

ORIGINAL ARTICLE

Posttraumatic stress disorder and preparatory grief in advanced cancer

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Summary

Purpose: The purpose of the current study was to investigate the prevalence of posttraumatic stress disorder (PTSD) and its association with sociodemographic variables and preparatory grief in patients with advanced cancer.

Methods: 195 advanced cancer patients participated in the study. Out of them, 170 had PTSD and 25 had other anxiety disorders. The diagnoses were made in strict accordance with Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I)-Clinician version. Patients completed also the Preparatory Grief in Advanced Cancer Patients (PGAC) scale.

Results: Patients with PTSD were younger (63.54 ± 12.07 years) than those without PTSD (70.36 ± 13.03 years, $p=0.010$). Patients with PTSD revealed more preparatory

grief (37.69 ± 12.11) than those without PTSD (29.58 ± 14.04 , $p=0.003$). Multiple logistic regression analysis showed that preparatory grief ($p=0.012$), and metastatic disease ($p=0.009$) remained in the model whereas age showed a trend for independent significance ($p=0.067$).

Conclusion: In advanced cancer stages, younger patients, those with metastatic disease or patients with elevated scores on preparatory grief seemed to have a greater likelihood to develop PTSD. Thus, given the prevalence of PTSD in advanced cancer patients, health care professionals should be able to better recognize those who are at risk for or exhibit symptoms of this disorder so that appropriate treatment referrals can be made.

Key words: advanced cancer, anxiety, palliative care, post-traumatic stress disorder, preparatory grief

Introduction

Many cancer patients have diagnosis of psychiatric disorders [1,2]. Anxiety disorders have been shown to be a complicating comorbid diagnosis in many patients with medical illness such as cancer [3]. PTSD is an anxiety disorder that develops in response to a severe trauma in which an individual experienced, witnessed, or was confronted by actual or threatened death, injury, or loss of physical integrity of self or others. Unfortunately, little data are available concerning PTSD in patients with cancer other than breast [4]. Since life-threatening diseases such as cancer have been included as a potential traumatic event in the DSM-IV [5], PTSD has been increasingly diagnosed as an additional morbidity among cancer patients [6]. A traumatic event is defined as an experience that is threatening oneself or a close person, accompanied by intense fear, horror, or helplessness [7].

It has been found that 0-32% of patients will devel-

op PTSD as a result of cancer [8]. Additionally, cancer experience has a traumatic quality producing intrusive thoughts (about cancer illness and treatment), avoidance behavior (i.e. patients trying not to think or discuss about the illness) and arousability (i.e. irritability), the 3 main cluster symptoms for PTSD diagnosis [9-11].

Preparatory grief is the grief that the terminally ill patient may undergo in order to prepare himself for his/her final separation from this world [12]. Patients may mourn the changes in their physical and mental capacities, or their role change within their family as they become more debilitated. Moreover, grief is the emotional response to a loss. Any change that the person perceives as negative in the way he/she relates to the environment can be considered a loss of self; the person begins to grieve for the ultimate loss - the loss of self, loss of privacy, independence, dreams, dignity, money, control, friendship or family role, autonomy, in other words, life itself [13,14].

Some researchers stated that grief and trauma should be distinct [15,16], while others reported that grief should be considered a traumatic event, and therefore pathological grief ought to fall under the rubric of PTSD [16]. A third opinion considers the overlap between grief and trauma proposing that a diagnostic category of “traumatic grief” should be developed based on the nature of the event [10,17] as they reflect symptoms of both separation distress and traumatic distress [18]. The traumatic distress component was frequently conceptualized as “PTSD-like” by researchers because it included symptoms like re-experiencing (intrusive thoughts), avoidance (avoidance of reminders) and increased arousal [19].

Due to the fact that little is known about the preparatory grief and the sociodemographic and clinical characteristics effects of advanced cancer patients on PTSD, we investigated the prevalence of PTSD, its relationship with preparatory grief and the sociodemographic and clinical characteristics of advanced cancer patients, as well as assessing factors that may influence PTSD.

Methods

Patients

The study was conducted in the Pain Relief and Palliative Care Unit, Areteion Hospital, University of Athens, in Greece between February 2008 to November 2009. One thousand six-hundred and thirty-four patients attended the unit between February 2006 to November 2009 for pain relief and cancer-related symptoms. From them, 1127 had cancer in advanced stages (stages III and IV). Eligibility criteria included >18 years of age, cancer diagnosis, anxiety disorders diagnosis, and ability to communicate effectively with the palliative care team. Exclusion criteria included a diagnosis of psychotic illness, or significant cognitive impairment. Written informed consent was obtained from all patients. One thousand and fifty-eight advanced cancer patients were judged eligible to participate in the study. From them 69 refused to answer to all the queries from the clinical interview and thus were excluded. One hundred ninety-five patients were diagnosed with anxiety disorders. Out of them, 170 patients had PTSD and 25 had other anxiety disorders. Disease status information also included performance status as defined by the Eastern Cooperative Oncology Group (ECOG PS, 0= optimum performance status, 4= worse performance status) [21].

The study was performed in accordance to the Helsinki Declaration and according to European guidelines for good clinical practice, and was approved by the Institution’s review board.

Measures

Traumatic event history was assessed using the Structured Clinical Interview for DSM-IV-TR (SCID-I). The SCID is a semi-structured clinical interview for the DSM psychiatric diagnosis [22]. Two interviewers who were clinical psychologists conducted the psychological assessment. They administered the interview assessment which included the traumatic event screening query from

the PTSD module that seeks to determine whether patients have experienced events that may qualify for the PTSD A1 event exposure criterion. Traumas were assessed by asking an open-ended question about stressful or disturbing events that may cause a patient to feel intense fear, helplessness or horror.

The next measure was the PGAC scale. This scale was designed to measure a set of preparatory grief responses to our sample. It has been shown to be acceptable by the population for which it was designed [23]. It is a 31-item scale. A 4-point Likert scale is used, ranging from 0 (disagree) to 3 (agree). The scale is interpreted as one dimension of overall preparatory grief, so the higher the score, the more the patient is experiencing preparatory grief. All scales met the minimal standards of reliability (Cronbach’s $\alpha = 0.838$). The test-retest reliability in terms of Spearman’s rho coefficient was also satisfactory ($p < 0.05$).

Statistical analysis

Data were expressed as mean±standard deviation (SD) or median for continuous variables, and categorical data were expressed as percentages. The Kolmogorov-Smirnov test was utilized for normality analysis of the parameters.

Univariate analyses were used (chi-square/Fisher’s exact tests) to analyse the relation between the outcome variable (presence or absence of PTSD) and the qualitative variables (gender, family status, ECOG PS, cancer location, metastasis, chemotherapy, radiotherapy, opioids, NSAIDs). Student’s t-test or Mann-Whitney U-test and One-Way ANOVA or Kruskal-Wallis were used to analyse the relation between the outcome variables and the quantitative measures, respectively.

All potential risk factors were included in the multivariate model, and stepwise elimination (Wald method) was used to arrive at the final model. Goodness of fit was evaluated using the Hosmer-Lemeshow statistic. The odds ratio (OR) of posttrauma was then estimated in a multivariable logistic regression model, and ORs and their 95% confidence intervals (95% CI) were presented [24].

All tests were two-sided, and a p-value of <0.05 was used to denote statistical significance. All analyses were carried out using the statistical package SPSS v. 13.00 (Statistical Package for the Social Sciences, SPSS Inc., Chicago, Ill., USA).

Results

Descriptive analysis

The mean age of the 195 participants was 64.41±12.37 years (range 34-93), and 178 (91.3%) were married. The patients’ mean education time was 7.51±4.70 years (range 0-16). The majority of the patients (64.1%) had good ECOG PS. The most frequent cancer location was the urogenital tract (26.7%). PTSD was revealed in 170 patients (87.2%) while 25 (12.8%) patients had other anxiety disorders. From the latter, who fulfilled criteria for anxiety disorders, 4 (16%) patients had panic disorder with agoraphobia, 2 (8%) had panic disorder without agoraphobia, 9 (36%) patients fulfilled the criteria for generalized anxiety disorders, 8 (32%) had anxiety disorders due to their cancer disease, and final-

ly, 2 (8%) patients had obsessive-compulsive disorder. Furthermore, 5 patients from those with anxiety disorders and 63 patients with PTSD reported higher scores on PGAC (>40).

The majority of the patients (66.7%) with PTSD reported that cancer diagnosis was the most traumatic event for them. In addition, 10.8% stated having experienced a death of a loved one, while the rest of them (22.5%) reported the following traumatic events: 4 patients: "exposure to earthquakes", 1 patient: his abandonment by father ("father leaving family"), 4: 2nd world-war experiences, 5 women: their experience of "mastectomy", 1 man: "orchiectomy", 1 patient: a history of childhood sexual abuse, 5 patients: "life-threatening accidents", 10 patients: "the suffering of their first-degree relatives with life-threatening diseases", and 8 patients reported their chemotherapy and/or radiotherapy treatment as traumatic.

Univariate analysis

Regarding comparison between patients with PTSD vs. those without with all the qualitative variables the only statistically significant tendency ($p=0.05$) was found in patients with metastatic disease (89.2%) vs. those without metastasis (15%) (table not included). Patients with PTSD were younger (63.54 ± 12.07 years) than those without PTSD (70.36 ± 13.03 years, $p=0.010$). Furthermore, patients with posttrauma revealed more preparatory grief (37.69 ± 12.11) than those without (29.58 ± 14.04 , $p=0.003$) (Table 1).

Multivariate regression analysis

Multiple logistic regression analysis indicated that 2 variables remained in the model ($\chi^2=19.05$, $p<0.0005$); with the increment of age, PTSD tended to lessen (95% CI: 0.93-1, $p=0.067$). Similarly, the increase of grief resulted in an increasing PTSD by 6% (95%, CI: 1.01-1.11, $p=0.012$). In categorical variables, patients with metastatic disease had 4.33% more probabilities to develop PTSD ($p=0.009$) (Table 2). In a sub-

sequent multiple logistic regression analysis assessing the probable factors that might influence our results it seemed that preparatory grief remained the same as in the previous analysis.

Discussion

Cancer is often perceived as life-threatening and many patients react to its diagnosis with fear or helplessness [25]. The current study examined the relationship between patients' PTSD, with preparatory grief, the sociodemographic and clinical characteristics of terminally ill cancer patients and then, the factors that might influence PTSD.

With regard to patients' traumatic experiences, cancer diagnosis as well as the death of a patients' beloved person was the most frequent traumatic events. From this view point, it seemed that loss leaves trauma victims vulnerable to develop PTSD, something consistent with the findings of other authors [26]. Patients with PTSD may react differently to cancer experience probably due to different types of trauma or even reporting different scores on preparatory grief. However, our findings regarding traumatic experiences are only descriptive. Therefore, further research would be essential in order to evaluate the relationship between different traumatic events with cancer diagnosis, prognosis and patients' quality of life. In the descriptive analysis, more patients revealed PTSD than other anxiety disorders, contrary to recent findings assessing cancer patients 6 and 12 months after their diagnosis [27-29]. A possible explanation for this finding might stem from the fact that all patients were at advanced disease stages (stages III and IV); 85.6% had a metastasis while those without metastatic disease had advanced localized disease. Furthermore, 5 patients from those with anxiety disorders and 63 patients with PTSD revealed high scores on preparatory grief.

In the univariate analysis, exploring PTSD with all the qualitative variables we found only a statistically significant trend in the relationship between PTSD and

Table 1. Univariate data analysis

	PTSD	N	Mean	SD	p-value
Age	No	25	70.36	13.03	0.010
	Yes	170	63.54	12.07	
Education	No	25	7.28	4.71	0.793
	Yes	170	7.55	4.75	
Grief total	No	24	29.58	14.04	0.003
	Yes	156	37.69	12.11	

PTSD: post traumatic stress disorder, SD: standard deviation

Table 2. Multivariate data analysis (Wald method)

	Reference category	Exp (B)*	95% CI		p-value
			Lower limit	Upper limit	
Age	---	0.96	0.93	1.00	0.067
Grief total	---	1.06	1.01	1.11	0.012
Metastasis	No	4.33	1.43	13.12	0.009
Constant	---	7.24			0.241

$\chi^2=19.05$, $df=3$, $p<0.0005$, Cox & Snell $R^2=0.185$, Exp (B): odds ratio, CI: confidence interval

metastasis. In other words, patients with metastatic disease had high levels of PTSD, probably due to the fact that patients with metastases have poor physical functioning and thus high levels of stress, contrary to other studies where the type or even the disease severity have not influence whether or not someone developed PTSD [30]. Statistically significant association was also found between PTSD and age. Patients with posttraumatic symptoms were younger than those without posttraumatic symptoms. A possible explanation for this result might be that younger patients have less experience than older ones in dealing with medical crises and life threats, and thus feeling more distressed [31].

Furthermore, patients with PTSD revealed more preparatory grief than those without PTSD. There was not any statistically significant association between PTSD and gender, contrary to the findings of other authors [32] where females were affected by both trauma and PTSD about twice as often than males.

Our analysis suggested that younger patients, those with metastatic disease or with high levels of preparatory grief have a greater likelihood to develop PTSD. A cancer patient may experience stress symptoms anytime from the diagnosis through the completion of treatment and cancer recurrence or metastasis [30], which might explain our finding where patients with metastatic disease had 4.33% probabilities to develop PTSD. Furthermore, some of the risk factors that play a role in the development of PTSD in cancer patients include poor physical functioning and high level of distress [8]. According to the literature, one of the sociodemographic variables that influence the risk of PTSD in patients with tumors includes also younger age [33]. Similarly, our results showed that age is an indicator for PTSD in cancer patients where older patients have 4% less probabilities to experience PTSD than younger patients consistent also with the Brewin et al. meta-analysis, where younger age was found a PTSD risk factor in trauma-exposed adults [34]. Presumably, in younger patients anticipation of death raises various existential concerns, a feeling of loss of control and psychological distress [35]. The best indicators of those who will develop PTSD often seem to be psychological [30]. Correspondingly, patients with high levels of preparatory grief were more likely to have PTSD. PTSD [10] and preparatory grief can have common precipitating events when the experience of cancer can be recognized as traumatic. Nevertheless, this does not permit equating preparatory grief with diagnostic entities like PTSD. Etiology, course, prognosis, and treatment must all be considered [36].

Contrary to the results of our study it has been previously estimated that the relationship between grief

and trauma may overlap [10,17]. In a subsequent multiple logistic regression analysis assessing factors that might possibly influence our results it was found that preparatory grief remains stable.

Symptoms of PTSD usually begin in the first 3 months after the trauma, but sometimes they do not appear for months or even years. Additionally, cancer patients should be involved in long-term monitoring. A limitation of the current study is that we did not identify prior research on whether or not prevalence rates of PTSD increase as death approaches which would be very interesting for further studies. Another limitation is that we did not clarify characteristics of the patients without PTSD and anxiety disorders but this does not concern the aims of the current study. Future research could reveal if the history of traumatic life events is associated with a shorter disease-free interval, indicating a potential effect of past traumatic experience in the diagnosis of cancer. It would be also interesting to assess whether pre-cancer mental disorders contribute significantly to cancer-related distress [7].

Concluding, these findings contribute to our understanding in predicting PTSD symptoms in patients with advanced cancer. As soon as patients report high levels of post-trauma, a search for the factors that might influence the experience of PTSD, such as metastatic disease, age and preparatory grief can be identified and treated, and additional benefits will include reduced posttraumatic stress symptoms.

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