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Screening for post-traumatic stress disorders in 1017 cancer patients and correlation with anxiety, depression, and distress

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Abstract

Objective: Post-traumatic stress disorder (PTSD) is a severe psychiatric disorder, which might develop after a traumatic event, like cancer diagnosis, and threatens the patient's psychological and/or physiological integrity. Anxiety, depression, and mental distress are known to be common in cancer patients; however, the frequency of PTSD was not investigated thoroughly in this patient group so far. Here, we aim to screen cancer patients for PTSD symptoms and determine a possible correlation with anxiety, depression, and distress.

Methods: The study was performed at the Divisions of Hematology and Oncology of the Medical University of Vienna from 2010 to 2018. Following written consent, patients were asked to fill out the validated self-assessment questionnaire for PTSS-10 and HADS. The study was approved by the institutional ethics committee of the Medical University of Vienna (EC Nr: 2255/2016).

Results: A total of 1017 adult cancer patients (513 male, 504 female) were included in a cross-sectional single-center study. Mean age was 57.6 years (SD 14.4 years); 31.7%, 14.6%, 13.2%, and 27.4% of patients outscored the predefined thresholds for self-assessed cases of PTSD, anxiety, depression, and distress, respectively. Compared with men, women showed a higher prevalence of symptoms for PTSD (38.9% vs 24.5%; $P < .001$) and anxiety (20.4% vs 8.6%; $P < .001$). The scores of HADS-A, HADS-D, and the combined HADS score (distress) were significantly correlated with PTSS-10 scores ($P < .01$). No differences in age were observed among the different score groups.

Conclusion: The study shows a significant prevalence as well as a correlation of PTSD symptoms with anxiety, depression, and distress among cancer patients. Findings underscore the necessity of a serious screening for psychiatric disorders, especially in female patients. In order to enable multidisciplinary care for cancer patients and to reduce the burden for psychiatric disorders, interdisciplinary screening and treatment concepts, which take into account gender aspects, are urged.

1 | BACKGROUND

In recent years, advances in early detection and treatment of tumors have greatly improved the prognosis of cancer patients.[1] Because of the life-threatening nature of cancer and the potentially severe side effects of treatment, psychiatric disorders such as anxiety and depression are common in cancer patients and greatly influence survival rate, adherence to treatment, and quality of life.[2,3] While depression and anxiety affects 10% to 20% of patients across all types and stages of cancer (compared to prevalence rates of 5% to 7% in the general population), psychiatric comorbidity seems to be underdiagnosed in the clinical routine, highlighting the need for standardized screening for psychiatric symptoms.[4-6]

Post-traumatic stress disorder (PTSD) is a psychiatric disorder, which develops after a traumatic event that threatens the patient's psychological and/or physiological integrity. Studies using the *Diagnostic and Statistical Manual, Fourth Edition* (DSM-IV) criteria for the diagnosis of PTSD reported a prevalence of lifetime cancer-related PTSD of 5% to 36%.[7,8] The core symptoms of PTSD are experiencing intrusion symptoms, showing avoidance behavior, negative alterations in cognitions and mood, and alterations in arousal and reactivity.[9] A meta-analysis has yielded a lifetime prevalence of cancer-related PTSD of 12.6% (7.4%-20.7%) as measured by a structured clinical interview,[10] and other studies found that an additional 10% to 20% of patients might experience subsyndromal levels of PTSD,[11] underlining the necessity for standardized screening for signs of distress in cancer patients and appropriate therapy.

To date, a potential correlation between distress and PTSD was not investigated so far, although the history of a recent trauma has been established as a risk factor for anxiety disorders in cancer patients recently.[12] It is noteworthy that the DSM-V criteria for PTSD have been profoundly adapted compared with DSM-IV-Text Revision (DSM-IV-TR). Diagnostic clusters, for example, were expanded from three to four, now also including negative cognition and mood. Further, which is from high relevance, a cancer diagnosis does not automatically qualify for criterion A, traumatic stressor. Only in those patients where extreme adverse events took place and six additional symptoms from criterions B to D are present, a diagnosis of cancer-related PTSD should be given. It can be assumed that these changes will influence the assessment of cancer-related PTSD in clinical practice as well as in scientific studies profoundly. Precise clinical assessment is also a necessity as it is a sophisticated task to distinguish between cancer-related PTSD and common differential diagnosis like adjustment disorder and mood disorders. Although depression, anxiety, distress, and PTSD have been identified as potentially relevant to overall survival (OS) and certainly to health-related quality of life (HRQoL), they have not yet been integrated into risk assessment, clinical trial design, and patient management.[12-14] Considering the influence on clinical trials, the impact of compliance and adherence to screening,

diagnostic, and therapeutic procedures as well as comorbidity and survival next to growing financial constraints and legal aspects (informed consent may be impaired by, eg, PTSD, and depression), the diagnosis for mental illnesses in cancer patients should gain more and more attention. However, no recommendations for the screening of PTSD in anxious or depressed patients nor cut-offs for scores in self-reported instruments, such as the Hospital Anxiety and Depression Scale (HADS), that could indicate the simultaneous presence of PTSD, do exist. Clinicians might therefore be interested in the prevalence and a possible correlation between self-reported symptoms of distress and PTSD to integrate psychological factors into clinical oncology. This would support the recent goal of personalized medicine to use each patient's unique characteristics to design optimal health care strategies.

2 | METHODS

2.1 | Ethical considerations

The study was conducted in convention 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).

2.2 | Study setting

This study was performed at the outpatient clinic of the Medical University of Vienna, Department of Medicine I, Divisions of Hematology and Oncology of the Comprehensive Cancer Center Vienna (www.ccc. ac.at) from March 2010 to November 2018. Patients who were attending the outpatient clinic and had a confirmed diagnosis of cancer, were aged 18 years or older, and were able to read and understand German were invited to participate in the survey. Questionnaires including socioeconomic questions, HADS-anxiety (HADS-A), HADS-depression (HADS-D), and Post-Traumatic Symptom Scale (PTSS)-10 were handed out at the time of registration. The patients were considered once in the context of a cross-sectional design. Of all the questionnaires that were handed out, 7244 were answered. Of these, 1017 patients completed both questionnaires (HADS and PTSD) and were included in the analysis.

2.3 | Questionnaires

The HADS, a self-administered rating scale, was specifically developed to identify anxiety, depression, and distress in nonpsychiatric medical patients. The questionnaire consists of 14 items and is separated into two subscales evaluating anxiety and depression, respectively, called

HADS-A and HADS-D. Some studies also used the combined score of HADS-A and HADS-D, HADS total (HADS-T), ranging from 0 to 42 for the measurement of general psychological distress.[15,16] For both depression and anxiety subscale, a score of less than 8 is determined to be for noncases, scores between 8 and 11 are for doubtful cases, and scores greater than 11 are for definite cases.[17] The optimal cutoff point for distress cases (HADS-T) is a score of greater than or equal to 16. Patients with scores between 13 and 16 are doubtful cases and less than 13 are noncases. These cutoff scores have been described to have an optimal combination of sensitivity (80%) and specificity (92%). Other cutoff points between 13 and 16 could also be used because of adequate calculated sensitivity and specificity.[18] Because of its shortness, it can easily be filled out by a patient while waiting for a consultation, and it has been in use for over 30 years without losing reliability or validity.[17,19]

The PTSS-10 is a 10-item self-report questionnaire that assesses the presence and intensity of PTSD symptoms.[12] Each of the 10 symptoms is rated on a 4-point Likert scale ranging from 0 (not at all/never) to 3 (very often). The PTSS-10 has been identified to be a reliable and valid instrument in screening for PTSD because of its high internal consistency (Cronbach α = .93) and high test-retest reliability (intraclass correlation coefficient [ICC] α = .89).[14] The total score ranges from 0 to 30. A cutoff score of greater than 12.5 was determined for diagnosis of PTSD.[13,14] As this study was launched in 2010, we assessed the prevalence of PTSD based on the DSM-IV criteria.

2.4 | Statistical considerations

All statistical analyses were performed using the open source software R version 3.5.2. (R Core Team, 2018). Absolute and relative frequencies were computed for categorical variables, mean, and standard deviation; median and interquartile range (IQR) were used for the descriptive analyses of continuous variables. Raw questionnaire scores were assumed to be interval-scaled. Pearson correlation coefficients were calculated to assess associations between variables (Table 1).

3 | RESULTS

3.1 | Patient characteristics

The mean age of the 1017 patients included in this study was 57.6 years (range 18 to 88 years). The most prevalent type of cancer was breast cancer (16.2%), followed by hematological tumors (14.2%) and lung cancer (11.7%). From those most frequent types of cancer (hematological tumors were combined because of statistical reasons), breast cancer showed the following mean scores: PTSS-10, 10.6 points (SD, 5.9); total HADS-T, 11.8 (SD, 7.5); HADS-A, 7.3 (SD, 3.9); and HADS-D, 4.5 (SD, 4.3). Hematological malignancies showed a mean PTSS-10 score of 8.7 (SD, 6.1); HADS-T, 10 (SD, 7); HADS-A, 5.7 (SD, 4); and HADS-D, 4.3 (SD, 3.6). Lung cancer patients had a mean PTSS-10 score of 10.2 (SD, 6.3); HADS-T, 13.7 (SD, 8.3); HADS-A, 7.1 (SD, 4.3); and HADS-D, 6.6 (SD, 4.9) (Table 2).

TABLE 1 Patient characteristics

Characteristic	Overall Cohort (n = 1017)
Age, mean (SD), y	57.6 (+/−14.4)
Sex, No (%)	
M	513 (50.4%)
W	504 (49.6%)
Cancer type, No (%)	
Brain	41 (4.8%)
Pancreas	48 (5.6%)
Hematological	122 (14.2%)
Female genital organs	9 (1.1%)
Lung	100 (11.7%)
Stomach/esophagus	41 (4.8%)
Head and neck	19 (2.2%)
Soft tissue	58 (6.8%)
Breast	139 (16.2%)
Testis	15 (1.8%)
Kidney/urinary tract/bladder	56 (6.5%)
Colon/rectum	81 (9.5%)
Hepatobiliary	21 (2.5%)
Malignant melanoma	2 (0.2%)
Prostate	12 (1.4%)
Other	93 (10.9%)
Missing	160

The duration of the disease, measured from the date of diagnosis until the time of questioning, did not show any influence on the values of HADS-T (P = .26), HADS-D (P = .19), HADS-A (P = .49), or PTSD (P = .45), respectively.

4 | DISTRIBUTION OF PTSD AND HADS

4.1 | Anxiety symptoms

The median HADS-A score (IQR) in this cohort was 6.[3-9] Of our 1017 patients, 642 (63.1%) had a HADS-A score of less than 8; 227 (22.3%) scored between 8 and 11; and 148 (14.6%) scored above 11 points (range 11-21), as shown in Table 2 as well as in Table S1. Of our male patients, 44 (8.6%) were above the threshold of 11+ points, compared with 103 (20.4%) of our female patients (P < .001). As shown in Table 2, the mean and median age of patients in the distinct groups of scores were evenly distributed with very little differences, which is true for all results reported in this study.

4.2 | Depression symptoms

Regarding the HADS-D subscale, the median score (IQR) we found was 4.[2-8] A total of 737 (72.5%) patients scored below 8 points, 146 (14.4%) patients reached a score between 8 and 11, and 134 (13.2%)

TABLE 2 HADS and PTSS-10 scores in respect to sex and age

		Sex			Age		
Scale	Score	Male	Female	All	n (missing)	Mean (SD)	Median (IQR)
HADS-A	All	511 (100%)	504 (100%)	1017 (100%)	945 (72)	57.6 (14.4)	59 (48-69)
	<8	364 (71.2%)	278 (55.2%)	642 (63.1%)	595 (47)	58.46 (15.08)	61 (49-70)
	8-11	103 (20.2%)	123 (24.4%)	227 (22.3%)	214 (13)	56.27 (13.05)	57 (48-66)
	11+	44 (8.6%)	103 (20.4%)	148 (14.6%)	136 (12)	55.92 (13.09)	58 (47-66)
HADS-D	All	511 (100%)	504(100%)	1017 (100%)	945 (72)	57.6 (14.4)	59 (48-69)
	<8	375 (73.4%)	362 (71.8%)	737 (72.5%)	688 (49)	56.83 (14.53)	58 (47-68)
	8-11	70 (13.7%)	74 (14.7%)	146 (14.4%)	130 (16)	59.32 (14.13)	61 (51-70)
	11+	66 (12.9%)	68 (13.5%)	134 (13.2%)	127 (7)	59.98 (13.61)	62 (52-71)
HADS-T	All	511 (100%)	504 (100%)	1017 (100%)	945 (72)	57.6 (14.4)	59 (48-69)
	<8	325 (63.6%)	271 (53.8%)	596 (58.6%)	554 (42)	57.58 (14.96)	60 (48-69)
	8-11	70 (13.7%)	72 (14.3%)	142 (14.0%)	133 (9)	56.63 (13.48)	57 (48-66)
	11+	116 (22.7%)	161 (31.9%)	279 (27.4%)	258 (21)	58.14 (13.63)	60 (49-68)
PTSS-10	All	511 (100%)	504(100%)	1017 (100%)	945 (72)	57.6 (14.4)	59 (48-69)
	<12.5	386 (75.5%)	308 (61.1%)	695 (68.3%)	641 (54)	57.36 (14.99)	59 (48-69)
	>12.5	125 (24.5%)	196 (38.9%)	322 (31.7%)	304 (18)	58.1 (13.07)	59 (50-67)

Abbreviations: HADS-A, Hospital Anxiety Depression Scale—anxiety; HADS-D, Hospital Anxiety Depression Scale—depression; HADS-T, Hospital Anxiety Depression Scale—total; IQR, interquartile range; PTSS-10, Post-Traumatic Symptom Scale.

surpassed the 11+ threshold. In contrast to the gender difference seen in the HADS-A scores, gender distribution was fairly even among the predefined subgroups.

4.3 | Total distress score

The combined result of both HADS-A and HADS-D, HADS-T, showed a median score of 11.[6-13,15-17,19,20] A total of 421 (31.4%) of patients scored above 13 points and 279 (27.4%) surpassed a score of 16

points. While 161 (31.9%) of the female patients had a score of 16+, only 116 (22.7%) male patients reached that score (P < .001).

4.4 | PTSD symptoms

Concerning PTSD, we found a median PTSS-10 score of 9 in our patients.[4-11,15,16,20] A total of 695 (68.3%) patients had a PTSS-10 score of less than 12.5 points, compared with 322 (31.7%) patients with a score of more than 12.5 (Table 2). While 125 (24.5%) of male
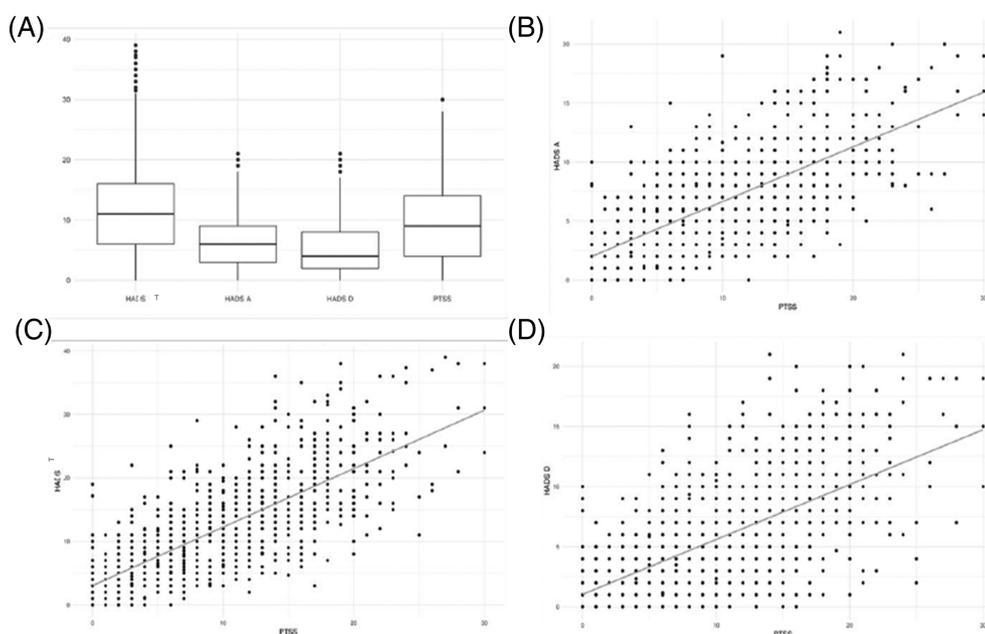

FIGURE 1 Distribution and correlation of the Hospital Anxiety Depression Scale (HADS) and Post-Traumatic Symptom Scale (PTSS) scores

patients reached a score of more than 12.5 points, 196 (38.9%) of female patients surpassed that threshold (P < .001).

4.5 | HADS scores significantly correlate with PTSS scores

The relation between HADS-A, HADS-D, or HADS-T with PTSS-10, combined with a depiction of the respective correlation coefficients, is visualized via scatterplots in Figure 1B-D, indicating a correlation between the respective scales. The calculated correlation coefficients between the scores of HADS-A, HADS-D, HADS-T, and PTSS-10 are shown in Table 3. All of the respective scores indicate a large correlation (correlation coefficient greater than 0.5). Most importantly, it was shown that the scores of HADS-A, HADS-D, and HADS-T were each significantly correlated with PTSS-10 scores, with the correlation coefficients being 0.708 (P < .01), 0.637 (P < .01), and 0.744 (P < .01), respectively.

5 | DISCUSSION

The present prospective study examined the occurrence of PTSD and its correlation with anxiety, depression, and distress in 1017 cancer patients. The study result concludes that nearly a third of all 1017 cancer patients exhibited clinical symptoms defined in PTSD and distress. In summary, a significant high percentage of patients outscored the predefined thresholds for self-assessed cases of PTSD, anxiety, depression, and distress, respectively. Women showed a higher prevalence of symptoms for PTSD (38.9% vs 24.5%, P < .001) and anxiety (20.4% vs 8.6%, P < .001) when compared with male patients. This fits to the fact that especially in breast cancer, patients show a higher incidence. This can probably be explained by the fact that most patients are female and therefore bear a higher risk for distress. Interestingly, the scores of HADS-A, HADS-D, and the combined HADS score (distress) were all significantly correlated with PTSS-10 scores.

Recent studies already suspected that the prevalence of PTSD and depression is increased in cancer patients.[5,8] However, previous data were gathered from small cohorts of patients suffering from specific types of cancer like breast cancer for instance.[8] Additionally, few studies investigated the simultaneous prevalence of PTSD and depression

in cancer patients. In this context, our data suggest for the first time that the prevalence of distress and PTSD in oncologic patients diagnosed with all different types of cancer might be higher than previously suspected.[5] Furthermore, this work also indicates a significant correlation between symptoms of anxiety, depression, and PTSD in cancer.

Interestingly, the prevalence of symptoms of PTSD in this study lies well above the prevalence rates reported in previously published studies.[8,10] This may be because of the fact that we recruited patients suffering from different kinds of cancer, while most of the previously conducted studies restricted to certain types of cancer, for instance breast cancer.[8] Another study by Nip et al, which recently investigated the prevalence of PTSD symptoms in a similar cohort also found a rate of PTSD that was higher than previously suspected.[21]

Our patients also reported higher rates of symptoms of anxiety and depression compared with the general population, but these are in accordance with prior work involving cancer patients.[22] Findings were demonstrated for all patients with different types of cancer and emphasize the importance of psychiatric screening in an outpatient ambulant setting.

A significant correlation between symptoms of distress and PTSD as measured by HADS and PTSS-10 was not yet described in patients suffering from different kind of malignancies. Since recent trauma was previously correlated with a higher rate of anxiety and depression in a small patient cohort without referring to PTSD in cancer patients, this finding is conclusive and new.[20] Our findings underline the relevance of screening for mental health if a patient shows symptoms of either anxiety, depression, or PTSD. Previous data have shown that both PTSD and depression strongly affect patient's quality of life, distress, and coping strategies.[22-24] Thus, proper screening and diagnosis of PTSD in anxious or depressed cancer patients may improve crucial patient outcome. Especially in respect to gender differences, those aspects are far to less considered in treatment concepts. These results provide further evidence for the remarkably high prevalence of PTSD and distress in female cancer patients. One explanation could be that women are more likely to perceive and articulate symptoms of emotional stress, and thus, it can be hypothesized that male patients underreport symptoms of psychological distress, resulting in underdiagnosis and undertreatment of psychiatric comorbidities.[21,25] This potential lack of diagnosis and treatment might contribute to a lower quality of life and a worse outcome in female and male cancer patients.

6 | CONCLUSION

One third of all cancer patients screened in this study suffered from serious psychological burden. Frequently, treatment efforts are focused on physical symptoms, while comorbid psychiatric conditions are often overlooked and therefore untreated in many of the cases.

The significant correlation between HADS and PTSS-10 scores in cancer patients emphasize the fact that mental health is still underrecognized in clinical routine. Further research might focus on gender differences and how the psychological burden on women

TABLE 3 Correlation of HADS and PTSS-10

	HADS-A	HADS-D	HADS-T	PTSS-10
HADS-A	1			
HADS-D	0.628**	1		
HADS-T	0.893**	0.911**	1	
PTSS-10	0.708**	0.637**	0.744**	1

Abbreviation: HADS-A, Hospital Anxiety Depression Scale—anxiety; HADS-D, Hospital Anxiety Depression Scale—depression; HADS-T, Hospital Anxiety Depression Scale—total; IQR, interquartile range; PTSS-10, Post-Traumatic Symptom Scale.

**P < .01.

and men could be treated best. In addition, patients should be accompanied continuously by psychological services throughout their disease trajectory to improve psychological management and quality of life. In addition, a connection between physical causes, such as anemia or infection, must be taken into account.

6.1 | Study limitations

Our study has several limitations that warrant discussion. We used self-reporting instruments, and no formal diagnosis was established by a structured clinical interview. The use of the PTSS-10 questionnaire is not able to determine the population's prevalence of cancer-related PTSD. It solely shows the presence of PTSD-associated symptoms in cancer patients. For exact PTSD diagnosis, further clinical diagnostics following the DSM-V criteria are required. However, the screening instruments we used are well-validated and highly correlate with diagnosis by structured clinical interview and are the gold standard for screening in clinical routine.[14,17] Furthermore, the included patients suffered from a wide range of different cancer types. The patients received a broad spectrum of anticancer treatment, depending on their symptoms, type of cancer, and stage, which was not determined in this study. This may result in different trauma and stress levels and different severities of the cancer-related PTSD symptoms. Furthermore, possible chronical aspects concerning mental health were not evaluated. Because of the cross-sectional data, we cannot infer causality concerning the duration of the disease and the correlation with HADS or PTSD. Lastly, we performed our study in a single health care center; hence, our results may not translate into the general population or regions that show socioeconomic diversity.

6.2 | Clinical implications

A vast number of cancer patients experience psychiatric symptoms at least at some point of their disease. The study shows a significant prevalence as well as a correlation of PTSD symptoms with anxiety, depression, and distress among cancer patients suffering from different malignancies.

In the outpatient setting, a serious screening procedure to exclude mental distress should be applied for all but especially for female patients. The proposed screening procedure could be conducted in a feasible manner by self-assessment questionnaires as used in this study. Early identification of patients with symptoms of psychological distress could help to improve the quality of life as well as the patient's outcome.

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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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.