Psychological distress in patients with pancreatic cancer—an understudied group

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Abstract

Background: Pancreatic cancer is the fourth leading cause of cancer-related death in the United States, unsuccessful in significantly improving 5-year survival. A diagnosis of pancreatic cancer may be associated with increased psychological distress, yet remarkably little is known about the degree of psychological distress experienced by these patients at the time of diagnosis and treatment.

Method: In a cross-sectional study, 304 patients with pancreatic cancer and 7749 patients with other cancer diagnoses completed the Brief Symptom Inventory (BSI) or the Brief Symptom Inventory-Shortened Version (BSI-18) and the Problem Common Checklist (PCL) during outpatient registration. Sociodemographic characteristics were collected from patients' clinical files.

Results: A higher percentage of pancreatic cancer patients reported elevated distress across each subscale of the BSI and BSI-18 when compared with those diagnosed with other cancer diagnoses as a group. The most notable difference was established on the depression subscale, with 28.8% of pancreatic patients reporting elevated depression compared with 18.5% of other cancer diagnoses. In pancreatic patients, a significant difference was also found in the percentage of males endorsing high depression levels when compared with females (34.0 vs 22.6%, p < 0.05).

Conclusions: Pancreatic cancer patients demonstrate elevated levels of psychological distress. This should alert providers to be vigilant in evaluating patients for distress and to provide appropriate referrals. The endorsement of fatigue and pain, along with the observed gender differences, suggest that early distress management interventions may need to include components targeted to these issues.

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Keywords: pancreatic cancer; psychosocial; distress; BSI; gender; depression

Introduction

Received: 12 August 2009

Revised: 25 November 2009

Accepted: 9 December 2009

Within the past decade, the importance of understanding, and subsequently treating, the emotional distress that can accompany a diagnosis of cancer has been increasingly recognized. This realization has led to a variety of screening approaches designed to match patients with the greatest need to the services best suited to care for those needs. For many, this screening occurs at, or shortly near, the time of the patient's diagnosis or first interaction with the cancer center.

Individuals with pancreatic cancer are one of the high-risk groups that need psychosocial services. Despite its history and current standing as the fourth leading cause of cancer-related death in the United States [1,2] there is remarkably little known about the degree of psychological distress experienced by these patients at the time of diagnosis.

Literature reviews and clinical studies of depression and anxiety in individuals with cancer have suggested that both issues are present in the majority of patients at some point during the cancer trajectory [3–9]. In individuals with pancreatic cancer, early studies reported that depressionrelated symptoms could be identified in 71% of patients [10]. Holland et al. [11] found that advanced pancreatic cancer patients reported significantly higher levels of psychological distress than patients with other types of advanced abdominal neoplasms. In contrast, more recent studies employing self-report measures, such as the Edmonton Symptom Assessment Scale (ESAS), have noted relatively low levels of depression and anxiety in pancreatic cancer patients [12]. Relatively

large standard deviations and small sample sizes in these studies, however, suggest that there is likely wide variability among pancreatic cancer patients and distress.

In one of the most comprehensive articles on distress in individuals with cancer, Zabora et al. [3] presented the prevalence of psychological distress in patients with different cancer diagnoses. In the sample of pancreatic cancer patients, mean depression, anxiety, hostility, and Global Severity Index (GSI) scores on the Brief Symptom Inventory (BSI) were 56.30, 56.71, 49.46, and 55.97, respectively. The depression and anxiety scores for pancreatic cancer patients were the highest among the cancer diagnoses reported, whereas the GSI score, an indication of global distress, was the second highest, only after lung cancer patients. Indeed, 36.6% of the pancreatic cancer patients could be identified as having elevated distress (positive cases), meaning that they had a T-score of ≥ 63 on the GSI or a T-score of ≥ 63 on any of the two subscales of the BSI. Interestingly, despite the high depression and anxiety individual subscale scores, individuals with pancreatic cancer were only fourth in the percentage of patients who were positive cases (as defined above), coming after those with lung cancer, brain cancer, and Hodgkin's disease. Although these results suggest that increased distress was evident in individuals with pancreatic cancer, it did not provide further understanding of psychological distress based on gender, age, or other variables.

Given the fact that there exists little information on the psychological distress levels or common problems of pancreatic cancer patients by either demographic or clinical subgroups, this study was designed to further characterize the levels of emotional distress and the perceived etiology present in individuals with pancreatic cancer. We hypothesized that pancreatic cancer patients would report elevated distress levels across each subscale of the BSI and Brief Symptom Inventory-Shortened Version (BSI-18) when compared with those diagnosed with other cancers. Further understanding of any potential differences in distress by gender, racial, or other demographic or clinical variables would serve to assist researchers and practitioners alike in developing screening, assessment, and intervention strategies to monitor and address the distress seen in this population.

Methods

The design was a cross-sectional survey of cancer patients seen at the Johns Hopkins Oncology Center outpatient clinics between 1987 and 2002. At the time of registration, patients who were beginning treatment or beginning a new treatment regime were asked to complete the BSI [13,14] or

the BSI-18 [3] and the Problem Common Checklist (PCL) [15]. Two separate databases were combined to maximize power for this secondary analysis, including the common subscales and global scales from the BSI and the BSI-18. For the purpose of this paper, the independent variable is diagnosis (pancreatic cancer vs all other cancers), the dependent variables are the anxiety, depression and somatization subscales, the general distress global scale of the BSI and BSI-18, age, gender, race, and marital status. Staging data was only available for 15% of the patient pool and, therefore, was omitted from the study as it would not accurately represent characteristics of the sample population. Reliable socioeconomic data were not available in the computer system and the date of diagnosis was missing for a third of the sample, so neither variable is included in this study.

Sample

The sample included cancer outpatients being treated for a new cancer diagnosis or a recurrence at the Johns Hopkins Oncology Center. Patients were in varying stages of the illness trajectory, from newly diagnosed to palliative care. The sample used in this study was a convenience sample of 8053 cancer patients with complete data for the variables of interest. This paper investigates the 304 patients with pancreatic cancer compared with the remaining 7749 patients with other cancer diagnoses. Diagnoses groups with less than 100 cases were excluded from the analysis. The types of diagnoses groups with the highest numbers represented (over 100 cases per diagnosis) include: breast (n = 2197), lung (n = 922), colon (n = 715), prostate (n = 646) lymphoma (n = 627), head and neck (n = 564), liver (n = 410), brain (n = 356), ovarian (n = 338), leukemia (n = 269), Hodgkin's (n = 198), bladder and kidney (n = 193), melanoma (n = 169) and multiple myeloma (n = 145).

Procedures

IRB approvals were obtained at The Johns Hopkins Oncology Center for the study and subsequently at the University of California, San Diego, for the secondary analysis of this data. Patients were handed a cover letter inviting them to complete the BSI or the BSI-18 and PCL along with standard registration forms. Those who accepted the invitation returned the BSI or the BSI-18 and the PCL to the registrar with the other registration paperwork. The registrar's office forwarded all BSI's to the Department of Patient and Family Services for scoring. The BSI and the BSI-18 has questions on date of birth, date the form was completed, and gender. The remaining variables were collected retrospectively from the computerbased decision support system within The Johns Hopkins Oncology Center. For the purpose of this paper, each patient was only included once.

Measures

The brief symptom inventory

The self-report BSI consists of 53 items designed to reflect psychiatric symptom patterns. Patients were asked to rate the severity of each of these symptoms on a 5-point scale of distress from 0 to 4 (with 0 = 'not at all' and 4 = 'always'). The BSI generates three global scales: GSI (based on intensity of distress and number of symptoms), positive symptom distress index (PSDI; intensity of distress), and positive symptom total (PST; number of symptoms respondents reported experiencing). The BSI also yields nine subscales: somatization (e.g. feeling weak in parts of your body), obsessive compulsive (e.g. excessive repetitive behaviors owing to doubts, worries or beliefs), interpersonal sensitivity (e.g. inability to take criticism or trouble interacting with others), depression (e.g. feeling lonely), anxiety (e.g. feeling so restless that you could not sit still), hostility (e.g. angry at others, inability to control anger), phobic anxiety (e.g. restlessness owing to fear), paranoid ideation (e.g. stress-induced feelings of being scrutinized or disliked by others), and psychoticism (e.g. lack of self-control). The BSI is scored by converting raw scores to T-scores, which will range from 30 to 80. A score of 63 or greater on a minimum of two of the subscales, or a GSI of 63 or greater, are considered to be indicative of elevated distress at a level that indicates that some form of psychosocial intervention is warranted [12–14]. T-scores are adjusted for gender, with a given raw score resulting in a higher T-score in men as indicated by Derogatis and colleagues [13]. The BSI has been normed, validated, and is a reliable measure of psychological distress [3].

Brief symptom inventory-shortened version

The original 53-item, self-administered BSI [13,14] was reduced to 18 items [15], thus requiring only 1-2 min to complete, and even less time to score the full scale and its three subscales [3]. The BSI-18 has been validated as an effective instrument for assessing psychological distress in patients with cancer. The BSI-18 can be given easily during patient care visits and repeated at appropriate intervals to monitor the psychosocial impact of the disease process and/or the effectiveness of psychological interventions [3]. The BSI-18 is scored by counting the number of positive responses on a 4-point Likert scale, which results in an overall distress score between 0 and 72. The three separate subscores are: depression (e.g. feeling lonely), anxiety (e.g. feeling so restless that you could not sit still), and somatization (e.g. feeling weak in parts of your body). A total distress score of 10 or more

for men and 13 or more for women, out of a total of 72, determines that some form of psychosocial follow-up intervention is warranted.

Problem checklist

In conjunction with the BSI-18, patients also completed the PCL [15]. The PCL covers 20 common practical problems in five general categories: emotional, social, physical, communication, and financial. The list encompasses the problems that patients most commonly report, including fatigue, pain, management of emotions, and communication with family members, as well as practical problems, such as transportation and parking, when receiving treatment. Patients are also asked to identify both their current and anticipated problems and are encouraged to add any other potential problems in the 'other' section. Given the frequency and adverse impact of two symptoms, pain and fatigue, patients were further asked to rate these symptoms on a visual analog scale. Finally, patients were asked whether they would like to talk with a member of the staff about any of the problems listed.

Statistical analysis

Independent *t*-tests and chi-square tests were conducted to examine possible differences on assessed demographic variables by cancer type. Specifically, independent *t*-tests compared the subscale scores on the BSI and the BSI-18 of those diagnosed with pancreatic cancer to all other cancer patients. Within the pancreatic cancer group, multiple regression analyses were conducted to examine the predictive capacity of age, gender, race, and marital status on the subscales of depression, anxiety, and somatization, as well as the global distress scale of the BSI and BSI-18. In the analyses that include race as a predictor, only Caucasians and African-Americans were included owing to the small number of other races assessed in this study. Furthermore, given that African-American participants constituted only 14% of the sample, analyses were also conducted with these individuals removed. Additionally, in the analyses that include marital status as a predictor, this variable was dichotomized to include two groups; married and non-married individuals, owing to the preponderance of married participants. Frequencies of the PCL items were run to determine the most common problems.

Results

Demographics

There were 304 patients diagnosed with pancreatic cancer assessed in this study. The majority of patients were Caucasian (81.8%) or African

	Pancreatic cancer (n = 304)		All other cancers $(n = 7749)$		Sig.
	n	%	n	%	
Gender					
Male	167	54.9	3441	44.4	p<0.001
Female	137	45.1	4308	55.6	p<0.001
Race					
Caucasian	255	83.9	6373	82.5	
African-American	41	13.5	1211	15.7	
Other	8	2.6	143	1.8	
Marital status					
Single	27	8.9	842	10.9	
Married	187	61.5	5354	69.1	p<0.001
Divorced/separated	25	8.2	614	7.9	
Widow	28	9.2	738	9.5	
Unknown	37	12.2	201	2.6	
	Mean (SD)	Range	Mean (SD)	Range	Sig.
Age	60.4 (10.78)	33–87 years	55.85 (13.78)	14–90 years	p<0.001

 Table I. Demographics by cancer group

 Table 2. Percentage of individuals reporting high distress scores by cancer group

	Pancreatic cancer	All other cancer	Sig.
General Distress Scale	26.4	21.0	p<0.05
Somatization	33.8	28.3	p<0.05
Depression	28.8	18.5	p<0.001
Anxiety	29.1	23.9	p<0.05

American (13.5%), with a relatively even male (54.5%) to female (45.5%) gender ratio (See Table 1). The mean age of this group was 61.18 (SD = 10.78) with ages ranging from 33 to 87 years old. The group that constituted all other cancer patients (n = 7749) had a similar demographic profile, with the majority being Caucasian (83.9%), female (55.6%), and married (70.5%). The mean age of this group was 55.85 (SD = 13.78) ranging from 14 to 90 years of age. There was a statistically significant difference in the mean age by cancer diagnosis, with those in the pancreatic cancer group being approximately 5 years older than in the other cancers group (t = -6.91,df = 319.39, p < 0.001). Chi-square analysis comparing pancreatic cancer patients to all other cancer patients were significant for gender, with more males in the pancreatic cancer group (54.9%) than the other cancers group (44.4%) ($\chi^2 = 13.11$, p < 0.001). Finally, there were no significant differences found between pancreatic cancer patients and all other cancer patients on martial status and race.

Brief symptom inventory and brief symptom inventory-shortened version

This study assessed three subscales and the general distress scale of the BSI and the BSI-18 in patients with pancreatic cancer and those diagnosed with all other cancers (Table 2). A greater percentage of

pancreatic cancer patients reported high scores on the general distress scale (26.4 vs 21%, p < 0.05), as well as the subscales of depression (28.8 vs 18.5%, p < 0.001), somatization (33.8 vs 28.3%, p < 0.05), and anxiety (29.1 vs 23.9%, p < 0.05) than those with other cancer types while controlling for age and gender. Because of the fact that there were a significantly greater number of older males in the pancreatic cancer group than in the other cancer groups, age and gender was held constant for the consequent analyses.

Further analysis was conducted in order to provide a detailed profile of this empirically underrepresented group. Chi-square and regression analyses enabled the role of demographic factors in predicting distress to be explored. Although results indicated that the pancreatic cancer patients assessed in this study were a relatively homogenous group across most subscales and demographic factors, a significant difference was found in the percentage of males endorsing high depression levels when compared with females (34.0 vs 22.6%, p < 0.05), and in the percentage of Caucasian participants endorsing high depression levels when compared with African-Americans (31.1 vs 15.0%, p < 0.05). Additional analyses conducted with Caucasian pancreatic cancer patients only revealed a similar trend, with males reporting higher levels of depression when compared with females (31.3 vs 20.5%, p < 0.05). A slight significant difference was also found between male and female pancreatic cancer patients on the general distress scale (33.6 vs 23.1%, $p \leq 0.05$).

Regression analyses were conducted to examine the predictive capacity of demographic factors across each subscale of the BSI (Table 3). It was established that demographic factors were significant predictors of variance in only one subscale, with gender, race, and marital status all predicting variance in levels of depression. Despite the

 Table 3.
 Multiple regression analysis models for BSI subscales and general distress

	В	Beta	t	Sig.
Dependent variable: depression				
Race ^a	-0.199	-0.151	-2.309	p<0.05
Gender ^b	-0.180	-0.199	-3.034	p<0.01
Marital status ^c	-0.141	-0.145	-2.138	p<0.05
Age	-0.005	-0.119	-1.843	
Constant	1.321		4.805	
$R^2 = 0.07, F = 4.355, p < 0.01$				

^aAfrican-American coded 0, Caucasian coded 1.

^bFemale coded 0, Male coded 1.

 $^{\rm c}{\rm Divorced/separated}$ coded 1, all other marital status coded 0. There are no statistically significant predictors of somatization, anxiety and general distress.

statistical significance of these predictors, only a minimal degree of total variance was predicted in this regression analysis.

Problem common checklist

Because of the small sample size of PCLs collected (n = 121), descriptive statistics only were run on the PCL for pancreatic cancer patients. This data can be used to explore the common problems that pancreatic cancer patients report. The most common problems reported by pancreatic cancer patients were: fatigue (31.9%), pain (24.8%), temporary housing while staying in Baltimore (13.3%), transportation (11.5%), and managing emotions (7.1%). It is important to acknowledge the low percentage of patients endorsing the 'Managing emotions' category in light of the high level of distress endorsed on the BSI. Although the small sample size of completers may be a contributing factor, it is also possible that this percentage may be indicative of a larger issue regarding the stigmatization of mental health issues in medical care [16]. Patients may have been unwilling to endorse this issue for a variety of reasons, including the view that emotional issues are not important to their physician, may be a sign of weakness, or may be less socially acceptable to endorse compared with physical symptoms that are also listed in this measure.

Discussion

The results of this study supported our primary hypothesis. A higher percentage of pancreatic cancer patients reported elevated distress across each subscale of the BSI and BSI-18 when compared with those diagnosed with other cancers. The most notable difference was established on the depression subscale, with 28.8% of pancreatic patients reporting elevated distress compared with 18.5% of other cancer diagnoses, whereas age and gender were held constant. Our results are consistent with earlier studies that have found depression to be highly correlated with a pancreatic cancer

diagnosis (33–50%) [17,18]. A greater percentage of pancreatic cancer patients also reported elevated symptoms of anxiety, somatization, and general distress. These results are in accordance with earlier research by Carlson et al. [4] who reported that pancreatic cancer patients reported the second highest rates of distress compared with all other cancer groups, including lung, brain, Hodgkin's disease, lymphoma, liver, head and neck, unknown primary, breast, leukemia, melanoma, colon, prostate, and gynecological. Our data also supports an earlier study by Holland et al. [11] who reported that pancreatic cancer patients had high distress scores and that they need to be screened for more than just depression symptoms. These results also reinforce the findings of the Institute of Medicine (IOM) [19] and National Comprehensive Cancer Network (NCCN) [20] that emphasize the importance of routine psychosocial distress screening in cancer care and the availability of a range of support services, including counseling, palliative care, and psychopharmacology. There is a growing consensus in the United States, Canada, Western Europe, and Japan for universal psychosocial screening of cancer patients. In fact, Bultz et al. [21] have advocated that distress be designated the Sixth Vital Sign in routine medical care. Further, pancreatic cancer patients as a group may be particularly susceptible to developing elevated distress, possibly owing to the poor prognosis and poorly understood underlying metabolic mechanisms of this disease.

In order to extend knowledge and raise awareness of this important and growing patient group, and to provide a more extensive clinical profile than earlier published articles, the relationship between demographic factors and levels of depression, anxiety, somatization, and general distress were examined. Few significant differences were established across these components of distress, indicating that the pancreatic cancer patients assessed in this study were a relatively homogeneous group. Significant differences were established in the endorsement of depression, with Caucasian male pancreatic cancer patients more likely to report elevated symptom levels. Our findings extend earlier research by Holland and her colleagues [11] who found that men with either pancreatic or gastric cancer had depression and distress scores equal or slightly higher than women with pancreatic or gastric cancer. These authors also reported that men with pancreatic cancer (but not women) had higher depression scores on the Profile of Mood States than men with gastric cancer. These results are in contrast to the general population where women typically report higher levels of depression than men [22].

The potential role of immunoregulatory mechanisms and substances (e.g. proinflammatory cytokines) in eliciting depression-like symptomology in cancer patients has prompted an increasing level of empirical interest [23]. Evidence from animal models and preliminary research in human subjects suggests that proinflammatory cytokines associated with the physiological response to illness may elicit depression-like symptoms, including depressed mood, anhedonia, fatigue, and cognitive dysfunction [24–26]. Although this fertile empirical domain may provide alternative treatment targets for symptom management in cancer, further research is needed to fully explicate the relationship between cancer and comorbid depression.

Higher levels of reported depression for Caucasian pancreatic cancer patients was not predicted, and do not lie in accordance with earlier literature that has established elevated rates of depression in African-American cancer patients [3]. It is noted that although the assessed sample is relatively large in comparison to earlier research of pancreatic cancer patients, African-American participants constituted less than 14% of this sample. Although this may have contributed to the significant race finding, noted above, these results warrant further investigation. Overall, analyses did not identify a particular demographic group as possessing significantly elevated distress and, therefore, reinforces the critical need to provide screening and support services to all patients in this group.

Depression in pancreatic cancer patients

Depression is one of the most frequently reported forms of distress in adult cancer patients [27,28] and has been associated with a range of negative health outcomes [29–31]. Consistent with earlier research conducted by Holland et al. [11], and as mentioned above, this study established that male pancreatic cancer patients were significantly more likely to endorse high levels of depression than female patients. This result was established within a relatively large sample of patients with a near-even gender split. Although further research and replication is needed, these important results challenge long-held assumptions within the domain of mental health research that consistently support higher levels of depression in females [32], and may have important implications for clinical care and the development of psychosocial support services. Male cancer patients have consistently been shown to be low users of cancer information services as well as other health and support services [33–36] and, therefore, health-care professionals may need to consider alternative methods by which to reach this subgroup in need. For example, studies have supported the use of problem-solving interventions for decreasing cancer-related distress [37–39]. Since for men turning inward, self-reliance, taking action, outcome orientation, and problem resolution are natural inclinations for managing stress, applying problem-solving methods to help male pancreatic cancer patients manage their distress seems like the next logical step.

Limitations

The results of this study provide important information regarding the experiences of pancreatic cancer patients and fertile ground for future research; however, they must be examined in light of the study's limitations. One obvious drawback is the age of the data used in this study, which was collected almost 10 years ago. However, given that there is a paucity of research concerning this group of patients, the opportunity to learn about this understudied population through this data outweighed the age of the data. It is important to note that despite the time that has elapsed since the collection of this data, there has been little change in the 5-year survival rate for those diagnosed with pancreatic cancer [40]. Furthermore, reports by the IOM [19] and the NCCN [20] continue to emphasize the need to enhance psychosocial care in the cancer setting and, therefore, this study remains pertinent and informative to health-care providers today. Two additional limitations that deserve mention include the fact that the cross-sectional methodology used did not allow for patients' distress to be examined over time and this study did not assess a comprehensive set of possible moderators of distress. The possible role of such moderating factors as social support and coping efficacy in buffering distress, or dissatisfaction with care in exacerbating distress or common problems related to their cancer care, remain to be fully elucidated in this patient population, particularly over the course of diagnosis, treatment, and transition to survivorship.

Despite these caveats, this paper reinforces earlier findings regarding the significant rates of cancer-related distress reported by patients, and extends our knowledge of an important but frequently understudied group who may be at high risk of elevated distress. In line with comprehensive recommendations by the IOM [19], these findings reinforce the need for psychosocial services to form an integral part of clinical cancer care, particularly given the negative outcomes associated with untreated distress and proven efficacy of psychosocial interventions. Future research examining the predictive validity of the BSI-18 and clinical depression is also warranted. In addition, the relationship between distress in cancer patients and physiological disease markers is needed to further advance this important domain of research.

Conclusion

Pancreatic cancer patients in this study demonstrated elevated levels of psychological distress. These findings reinforce the need for psychosocial screening, using instruments, such as the BSI or BSI-18 and the PCL, to help clinicians identify patients with pancreatic cancer who have increased levels of psychological distress, and targeting interventions and referrals for psychosocial issues in the initial management of this disease.

Because men can manifest depression in different ways to that of women, it may be important to study gender specific screening tools and interventions in this group. Finally, it may also be helpful, given the heightened depression levels reported by men in this sample, to develop programs that enable men and women to identify, understand, and work together to manage the pancreaticrelated distress and cope with this often fatal diagnosis.

Given the poor prognosis of this patient population, it is especially essential to provide a proactive, targeted approach for identifying distress and common problems reported by this understudied group. There are now a large number of screening instruments that are practical and patient friendly, both in paper [41] and electronic mediums [42] that can be used to identify distress in this underserved population. Early interventions, such as supportive counseling, problem-solving therapy, and pharmacotherapy, may lead to amelioration of many of the psychological issues associated with pancreatic cancer, and thus lead to improved quality of life and disease management.

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