Published in final edited form as:
J Pain Symptom Manage. 2014 September ; 48(3): 465–470. doi:10.1016/j.jpainsymman.2013.10.021.

Dyspnea and Panic Among Patients With Newly Diagnosed Non-Small Cell Lung Cancer

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Abstract

Context—Among patients with lung cancer, dyspnea is associated with psychological distress, fatigue, and poor coping. Respiratory symptoms are also a common trigger for panic attacks in the general population. Minimal research has addressed the prevalence of panic disorder or the association of dyspnea with risk of panic disorder in lung cancer.

Objectives—We explored the frequency of panic disorder symptoms and the association of dyspnea with risk of panic disorder symptoms among patients with newly diagnosed non-small cell lung cancer (NSCLC).

Methods—During 2006–2010, consecutive patients presenting for initial consultation at a thoracic oncology clinic completed a survey of current symptoms, including dyspnea and panic disorder symptoms. We evaluated the frequency of panic disorder symptoms. Logistic regression was used to test the association of dyspnea with risk of panic disorder symptoms, adjusting for age, gender, disease stage, performance status, and major depression symptoms.

Results—Among 624 patients (*M* age=63.7 [*SD*=12.1]; 52.6% female), 48.1% reported that breathing was at least somewhat difficult and 11.2% endorsed panic disorder symptoms. Dyspnea was independently associated with higher risk of panic disorder symptoms (OR=2.19, 95% CI=1.11–4.31, *P*=0.02). Younger age and major depression symptoms also were associated with higher risk (*P*'s<0.01).

Conclusion—Almost half of patients with newly diagnosed NSCLC reported dyspnea, and patients with dyspnea were over twice as likely to endorse panic disorder symptoms relative to patients without dyspnea. Results highlight the need to differentiate panic disorder symptoms among patients who report dyspnea, particularly those who are younger or experiencing major depression symptoms.

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Disclosures
The authors declare no conflicts of interest.

Keywords

dyspnea; panic disorder; lung carcinoma; anxiety

Introduction

Dyspnea is a common and distressing problem experienced by patients with non-small cell lung cancer (NSCLC), with about half of patients reporting clinically significant symptoms (1,2). Among patients with NSCLC, dyspnea is associated with reduced quality of life, impaired sleep, restricted physical activity, occupational dysfunction, and more frequent emergency department visits (3–8). Patients with lung cancer who experienced dyspnea also have reported acute fear and the sensation of impending death (7). Findings suggest that for some patients, dyspnea episodes may increase risk for panic-related symptoms.

A panic attack refers to an acute, intense fear response characterized by autonomic arousal (9). During a panic attack, an individual may experience distressing somatic symptoms like breathlessness, palpitations, sweating, trembling, and nausea, as well as a fear of dying or losing control. When panic attacks lead to persistent worry about future attacks, avoidance of situations that might trigger an attack, or frequent health care seeking, an individual may meet criteria for panic disorder (10). Panic disorder is often chronic and associated with poor general and psychological health. Panic disorder also overlaps with dyspnea in predicting lower quality of life, impaired functioning, and excessive health care utilization (11–14). Among patients with cancer, panic disorder might place patients at risk for serious distress and treatment discontinuation (15,16).

Despite the prevalence of dyspnea in NSCLC and the association of dyspnea with panic in the general population, few studies have examined risk of panic in patients with NSCLC. Notably, the prevalence of panic disorder is elevated in other chronic respiratory conditions such as asthma and chronic obstructive pulmonary disease (COPD), underscoring the potential for dyspnea to increase the risk for panic disorder in patients with NSCLC (17–23). In the current study, we aimed to identify the prevalence of panic disorder symptoms among patients with NSCLC. Secondly, we examined the association of dyspnea with risk for panic disorder symptoms, independent of other demographic, clinical and psychological correlates of panic disorder symptoms. We hypothesized that patients with dyspnea would show higher risk for panic disorder symptoms relative to those without dyspnea, based on the potential for breathlessness to trigger the development of panic pathology in some patients. Data were drawn from a survey of current symptoms in patients attending initial consultation at an outpatient thoracic oncology clinic.

Methods

Patients

The study sample included adult patients who presented for initial consultation at the Massachusetts General Hospital Center for Thoracic Cancers (MGHCTC) and who consented to participate in a longitudinal study of current symptoms. Patients were eligible

for study participation if they were between 18 to 95 years of age, were fluent in English, and had a confirmed NSCLC diagnosis.

Procedures

Study procedures were approved by the Partners Human Research Committee Institutional Review Board prior to study conduct. Between July 2006 and December 2010, a research assistant approached consecutive patients attending initial consultation at the MGHCTC. During the scheduled clinic visit, the research assistant screened interested patients for eligibility. Eligible and interested patients provided informed consent and completed a baseline survey. We also reviewed patients' electronic health records (HER) to obtain data on disease characteristics. The current study is a secondary analysis of baseline survey data.

Measures

Outcome: Panic Disorder Symptoms—The Patient Health Questionnaire (PHQ) is a commonly used instrument for mental health screens in health care settings (24). We used the 15-item PHQ panic module to screen for panic disorder symptoms in the past four weeks. This module follows Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) criteria for panic disorder (10), and has shown good sensitivity (86%) and specificity (91%) in detecting panic disorder in outpatient settings (25). Respondents screen positive for panic disorder symptoms if they have recently experienced sudden anxiety attacks that were bothersome or worrisome, and if these attacks were associated with at least four physiologic (e.g., heart racing) and/or cognitive (e.g., fear of dying) symptoms.

Primary Factor: Dyspnea—The well-validated Functional Assessment of Cancer Therapy–Lung (FACT-L) module was used to assess lung cancer-related symptoms during the past week (26). We used a single item ("I have been short of breath") to measure dyspnea. Continuous responses (0–4 scale) were dichotomized to identify the presence (i.e., "somewhat," "quite a bit," "very much") or absence (i.e., "not at all," "a little bit") of dyspnea.

Covariates—We selected demographic, clinical and psychological factors based on known or hypothesized correlations with panic disorder symptoms. *Demographic:* Patients reported age, gender, and racial/ethnic identification. *Clinical:* We reviewed EHR data to identify cancer stage and Eastern Cooperative Oncology Group (ECOG) performance status (27). *Psychological:* Depression and anxiety symptoms commonly co-occur in lung cancer (28). The 9-item PHQ depression module (PHQ-9) (29) was used to screen for major depression symptoms in the current study. This module follows DSM-IV criteria for depressive disorders, and has shown good sensitivity (88%) and specificity (88%) in detecting depression in medical settings (30). Respondents screen positive for major depression symptoms if they are experiencing depressed mood and/or anhedonia for more than half the days over the past two weeks, and if they endorse at least five depression symptoms overall (may include disruptions in sleep, energy, appetite, and concentration, and guilty thoughts).

Statistical Analysis

Prevalence of panic disorder symptoms was calculated. Differences between patients with or without panic disorder symptoms were evaluated using independent samples *t*-tests for continuous variables and Chi-square tests or Fisher's exact tests for categorical variables. We used multiple logistic regression to evaluate whether dyspnea was associated with risk of panic disorder symptoms, adjusting for age, gender, disease stage (I/II versus III/IV), performance status (0–1 versus 2 or higher) and major depression symptoms (positive screen: yes/no).

Results

Sample Characteristics

Approximately 85% of consecutive patients enrolled in the study and completed a baseline survey (*n*=624). Data were not collected from patients who chose not to enroll. The mean age of patients was 63.7 years (SD=12.0). Most patients identified as non-Hispanic white (91.0%) and approximately half were female (52.6%). Patients represented disease stages I (18.3%), II (6.9%), III (18.9%), and IV (52.7%), and most had an ECOG performance status of 0 (44.9%) or 1 (38.5%). Almost half (48.7%) reported experiencing dyspnea during the past week.

Panic Disorder Symptoms

Approximately 12.3% of patients endorsed experiencing at least one panic attack in the past four weeks, and 11.2% met screening criteria for panic disorder symptoms. Panic disorder symptoms were more common among patients with dyspnea relative to those without dyspnea (14.7% vs. 7.6%, $P = 0.004$). Additionally, panic disorder symptoms were more common among females (13.7%) relative to males (8.4%; $P=0.04$) and among those with major depression symptoms versus those without major depression symptoms (25.0% vs. 9.1%; $P=0.001$). Finally, patients with panic disorder symptoms were younger than those without symptoms (M=56.0 years [SD=9.0] versus 64.7 years [SD=12.0]; t=5.79, $P<0.001$). Panic disorder symptom status did not vary by disease stage (I/II vs. III/IV) or performance status (0–1 vs. 2+).

Adjusted Model of Dyspnea Predicting Panic Disorder Symptoms

In a multiple logistic regression model of panic disorder symptoms (Table 1), dyspnea remained independently associated with higher risk of panic disorder symptoms after adjusting for all covariates (OR=2.19, 95% CI=1.11, 4.31). Older age was associated with lower risk (OR=0.94, 95% CI=0.92, 0.97) whereas major depression symptoms were associated with higher risk (OR=3.40, 95% CI=1.50, 7.73). In comparison, gender, disease stage and performance status were not associated with risk of panic disorder symptoms.

Discussion

To our knowledge, this is the first study to examine prevalence of panic disorder symptoms in patients with NSCLC and the association of dyspnea with risk of panic disorder symptoms in this population. Study strengths included enrollment of a large sample of

consecutive NSCLC patients at approximately the same point in care (initial consultation) and the use of a brief, validated screening instrument for panic disorder symptoms. Among participants, 11.2% had experienced panic disorder symptoms within the past four weeks. These results build on prior large-scale work indicating that cancer is associated with increased odds of panic attacks compared with the general population (31). Additionally, whereas panic disorder typically presents earlier in adulthood, a review of inpatient psychosomatic consultations at a regional cancer center showed that approximately half of patients presenting with panic attacks or panic disorder were experiencing panic for the first time (15).

Because the sensation of breathlessness is a common initiating symptom for panic attacks, we examined whether dyspnea was associated with risk for panic disorder symptoms. In the current sample, nearly half of patients reported dyspnea. This is consistent with prior evidence that breathlessness is common among patients with lung cancer, both before and after disease-directed treatments (32). Moreover, patients who reported dyspnea were more than two times as likely to have panic disorder symptoms relative to those without dyspnea, independent of age, gender, disease stage, performance status, and major depression symptoms. These findings strengthen prior observations that lung cancer patients with dyspnea may be at risk for panic symptoms (7).

Identifying the association of dyspnea with risk of panic disorder in patients with NSCLC is clinically meaningful, given the high disease burden in this population and the symptom overlap between these two specific problems. When a patient with NSCLC and a history of panic presents with acute dyspnea, a clinician must determine whether these symptoms are the result of panic, progressive cancer, or a host of other conditions with serious treatment implications. Acute medical diagnoses such as pulmonary embolus first must be ruled out. Subsequently, although opioids are commonly prescribed to alleviate persistent breathlessness in patients with NSCLC, benzodiazepines and/or cognitive-behavioral therapy for anxiety may be indicated to treat underlying panic disorder (33). With regard to risk reduction, longitudinal studies are needed to help identify the extent to which dyspnea increases risk for developing panic disorder and/or panic pathology exacerbates breathlessness associated with NSCLC burden.

Among the covariates, both major depression symptoms and younger age were associated with higher risk for panic disorder symptoms. Research in both cancer and the general population has established that depression and anxiety symptoms commonly co-occur (28,34,35). Results also support findings that young patients with cancer report more psychiatric symptoms, including anxiety, relative to older patients (36). In a nationally representative survey study, cancer was associated with an increased odds of panic attacks in respondents aged 15–54 but not in older age groups (31). Oncology providers may consider having a lower threshold to proactively assess panic disorder symptoms in patients with dyspnea, and particularly younger patients and those with mood symptoms, to direct symptom management and prompt specialty mental health evaluation as needed.

Several study limitations warrant consideration. First, we collected data at a single institution from patients who were primarily non-Hispanic white and had a relatively good

performance status, which may limit the extent to which findings generalize to other groups. In addition, analyses were conducted using cross-sectional data and we did not have retrospective data on history of panic; therefore, we are unable to draw causal conclusions regarding the observed associations. We also did not collect data on comorbid respiratory illnesses (i.e., COPD) which may increase risk of panic in this population. Furthermore, other lung cancer disease and treatment-related symptoms may contribute to risk of panic, and should be explored in future work. Finally, the use of a brief self-report instrument to screen for panic disorder symptoms may have led to misclassification of some cases.

Conclusion

In a cohort of patients with NSCLC presenting for initial outpatient oncology consultation, a significant minority endorsed panic disorder symptoms. The odds of endorsing panic disorder symptoms were more than two times higher among those reporting dyspnea. Findings highlight the need to further examine treatment planning, health care utilization, and health outcomes among patients who are experiencing dyspnea and who may be at risk for developing panic pathology. Clinicians should consider assessing panic symptoms in the context of dyspnea, to facilitate differential diagnosis, symptom management and alleviation of distress. Interventions may be designed to educate patients on symptom management and address breathlessness and panic comorbidity.

Acknowledgments

This research was supported in part by National Cancer Institute grants K23 CA115908 (Pirl) and R25 CA092203 (Shin).

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Table 1

Logistic Regression Model of Panic Disorder Symptoms in Patients With Metastatic Non-Small Cell Lung Cancer

Factors	OR	95% CI	*P*
Age	0.94	0.92 – 0.97	<0.001
Female gender	1.79	0.93 – 3.47	0.08
Disease stage III/IV (versus I/II)	1.33	0.61 – 2.89	0.47
Performance status ≥2 (versus 0–1)	0.25	0.05 – 1.29	0.10
Major depression symptoms	3.40	1.50 – 7.73	<0.01
Dyspnea	2.19	1.11 – 4.31	0.02