured diagnostic interview was carried out in our study, a comparison to full-syndrome PTSD prevalence rates was not possible. Yet, our findings are in line with recent studies showing PTSS rates in cancer patients ranging from 30% to 60%.¹⁶

Whereas the prevalence for anxiety symptoms found in this study was in line with previous research,^{9,27} the prevalence for depressive symptoms was in the lower spectrum, ranging from 11% to 57% in the literature.^{10,28} This may be explained by the outpatient treatment setting of the current study as well as by sample characteristics. The present sample included a wide range of underlying cancer types, whereas previous studies included small cohorts of patients suffering from specific cancer types like colorectal or breast cancer.^{10,28}

The present study's observation of an equal gender distribution across all pain-subcategories is supported by current literature.^{29,30} While women compared to men reported more often symptoms of distress, anxiety and post-traumatic stress, no sex difference was observed in regard to depressive symptoms in the present sample. The increased prevalence of distress, anxiety and post-traumatic stress in women compared to men is well documented in cancer and non-cancer patients.^{31–33} Yet, most studies also showed increased rates of depression in women suffering from cancer or even when cancer was survived.^{28,31,32} However, a recent linkage study in a representative community sample showed that cancer doubled the risk of depression during life in men, and correlated with symptoms of anxiety in men but not in women.³⁴ Hence, further research is needed to examine the distinct effects of gender on mental health problems in cancer patients. Future work could examine mental health problems in relation to cancer types and perceived stigma. Men may tend to underreport psychiatric symptoms due to feelings of shame and labelling. Additionally, a focus on positive mental health, resilience and coping strategies may provide new insights on gender differences in cancer patients, as these factors have been found to be gender-sensitive.^{7,35}

The main outcome of our study underscores the connection of pain perception with mental health problems in a large outpatient cohort, which is consistent with previous research.^{13–16} Our analysis revealed that only depression, but not anxiety had a significant association with experiencing pain. Similar results could be shown in a sample of Chinese cancer patients, revealing that depression was linked to pain, but anxiety was mostly linked to other disease-related factors like perceived treatment effects and functional status.¹³ Furthermore, depression was found to have a far more pervasive association than anxiety with multiple health-related domains in a US study on cancer patients.¹⁴

Our study revealed a strong association between symptoms of PTSD and elevated pain levels in an outpatient setting. Similar associations were also found in hospitalized cancer patients, where a study showed PTSD symptoms to be associated with elevated pain levels as well as increased psychological symptom burden.³³ Comparable findings were shown in (non-cancer) chronic pain patients, where a comorbid PTSD was associated with increased levels of pain and reduced quality of life.¹⁵

In cancer patients, the underlying mechanisms of the relationship between pain perception and symptoms of PTSD are still fairly unknown. However, the association might be mediated by pain coping strategies, depressive symptoms or sleep disturbances.^{15,16} In an outpatient setting, effective pain management is more complicated than for inpatients. As (non-cancer) chronic pain patients show higher rates of opioid prescriptions,¹⁵ cancer patients with PTSD might be at risk for opioid misuse due to the strong association of PTSD and pain perception.

As the present study had a cross sectional design, causality of the results in neither direction can be inferred. In non-cancer patients, epidemiological and functional imaging studies indicate a bidirectional relationship of mental health problems and chronic pain, which could partly be due to shared neural mechanisms.³⁶ However, there is evidence indicating pain precedes depression, more significantly in low pain than in high pain groups.³⁷ Studies also suggest pain being the predecessor of psychological distress rather than the other way around.³⁷ In a Japanese longitudinal study of cancer patients in palliative care, pain was associated with depression at baseline, but was not a predictive factor of depression at follow-up.¹⁷ To determine causal relation, longitudinal studies are needed. A better understanding of the interplay of pain and mental health in cancer patients could improve interdisciplinary care and prevention.

4.1 | Study limitations

Although outpatient treatment at the Vienna General Hospital is not restricted to inhabitants of Vienna, patients from rural regions are a minority. Therefore, our results may not be translatable to the general population of Austria. The questionnaires we used for the assessment of psychiatric symptoms are screening instruments and are no substitute for a thorough psychiatric diagnosis via clinical interviews. Yet, we selected instruments that offer feasible and validated methods for assessing symptoms of mental health disorders in a large sample.

Concerning PTSD, we know that DSM-V criteria have been profoundly revised compared to DMS IV-TR. Diagnostic clusters, for instance, were expanded from 3 to 4, now also including negative cognition and mood. Additionally, a cancer diagnosis does not automatically qualify for criterion A, traumatic stressor. These changes might influence the assessment of cancer-related PTSD.

Additionally, due to statistical reasons and the power of the analysis, we could not include a large amount of influencing factors in our regression model. Future research could examine the prevalence

of pain and mental health problems in relation to cancer type or to a possible psychiatric condition prior to the onset of cancer.

Furthermore, the questionnaire was only available in German language. Persons with limited German-language skills or reduced intellectual capacity were not included in this study. It could be assumed, that due to communication difficulties and resulting uncertainties this group could be even more at risk for psychiatric disorders. Future work might explore the experience of special cancer patient groups, like refugees or persons with intellectual disabilities.

4.2 | Clinical implications

Our findings emphasize the importance of psychiatric screening in the outpatient oncological setting. To optimize prevention and treatment options, a positive screening result should be followed by a thorough psychiatric diagnostic interview. Accordingly, adequate treatment options should be discussed and provided, both psychosocial and psychopharmacological. Our results support a gender-sensitive approach for mental health care in cancer patients. On the one hand, mental health treatment options for women should to be intensified to reduce the increased burden of psychiatric symptoms. On the other hand, clinicians should be especially attentive to mental health problems in men, as they may underreport psychiatric symptoms. Our study further highlights the need and importance of psycho-oncological and multidisciplinary support. Treatment options for patients that target both, pain and mental health problems, may be beneficial in reducing pain and improving mental health status concomitantly.³⁶ Research indicates that behavioural interventions frequently used for mental health problems are promising in reducing pain, but cancer-related pain is understudied in this context.³⁸

5 | CONCLUSIONS

The results of this study revealed clear associations of pain with PTSD, depression and psychological distress, but not anxiety in cancer outpatients by using internationally recognized and reliable screening instruments. Pain management and psychosocial care should be considered a primary goal in cancer outpatients, considering the psychological health and quality of life of patients.

CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

Data cannot be shared for ethical reasons. However, data can be shared on specific request.

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