Original Article

Relationship Between Pain and Post-Traumatic Stress Symptoms in Palliative Care

Maya L. Roth, PhD, CPsych, Kate St. Cyr, MScPPH, Ingrid Harle, MD, and Joel D. Katz, PhD, CPsych

Parkwood Hospital Operational Stress Injury Clinic (M.L.R., K.S.C.), London, Ontario; Palliative Medicine Program (I.H.), Queen’s University, Kingston, Ontario; and Department of Psychology (J.D.K.), York University, Toronto, Ontario, Canada

Abstract

Context. Previous research suggests that patients receiving palliative care may simultaneously experience poorly managed pain and post-traumatic stress disorder (PTSD)-related symptoms as a result of their deteriorating health.

Objectives. To: 1) examine predictors of PTSD-related symptoms in patients requiring palliative care; 2) assess whether anxiety, depression, pain catastrophizing, and pain anxiety mediate the relationship between pain interference and PTSD-related symptoms; and 3) evaluate the impact of these variables on pain interference and PTSD-related symptoms.

Methods. One hundred patients receiving palliative care at one of two palliative care sites in London, ON, Canada, completed the PTSD Checklist—Civilian version (PCL-C), the Hospital Anxiety and Depression Scale (HADS), the Pain Catastrophizing Scale (PCS), the Brief Pain Inventory-Short Form (BPI-SF), and the Pain Anxiety Symptoms Scale-20 (PASS-20). Hierarchical multiple regressions were used to examine HADS-Anxiety, HADS-Depression, PCS and PASS-20 scores as predictors of PCL-C scores; and mediation analyses were used to test the effect of HADS-Anxiety, HADS-Depression, PCS, and PASS-20 on the relationship between BPI-SF interference and PCL-C. Mediators that significantly affected this relationship in the individual mediator models were entered into a multiple mediator model.

Results. Only pain anxiety and pain catastrophizing emerged as significant mediators of the relationship between pain interference and PTSD-related symptoms. After being entered in a multiple mediator model, pain anxiety emerged as the strongest mediator.

Conclusion. The findings of the present study reveal that pain and PTSD-related symptoms are important concerns in palliative care, and that pain must be addressed to best meet the needs of this population.

Address correspondence to: Maya L. Roth, PhD, CPsych, Operational Stress Injury Clinic, Parkwood Hospital, Third Floor, Hobbins Building, Room H3012, 801 Commissioners Road East, London, Ontario N6C 5J1, Canada. E-mail: maya.roth@sjhc.london.on.ca

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Introduction

Despite the advances in the management of physical symptoms and psychological issues in patients requiring palliative care, pain and psychological distress remain significant concerns. Pain and its related suffering, including depression, feelings of isolation, and anxiety, are often accepted as “normal” experiences along the trajectory of dying\(^1\) and these conditions may be somewhat overlooked as a result of this perception. Although palliative care aims to control pain and distress, and to provide comfort to patients as their health progressively deteriorates,\(^2\)\(^-\)\(^5\) it is a complex field, and care is best provided by a multidisciplinary team and approach.\(^6\)\(^,\)\(^7\) To effectively meet the needs of this population, the issue of pain must be addressed.

Previous research suggests that pain, conceptualized by the International Association for the Study of Pain as a product of noxious stimulation that causes an emotionally evocative reaction,\(^8\) is prevalent among patients with cancer\(^9\)\(^-\)\(^15\) and those requiring palliative care services.\(^9\)\(^,\)\(^14\)\(^-\)\(^18\) Pain in the oncology and palliative care settings tends to be underdiagnosed and poorly treated.\(^9\)\(^,\)\(^11\)\(^,\)\(^13\)\(^,\)\(^19\)\(^,\)\(^20\) Inadequate pain assessment may lead to insufficient analgesia, which may subsequently lead to increased psychological and physical distress.\(^12\)

Emerging research has focused on exploring the implications of psychological distress, including post-traumatic stress disorder (PTSD)-related symptoms, in the oncology and palliative domains of care. PTSD-related symptoms, such as avoidance and emotional numbing, a feeling of detachment from others, and irritability and anger,\(^21\) have been associated with cancer-related symptoms, diagnosis, and treatment,\(^22\) and many researchers support the validity of PTSD-related symptoms in patients with cancer and those requiring palliative care services.\(^23\)\(^-\)\(^28\) Despite this, the nature of the relationship between psychological distress and pain among palliative care patients has not been widely studied to date.

However, outside of the realm of palliative care, pain researchers have aimed to better understand the relationship between PTSD-related symptoms and pain. The mutual maintenance model of pain and PTSD, which suggests that pain and PTSD are mutually maintained by seven possible mechanisms, may be an exceptionally useful model in exploring the relationship between pain and PTSD-related symptoms in patients requiring palliative care. These mechanisms are: 1) attention and reasoning biases, 2) anxiety sensitivity, 3) reminders of the trauma, 4) avoidance, 5) depression and reduced activity levels, 6) anxiety and pain perception, and 7) cognitive demand from symptoms limiting the use of adaptive strategies.\(^29\) As such, the objectives of the present study are to: 1) examine correlates of PTSD-related symptoms in patients requiring palliative care; 2) assess whether anxiety, depression, pain catastrophizing, and pain anxiety mediate the relationship between pain interference and PTSD-related symptoms; and 3) evaluate the relationship of these variables on pain interference and PTSD-related symptoms in a multiple mediator model.

Methods

Ethics approval for this study was obtained from the Human Participants Review Committee at York University and the University of Western Ontario Health Sciences Research Ethics Board.

Participant Data

A total of 168 participants older than 18 years with a cancer diagnosis were approached for recruitment from two primary sites: the London Regional Cancer Program (Palliative Medicine Outpatient Clinic and Lung Cancer Clinic) and the London Health Sciences Centre—Victoria Hospital campus (Palliative Care Unit and Palliative Medicine Consultation Service). Participants were excluded if they: 1) could not read or understand English; 2) were deemed not appropriate (i.e., had a visual or hearing impairment, could not speak because of a medical procedure, were nonpalliative medicine patients attending an appointment at the Palliative Medicine Outpatient Clinic or occupying an inpatient bed in the palliative care unit), or deemed too ill to
participate by palliative medicine physicians and nurses; or 3) were confused, delirious, or did not score above the cutoff of 24 of 30 on the Mini-Mental State Examination (MMSE).

**Measures**

Participants completed the following measures, which are briefly described in the following sections.

**Brief Pain Inventory-Short Form.** The Brief Pain Inventory-Short Form (BPI-SF) measures the past 24 hour pain intensity and pain interference, which can be described as the disruption of activity or functioning because of pain or fear of pain. Total pain intensity scores range from zero to 10, and pain interference scores range from zero to 70, with higher scores indicating greater pain intensity and interference, respectively. The BPI-SF has demonstrated adequate reliability, sensitivity, and validity in previously conducted multicenter studies. In the present study, Cronbach’s alpha for pain interference was 0.87. Internal consistency could not be calculated for pain intensity because a single numerical rating scale of current pain intensity was used for this variable.

**Hospital Anxiety and Depression Scale.** The Hospital Anxiety and Depression Scale (HADS) is a 14-item self-report questionnaire that measures the severity of anxiety and depressive symptoms. Depression and anxiety subscale scores range from zero to 21, with higher scores indicating greater symptom severity. Both the HADS-A (anxiety subscale) and the HADS-D (depression subscale) have been demonstrated to have good sensitivity and specificity. In the present study, Cronbach’s alpha for the HADS-A and HADS-D subscales were 0.82 and 0.80, respectively.

**Mini-Mental State Examination.** The MMSE is a brief quantitative measure of cognitive status and was used in this study to determine whether a potential recruit was cognitively suitable for participation in the study. A cutoff score of 24 out of 30 is recommended when screening medical populations for impairment. High levels of internal consistency and test-retest reliability have been reported in mixed medical samples, and the measure demonstrates moderate-to-high levels of sensitivity and specificity in a variety of clinical and control samples.

**Pain Anxiety Symptoms Scale-20.** The Pain Anxiety Symptoms Scale-20 (PASS-20) is a 20-item self-report questionnaire that assesses four components of pain anxiety: cognitive anxiety, escape/avoidance behaviors, fear of pain, and physiological symptoms of anxiety. A total score is generated by summing all responses and ranges from zero to 100, with higher scores indicating higher pain anxiety. The PASS-20 has demonstrated good reliability and validity in individuals with pain attending physiotherapy clinics. In the present study, Cronbach’s alpha for the total score and fear of pain, cognitive anxiety, escape/avoidance behaviors, and physiological symptoms of anxiety subscale scores were 0.93, 0.83, 0.87, 0.78, and 0.72, respectively.

**Pain Catastrophizing Scale.** The Pain Catastrophizing Scale (PCS) measures “an exaggerated negative ‘mental set’ brought to bear during actual or anticipated pain experience.” A total score ranging from zero to 52 is tabulated, with higher scores indicating greater pain catastrophizing. Scores for three subscales (rumination, magnification, and helplessness) also are generated. The PCS shows high internal consistency and validity in adult community and clinical pain samples. In the present study, Cronbach’s alpha for the total score and rumination, magnification, and helplessness subscale scores were 0.93, 0.89, 0.74, and 0.85, respectively.

**PTSD Checklist—Civilian Version.** The PTSD Checklist—Civilian version (PCL-C) is a 17-item self-administered questionnaire that assesses severity of PTSD symptoms. Scores range from 17 to 85, and cutoff scores that reliably predict a diagnosis of PTSD range between 44 and 50. A validation study of university students revealed high levels of internal consistency, test-retest reliability, and convergent and discriminant validity. In the present study, Cronbach’s alpha for the total score and re-experiencing, avoidance, numbing, and hyperarousal subscales were 0.89, 0.74, 0.80, 0.78, and 0.74, respectively.

Scores from two previously completed questionnaires—the Edmonton Symptom Assessment System (ESAS) and the Palliative Performance Scale—were extracted from participants’ medical charts. The ESAS is a self-report questionnaire that assesses the presence
and severity of nine symptoms commonly experienced by patients requiring palliative care: pain, fatigue, nausea, depression, anxiety, drowsiness, appetite, sense of well-being, and shortness of breath. Scores for each of the nine items range from zero to 10, with higher scores indicating greater symptom severity. In the present study, Cronbach’s alpha for the ESAS severity score was 0.88. The Palliative Performance Scale is a clinician-rated measure of functional performance and allows for the measurement of progressive decline in patients requiring palliative care. Scores range from zero to 100, in 10% increments, where zero indicates death and 100 is indicative of a fully functioning and ambulatory patient.

Recruitment and Data Collection
A total of 168 patients were identified during the recruitment period from May 30 to December 19, 2008. Of these, 24 declined participation; a further 38 were missed by the study investigator (investigator not available, patient not available, or patient died before being reached by investigator). Three more patients did not meet the MMSE cutoff criterion, two withdrew consent partway through completing the questionnaires, and one patient was identified as nonpalliative after completion of the study questionnaires, leaving a sample size of 100 (response rate of 59.5%).

Participants completed the aforementioned questionnaires after providing written informed consent. A total of 89 participants completed the questionnaires in the presence of the study investigator (M. L. R.), and the remaining 11 participants completed the questionnaires independently. Demographic and disease-related data, including age, sex, marital status, cancer diagnosis, stage of cancer at date of diagnosis, and current state of diagnosis, were extracted directly from participants’ medical records. Questionnaire data were manually entered into the Statistical Package for the Social Sciences, version 15.0 (SPSS Inc., Chicago, IL), and questionnaire-scoring syntax statements were created to compute summary scores for the BPI-SF, ESAS, HADS, PASS-20, PCS, and PCL-C.

Statistical Analyses
All data were screened for missing data, univariate and multivariate outliers, and skewed distribution as per procedures described by Tabachnick and Fidell and Field. Missing data, which represented 4% of all data, appeared to be random and, therefore, was not imputed, as per Tabachnick and Fidell. Rather, total scores were calculated by summing the items without creating a weighted total based on the missing items. Visual inspection of frequency distributions ensured that all scale summary scores fell within the expected ranges.

Hierarchical multiple regressions were used to examine HADS-A, HADS-D, PCS, and PASS-20 scores as statistical predictors of PCL-C scores, after controlling for BPI-SF intensity, BPI-SF interference, and ESAS.

Simple mediation analyses (Fig. 1) were tested using Baron and Kenny’s linear multiple regression model. These analyses were used to test the effect of four independent variables on the relationship between BPI-SF pain interference and PTSD-related symptoms (PCL-C scores): HADS-A (Model 1), HADS-D (Model 2), pain catastrophizing (PCS scores; Model 3), and pain anxiety (PASS-20 scores; Model 4). For each unique model, four steps were taken. In

Fig. 1. Path diagram of simple mediation models. Path a is the path between the independent variable and the mediator variable. Path b is the path between the mediator variable and the dependent variable. Path c’ is the direct effect between the independent variable and dependent variable. HADS = Hospital Anxiety and Depression Scale; PCS = Pain Catastrophizing Scale; PASS-20 = Pain Anxiety Symptoms Scale-20; BPI-SF = Brief Pain Inventory-Short Form; PCL-C = Post-Traumatic Stress Disorder Checklist—Civilian version.
Step 1 of each model, BPI-SF pain interference was assessed as a predictor of PCL-C scores. In Step 2, BPI-SF pain interference was assessed as a predictor of the model’s independent variable (i.e., HADS-A in Model 1). In Step 3, controlling for BPI-SF pain interference, the independent variable (i.e., HADS-A in Model 1), was assessed as a predictor of PCL-C scores. In the final step, controlling for the independent variable (i.e., HADS-A in Model 1), BPI-SF interference was assessed as a predictor of PCL-C scores. Bootstrap-significance tests were applied to each model, using \( n = 5000 \) bootstrap resamples, to assess the independent variable as a mediator of the relationship between pain interference and PTSD-related symptoms. A Bonferroni correction was applied to the Type I error rate to control the overall Type I error when multiple tests of significance are conducted. For all analyses, bootstrapped confidence intervals (CIs) were used to evaluate the statistical significance of the mediated models.

Lastly, a separate multiple mediator model, which followed the same approach as the four simple mediation analyses, was used to assess the effect of multiple mediator variables on the relationship between BPI-SF interference and PCL-C scores. Standardized regression coefficients were generated for each of the mediators, and bootstrapping was again used to construct CIs around the regression coefficients in the mediation analysis to test the significance of indirect effects. Mediators for the multiple mediator model were selected based on the results of the individual mediator models. If a mediator was found to significantly affect the relationship between the independent and dependent variables in its own unique individual mediator model, it was entered into the multiple mediator model (Fig. 2).

**Results**

Table 1 presents a summary of demographic, cancer-, and pain-related information. Twenty-five percent (\( n = 25 \)) reported clinically significant symptoms of anxiety, and 43% (\( n = 43 \)) reported clinically significant symptoms of depression, as measured by the HADS-A and HADS-D subscales, respectively. Seven percent (\( n = 7 \)) of participants met or exceeded the cutoff score of 44 for clinically significant PTSD-related symptoms. The mean PCL-C score was 25.88 ± 10.40.

**Hierarchical Regression Analysis**

The hierarchical regression analysis (Table 2) showed that pain intensity and pain interference significantly predicted PCL-C scores in Step 1 and accounted for 22% of the variance in PCL-C scores. The addition of symptom distress in Step 2 was not a significant predictor of PCL-C scores. After controlling for all variables in the model, pain anxiety scores accounted for a significant proportion of the variance in PCL-C scores and was the only variable that significantly predicted PCL-C scores.

**Simple Mediation Analyses**

The results of the mediation analyses are presented step by step in Table 3. It is worthwhile to note that neither anxiety nor depression emerged as a significant mediator of...
BPI-SF interference and PCL-C scores. However, pain catastrophizing emerged as a significant mediator of BPI-SF pain interference and PCL-C scores (63% of total effect mediated by pain catastrophizing), as did pain anxiety (79% of total effect mediated by pain anxiety).

Multiple Mediation Analysis

Pain catastrophizing and pain anxiety were entered into the multiple mediation model (Table 4); because anxiety and depression were not statistically significant mediators of the relationship between BPI-SF interference and PCL-C scores, they were not entered into the model. In Step 1 of the multiple mediation model, BPI-SF interference significantly predicted PCL-C scores and in Step 2, BPI-SF interference significantly predicted both pain catastrophizing and pain anxiety. In Step 3, controlling for BPI-SF interference and pain anxiety, pain catastrophizing did not significantly predict PCL-C scores, whereas controlling for BPI-SF interference and pain catastrophizing, pain anxiety significantly predicted PCL-C scores. In this step, pain catastrophizing did not mediate the relationship between BPI-SF interference and PCL-C scores above and beyond pain anxiety. In Step 4 of the multiple mediation model, controlling for pain catastrophizing and pain anxiety, BPI-SF interference did not significantly predict PCL-C scores, which suggests complete mediation.

The indirect effect of pain catastrophizing and pain anxiety combined with the relationship between BPI-SF interference and PCL-C scores was significant (indirect effect = 0.27; 99% bias-corrected CI = 0.0928–0.5108). An examination of the individual indirect effects of pain catastrophizing and pain anxiety show that only pain anxiety is a mediator because the 99% bias-corrected CI did not contain zero (CI = 0.1016–0.3441), meaning that pain catastrophizing does contribute to the overall indirect effect above and beyond pain anxiety. Therefore, pain anxiety emerged as the strongest mediator of the relationship between BPI-SF interference and PCL-C scores.

Discussion

The aim of the present study was to examine correlates of PTSD-related symptoms as determined by PCL-C scores in addition to the relationship between pain interference and PTSD-related symptoms in a sample of patients receiving palliative care. The results show that in the hierarchical regression model used to identify statistical predictors of PCL-C scores, only pain interference was significant. This finding suggests that pain interference is more relevant than pain anxiety to the transitional oncology palliative care experience, when patients are functionally declining from a stable palliative care stage toward an end-of-life palliative care stage, and pain intensity is mild and well

<table>
<thead>
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<th>Parameters</th>
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<td>Age (yrs)*</td>
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</tr>
<tr>
<td>Sex*</td>
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<tr>
<td>Age groups (yrs)*</td>
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<tr>
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<td>Cancer type*</td>
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<td>Metastases at diagnosis*</td>
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<td>Pain category*</td>
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</table>

*N = 100.

*N = 85.
managed. This is consistent with the findings of Asmundson et al., which linked pain interference to PTSD. It also relates to the suggestion that daily awareness of pain interference may act as a reminder of cancer-related trauma and thus acts to maintain the relationship between pain and PTSD-related symptoms in the transitional oncology palliative care experience.

Although previous research has not examined pain and psychosocial predictors of PTSD-related symptoms in palliative care, previous studies suggest a significant comorbidity of chronic pain and PTSD in other patient populations. In the present study, pain catastrophizing and pain anxiety were identified as individual mediators of the relationship between pain interference and PTSD-related symptoms, which provides support for these previous findings.

However, neither HADS-A nor HADS-D emerged as a significant mediator of the relationship between BPI-SF interference and PCL-C scores, which is contrary to Sharp and Harvey’s mutual maintenance model of pain and PTSD. Pain anxiety emerged as the strongest mediator of the relationship between BPI-SF interference and PCL-C scores, above and beyond the effect of pain catastrophizing; thus, preoccupation with and worry over pain may trigger PTSD-related symptoms in this cohort. Pain anxiety is conceptualized as fear of pain, cognitive anxiety, escape/avoidance behaviors, and physiological symptoms of anxiety, all of which map onto Sharp and Harvey’s mutual maintenance model. This finding imparts clinical implications. First, clinicians should be aware of the co-occurrence of pain interference and PTSD-related symptoms in transitional oncology palliative care populations. Failure to assess the possibility of pain interference may lead to the exacerbation of symptomatology and increased distress for already vulnerable patients. Second, pain anxiety and pain catastrophizing should be considered as possible focal points of intervention in patients requiring palliative care. Previous research has shown that cognitive-behavioral therapy is an efficacious treatment for both pain and PTSD-related symptoms, and may be a valuable tool when working with this population.

<table>
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<th>Step</th>
<th>Variable</th>
<th>Total $R^2$</th>
<th>$R^2$ Change</th>
<th>$F$ Change</th>
<th>$\beta$</th>
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<td>1 ($n = 73$)</td>
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<td>0.22</td>
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<td>0.31</td>
<td>$-0.27^b$</td>
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<tr>
<td>2 ($n = 73$)</td>
<td>BPI-SF intensity</td>
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<td>0.00</td>
<td>0.31</td>
<td>$-0.27^b$</td>
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<tr>
<td></td>
<td>BPI-SF interference</td>
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<td>0.00</td>
<td>0.31</td>
<td>$-0.27^b$</td>
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<tr>
<td>3 ($n = 73$)</td>
<td>BPI-SF intensity</td>
<td>0.43</td>
<td>0.21</td>
<td>5.85</td>
<td>$-0.20$</td>
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<tr>
<td></td>
<td>BPI-SF interference</td>
<td>0.43</td>
<td>0.21</td>
<td>5.85</td>
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<td></td>
<td>ESAS distress</td>
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<td>5.85</td>
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</table>

PCL-C = Post-Traumatic Stress Disorder Checklist—Civilian version; BPI-SF = Brief Pain Inventory-Short Form; ESAS = Edmonton Symptom Assessment System; PCS = Pain Catastrophizing Scale; PASS-20 = Pain Anxiety Symptoms Scale-20; HADS = Hospital Anxiety and Depression Scale.

$^aP < 0.05$.

$^bP < 0.01$.
PTSD-related symptoms also has proven to be beneficial.58

There are some limitations to the present study. The cross-sectional study design does not allow for the inference of causality, particularly related to the direction of the relationships between variables. The relatively small sample size also limits generalizability to other populations. The convenience sampling strategy of the present study may have introduced bias into the data, and the fact that only patients who were deemed well enough to participate by health care professionals or who could read and write English were included in the study may have resulted in some selection bias. The present study’s response rate of 59.5% may have introduced further bias into the study, particularly if significant differences existed between participants and nonparticipants. Additionally, the MMSE has not been widely accepted as a tool for delirium screening because it is possible that individuals with a score higher than 24 could potentially still fulfill the criteria for delirium. The self-report ESAS scores were extracted from hospital charts of inpatients one to two days before the remainder of study data was completed; therefore, the possibility exists that the results of these measures were not accurate at the time the other measures were collected. Finally, age differences in the variables of interest were not examined. Given the wide age range of participants in the present study (19–87 years), it is possible that differences in the relationships between independent and dependent variables may exist between narrower age categories.

Notwithstanding these limitations, the findings of the present study reveal that pain and PTSD-related symptoms are important concerns in palliative care. As the population of Canada continues to age and more Canadians are faced with terminal illness and its associated pain and psychological distress, the need for palliative care services will increase. An important next step would be to further examine the prevalence and validity of PTSD and PTSD-related symptom constructs in palliative care. Not surprisingly, the findings of the present study also indicate that transitional oncology palliative care patients may experience their cancer diagnosis as a traumatic event; however, this requires replication in further studies. Future research studies also would benefit from including a clinically valid assessment to establish a diagnosis of PTSD, which would systematically address concerns about the validity of PTSD in palliative care. Lastly, a longitudinal study with a larger sample size may broaden the generalizability of the study, provide an opportunity to detect changes in pain and PTSD-related symptoms over time, identify possible differences in the relationship between pain and PTSD-related symptoms by age and sex, and identify potential risk factors for PTSD-related symptoms and PTSD. A better understanding of the prevalence, interrelationship, and mutual maintenance variables of pain and PTSD-related symptoms may lend itself to improved assessment strategies and treatment options for patients requiring palliative care.

Disclosures and Acknowledgments

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Table 4

<table>
<thead>
<tr>
<th>Step</th>
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<th>β</th>
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<th>P</th>
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<td>2</td>
<td>Pain catastrophizing (BPI-SF interference)</td>
<td>0.62</td>
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<td>Pain anxiety (BPI-SF interference)</td>
<td>0.38</td>
<td>6.45</td>
<td>&lt;0.01</td>
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<tr>
<td>3</td>
<td>PCL-C scores (pain catastrophizing)a</td>
<td>0.16</td>
<td>1.25</td>
<td>0.22</td>
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<tr>
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<td>PCL-C scores (pain anxiety)b</td>
<td>0.50</td>
<td>4.11</td>
<td>&lt;0.01</td>
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<tr>
<td>4</td>
<td>PCL-C scores (BPI-SF interference)c</td>
<td>0.04</td>
<td>0.33</td>
<td>0.74</td>
</tr>
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</table>

BPI-SF = Brief Pain Inventory-Short Form; PCL-C = Post-Traumatic Stress Disorder Checklist—Civilian version.

aControlling for BPI-SF interference and pain anxiety.
bControlling for BPI-SF interference and pain catastrophizing.
cControlling for pain catastrophizing and pain anxiety.
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