Original Article

Lung Cancer and Posttraumatic Stress Symptoms: Predictive Factors and Subgroup Analysis

*Pei-Lun Chung, M. D.[1,2], Shu-I Wu, MD., PhD[3,4], Hong-Ming Chen, M. D.[1,2], Vincent Chin-Hung Chen, M.D., Ph.D.[1,2], Min-Jing Lee, M. D.[1,2]**

[1]Department of Psychiatry, Chang Gung Memorial Hospital, Chiayi Branch, Chiayi, [2]Department of Medicine, School of Medicine, Chang Gung University, Taoyuan, [3]Department of Psychiatry, Mackay Memorial Hospital, Taipei, [4]Department of Medicine, Mackay Medical College, New Taipei City, Taiwan

Abstract

Objective: Lung cancer is the most common cancer and the leading cause of cancer death worldwide. Research on the correlation between posttraumatic stress symptoms (PTSSs) and lung cancer is limited. In this study, we intended to study PTSS predictors in patients with lung cancer and their subgroups. **Methods:** Patients aged ≥ 20 years with lung cancer diagnosis were recruited. We collected information on demographic characteristics, depressive symptoms, and cognitive function, to examine the effect on PTSSs. With the Chinese version of the startle, physiological arousal, anger, and numbness questionnaire, we analyzed the variables to identify the independent correlates of PTSSs and to compare differences among treatment and cancer stage subgroups. **Results:** A total of 329 lung cancer patients were included with prominent male, below senior high school education level, married status, unemployment, smoking history, non-alcohol drinker, without psychiatric history and comorbid diabetes and hypertension. The correlates of PTSSs were significantly higher in education level ($\beta = 0.197$, $p < 0.01$), cognitive function ($\beta = -0.269$, $p < 0.001$), and depressive symptoms ($\beta = 0.294$, $p < 0.001$). In subgroup analysis, high education level was significantly correlated of PTSSs in different treatment groups surgery group ($\beta = 0.266$, $p < 0.05$), nonsurgery group ($\beta = 0.204$, $p < 0.05$), chemotherapy group ($\beta = 0.189$, $p < 0.05$), and nonchemotherapy group ($\beta = 0.220$, $p < 0.05$). Cognitive function was significantly correlated of PTSSs in different cancer stages in early stage ($\beta = -0.401$, $p < 0.01$) and advanced stage ($\beta = -0.182$, $p < 0.05$). **Conclusion:** Depressive symptoms, high education level, and the poor cognitive function were significantly associated with PTSSs in patients with lung cancer. Health professionals in oncology should consider psychological burden screening, cognitive function examination, and rehabilitation in clinical practice.

Key words: depressive symptoms, chemotherapy, surgery, education level
Taiwanese Journal of Psychiatry **(Taipei) 2022; 36: 157-163**

Introduction

Research indicates that a cancer diagnosis considerably affects mood and stress levels, and may be a precipitating stressor to posttraumatic stress symptoms (PTSSs) [1, 2]. Cancer-related stressors are associated with the diagnosis; living with the burden of a progressive life-threatening disease; the severity of the disease and prognosis; the discomfort and side effects of treatment; disfigurement and dysfunction, as well as and potential physical, social, and occupational impairments [3]. Evidence showed that individuals exposed to prolonged, repeated, or multiple stressful events exhibit greater PTSS compared with individuals who experienced discrete and a single event [4-6]. Cancer-related stressors are long-term, recurrent, and complex, causing this population to be particularly at risk of posttraumatic stress disorder (PTSD). Therefore, exploration of the PTSSs of patients with cancer is warranted.

Lung cancer is one of the most common cancers and the leading cause of cancer death worldwide [7]. Stress-related psychological symptoms in patients with lung cancer, such as PTSSs, should be studied. Research has been focused on breast cancer and has primarily been conducted in the United

Received: Aug. 22, 2022 revised: Oct. 18, 2022 accepted: Oct. 19, 2022
date published: Dec. 27, 2022

Access this article online

Quick Response Code:

Website: www.e-tjp.org

DOI: 10.4103/TPSY.TPSY_32_22

[1]*Corresponding author. No. 8, West Section, Jiapu Road, Puzi City, Chiayi County 613, Taiwan.
E-mail: Min-Jing Lee <8035c@cgmh.org.tw>

How to cite this article: Chung PL, Wu SI, Chen HM, Chen VC, Lee MJ. Lung cancer and posttraumatic stress symptoms: Predictive factors and subgroup analysis. Taiwan J Psychiatry 2022;36:157-63.

States, with only a few small-sample studies from Asia [3]. Ni et al. [8] conducted a longitudinal observational study in China involving 93 patients newly diagnosed as having lung cancer to study PTSSs among patients with lung cancer. According to the results, about half of patients experience mild-to-moderate PTSSs at baseline or in the previous six months. Another observational study done in France involving 47 patients with lung cancer undergoing lung resection therapy reported that about half of the patients experiences PTSSs during the three-month assessment period [9]. Dougal et al. [10] did a longitudinal observational study of 93 patients with lung cancer, and 57 of them completed the study. The investigators estimated the prevalence of PTSD being ranged from 5% to 16% across the assessments.

In addition to the incidence of PTSSs, studies have studied the risk factors associated with PTSSs among patients with lung cancer. One meta-analysis identified young age, low socioeconomic status, limited social support, precancer diagnosis or lifetime trauma history, advanced disease, invasive treatment, and recently completed treatment as risk factors for increased cancer-related PTSD [11]. But most research included in the meta-analysis focused on breast cancer, and only two studies studied the risk factors in patients with lung cancer. One observational study reported that the risk factors that predicted poor PTSS in the preceding six months are younger age, a history of smoking relatively few cigarettes, relatively less sedentary behavior, and more severe initial cancer symptoms (including fatigue or poorer quality of life) [9]. Another report showed that anxiety and acute postoperative pain in the early period strongly predict PTSD-related symptoms [10].

Studies reported that the adverse effects of treatment cause substantial stress on patients with cancer [12]. Cancer treatments (including surgery, chemotherapy, radiation, immunotherapy, and hormonal therapy) and their related side effects, as well as medical complications that occur as a result of the disease, treatment, or comorbid conditions, are all studied in the study [12]. Patients with lung cancer usually receive surgery or chemotherapy, resulting in pain, fatigue, disfigurement, and gastrointestinal upset. But no study has been studied PTSSs among patients with lung cancer receiving different treatment types. In this cross-sectional study, we intended to study the incidence of PTSSs among patients with lung cancer with a larger sample than those of previous studies. Furthermore, we also did a subgroup analysis to explore the individual risk factors among patients of different disease stages and patients receiving different treatment types.

Methods

Participants

We did a cross-sectional study at the oncology clinic of Chiayi Chang Gung Memorial Hospital. Initially, we enrolled 308 patients aged ≥ 20 years who had been diagnosed as having stages 1 to 4 lung cancer between November 2017 and August 2019 in this study. Excluded from the study were those with difficulty completing interviews, such as those with neurological disorders; a lifetime history of severe head trauma; a history of intellectual disability, bipolar disorder, schizophrenia, or substance-related disorders within the preceding 12 months or a past suicide attempt; illiteracy; a history of developmental delay; severe visual impairment (e.g., cataract or glaucoma); as well as and current pregnancy. Eligible participants from inpatient and outpatient clinics were recruited by the study assistants who have bachelor's degrees in nursing and broad working experience in the field of psychiatry. Finally, 239 participants were included in this study. This study was approved by the institutional review board of Chiayi Chang Gung Memorial Hospital (IRB protocol number = 201700252B0 and date of approval = March 16, 2017), requiring to obtain signed informed consents before their participation.

Measures

We collected the following demographic data (sex, age, body mass index, education level, marital status, and employment status). We also collected information on smoking history, drinking history, systemic treatments received (i.e., chemotherapy, radiotherapy, targeted therapy, and surgery), existing comorbidities (i.e., diabetes and hypertension), chronic pain and pain scores, psychiatric history, and cancer staging. The participants decided whether to receive treatment for cancer on the basis of the physicians' clinical assessment and the medical guidelines for each cancer stage. The following self-reported copies of the questionnaire were given to all study participants.

Posttraumatic stress symptoms

The startle, physiological arousal, anger, and numbness (SPAN) scale uses a four-point Likert scale ranging from 0 (not at all distressing) to 4 (extremely distressing) to assess the frequency and severity of PTSSs. A higher score indicates a more severe PTSS. The Chinese version of the SPAN scale (SPAN-C) that we used was validated in 2003. In psychometric strength, the SPAN-C scale has satisfactory consistency and reliability, with a Cronbach's α of 0.77 and test–retest reliability of 0.90 [13].

Depressive symptoms

The Patient Health Questionnaire-9 (PHQ-9) is a nine-item depression scale module adapted from the full PHQ that screens for depressive symptoms in two weeks before testing using a four-point Likert scale ranging from 0 (not at all) to 3 (nearly every day). The total score ranges from 0 to 27. A higher score for the PHQ indicates more severe depressive symptoms. The PHQ has high reliability and excellent internal consistency, with a Cronbach's α of 0.89 [14].

Self-perceived health

The EuroQol visual analog scale (EQ-VAS) was used to assess the participants' self-rated health in this study. The EQ-VAS is a standardized instrument for measuring generic health status. The measure consists of a vertical line marked from 100 (best imaginable health state) to 0 (worst imaginable

health state). Respondents are asked to draw a line to the VAS to describe their condition [15]. The validity and reliability of the EuroQol for use in patients with cancer have been verified [16].

Cognitive function

We used the functional assessment of cancer therapy-cognitive function (FACT-Cog) to examine the cognitive function of patients with cancer in the seven days before, during, and after receiving chemotherapy. It is a self-report questionnaire that comprises 37 items evaluated using a five-point scale from 0 (never) to 4 (several times a day). A higher score indicates better cognitive function and a lower impact on patient quality of life. It has satisfactory reliability and validity for clinical and research use. The internal consistency of the Chinese version of the FACT-Cog cognitive domain has a Cronbach's α ranging from 0.71 to 0.85 [17].

Chronic pain

We used the VAS for chronic pain to assess participants' chronic pain on an 11-point rating scale ranging from 0 to 10. A higher score indicates higher self-perceived intensity of pain. One study indicated that the VAS for chronic pain is a simple, frequently used, reliable tool to assess variations in the intensity of pain [18].

Statistical analysis

Univariate analyses of the associations between the categorical characteristics and PTSSs of patients with lung cancer were performed, and the results are presented as percentages, means, and standard deviations for categorical variables. The γ of the Pearson correlation analysis was used to examine the association between the continuous variables and PTSSs. A $p = 0.05$ was considered statistically significant. All copies of the questionnaire were examined for the normality of continuous variables in skewness and kurtosis. A linear regression model was used to determine the correlations of PTSS with and without adjustment for the variables. The adjusted multiple regression model included all significant correlates from the unadjusted model. We also did subgroup analyses of different lung cancer treatments (with or without surgery, with or without chemotherapy) and different cancer stages. We used the adjusted R^2 to quantify the variance of PTSS from the regression models. The variance inflation factor, with a recommended level of greater than 5, was used to examine the severity of multicollinearity [19]. We did the Durbin–Watson test to determine whether the residuals from the regression models were independent.

Analyses were done using statistical analytic system version 9.4 (SAS Institute, Cary, North Carolina, USA). An alpha level of 0.05 was considered significant for all analyses.

Results

We recruited 239 patients with lung cancer for this study. Tables 1 and 2 display the associations between PTSD symptom score and demographic characteristics in categorical and continuous variables separately. Higher level of education ($p < 0.01$) and comorbid psychiatric disorders ($p < 0.05$) were significantly associated with PTSSs, and comorbid diabetes

Table 1. Univariate analysis of associations between patients with lung cancer's characteristics and posttraumatic stress symptom ($n = 239$)

Characteristics	*n* (%)	PTSD symptom scores (mean ± SD)
Gender		
Male	161 (67.4)	0.40 ± 1.41
Female	78 (32.6)	0.78 ± 1.86
Education*		
Below senior high school	160 (66.9)	0.28 ± 1.02
Senior high school or higher	79 (33.1)	1.03 ± 2.26
Marital status		
Married	208 (87.0)	0.45 ± 1.43
Not married, widowed or divorced	31 (13.0)	0.54 ± 1.6
Employment		
Full-time	41 (7.2)	0.88 ± 2.48
No	198 (82.8)	0.45 ± 1.32
Smoking		
Never	103 (43.1)	0.71 ± 1.71
Past smoker	126 (52.7)	0.41 ± 1.51
Current smoker	10 (4.2)	0.1 ± 0.32
Drinking		
Yes	23 (9.6)	0.54 ± 1.64
No	216 (90.4)	0.39 ± 0.89
Comorbidity		
Psychiatric history*		
Yes	28 (11.7)	1.68 ± 3.06
No	211 (88.3)	0.37 ± 1.19
Diabetes**		
Yes	51 (21.3)	0.14 ± 0.49
No	188 (78.7)	0.63 ± 1.75
Hypertension		
Yes	98 (41.0)	0.54 ± 1.75
No	141 (59.0)	0.52 ± 1.45
Systemic treatments		
Surgical		
Yes	102 (42.7)	0.61 ± 1.78
No	137 (57.3)	0.47 ± 1.41
Chemotherapy		
Yes	134 (56.1)	0.54 ± 1.75
No	105 (43.9)	0.5 ± 1.35
Radiotherapy		
Yes	68 (28.5)	0.37 ± 1.17
No	171 (71.5)	0.59 ± 1.71
Target therapy		
Yes	54 (22.6)	0.33 ± 0.82
No	185 (77.4)	0.58 ± 1.74
Cancer stage		
I-II	93 (38.9)	0.61 ± 1.71
III-IV	145 (60.7)	0.48 ± 1.5

*$p < 0.05$; **$p < 0.01$ using Chi-square test or *t*-test (or other tests) when appropriate
SD, standard deviation; PTSD, posttraumatic stress disorder

was significantly associated with lower PTSS score ($p < 0.01$). In addition, younger age ($p < 0.01$), depressive symptoms ($p < 0.001$), self-rated health status ($p < 0.05$), and cognitive function ($p < 0.001$) were significantly associated with PTSS score, whereas receiving chemotherapy, surgical intervention, and cancer stage were not associated with PTSS scores. Those variables were generally normally distributed and exhibited appropriate levels of skewness (maximum skewness = 1.912) and kurtosis (maximum kurtosis = 5.257).

In Table 3, we found that the predictors for PTSS among patients with lung cancer in the regression analysis were significantly higher education level ($B = 0.698$, $\beta = 0.197$, $p < 0.01$), significantly poorer cognitive function ($B = -0.037$, $\beta = -0.269$, $p < 0.001$), and depressive symptoms ($B = 0.097$, $\beta = 0.294$, $p < 0.001$) retained their independent associations with PTSSs after adjustment for significant confounders in univariate analyses.

We did subgroup analysis to identify the predictors in patients undergoing surgery and chemotherapy and in patients of different cancer stages. The subgroup analyses indicated that, for patients receiving surgery and those not receiving surgery, higher education level ($B = 1.016$, $\beta = 0.266$, $p < 0.05$; $B = 1.056$, $\beta = 0.204$, $p < 0.05$), and depressive symptoms ($B = 0.154$, $\beta = 0.351$, $p < 0.01$; $B = 0.055$, $\beta = 0.199$, $p < 0.05$) were significant risk factors for PTSS in both groups. Poor cognitive function was a significant risk factor for PTSS in patients undergoing surgery ($B = -0.061$, $\beta = -0.348$, $p < 0.01$). The subgroup analyses comparing patients receiving chemotherapy and those not receiving chemotherapy indicated that higher education level ($B = 0.709$, $\beta = 0.189$, $p < 0.05$; $B = 0.698$, $\beta = 0.220$, $p < 0.05$), psychiatric history ($B = 0.919$, $\beta = 0.162$, $p < 0.05$; $B = 1.095$, $\beta = 0.202$, $p < 0.05$), and poor cognitive function ($B = -0.039$, $\beta = -0.269$, $p < 0.01$; $B = -0.036$, $\beta = -0.283$, $p < 0.05$) were the common significant risk factors for PTSS in both groups. Depressive symptoms ($B = 0.156$, $\beta = 0.478$, $p < 0.001$) were a significant risk factor for PTSS in patients not receiving chemotherapy. Among patients with early-stage lung cancer, higher education level ($B = 1.15$, $\beta = 0.304$, $p < 0.01$), poor cognitive function ($B = -0.061$, $\beta = -0.401$, $p < 0.01$), and depressive symptoms ($B = 0.187$, $\beta = 0.426$, $p < 0.001$) were significantly associated with PTSS score. Among patients with late-stage lung cancer, psychiatric history ($B = 1.095$, $\beta = 0.202$, $p < 0.05$) and poor cognitive

Table 2. Univariate analysis of Pearson correlation between patients with lung cancer's characteristics and posttraumatic stress symptom

Characteristics	Mean ± SD	PTSD (*r*)
Age (year-old)	63.75 ± 9.75	−0.171**
BMI (kg/m^2)	24.46 ± 3.86	0.062
Chronic pain (score)	0.44 ± 0.5	0.116
Depression (PHQ-9)	4.98 ± 4.91	0.44***
EQ-VAS	66.69 ± 17.02	−0.167*
FACT-Cog		
Perceived cognitive impairments	67.6 ± 6.89	−0.413***
Comments from others	15.67 ± 1.18	−0.203**
Perceived cognitive abilities	22.28 ± 5.22	−0.121
Impact on quality of life	15.46 ± 1.72	−0.433***
Total score	120.35 ± 11.87	−0.403***

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$ using Chi-square test or *t*-test (or other tests) when appropriate
BMI, body mass index; FACT-Cog, functional assessment of cancer therapy-cognitive; PHQ-9, Patient Health Questionnaire-9; EQ-VAS, EuroQol visual analog scale; SD, standard deviation; PTSD, posttraumatic stress disorder

Table 3. Predictors for posttraumatic stress symptom in patients with lung cancer ($n = 239$)

Variable	Unadjusted model					Adjusted model					
	B	SE	β	Adjusted R^2	DW	*B*	SE	β	VIF	R^2	DW
Age (years)	−0.028	0.010	−0.171**	0.025	2.080	-	-	-	-	0.305	2.019
Education											
Below senior high school (reference)	-	-	-	-	-	-	-	-	-		
Senior high school or higher	0.774	0.212	0.222**	0.045	2.09	0.698	0.23	0.197**	1.292		
Psychiatric history											
No (reference)	-	-	-	-	-	-	-	-	-		
Yes	1.304	0.307	0.266***	0.067	2.09	-	-	-	-		
Diabetes											
No (reference)	-	-	-	-	-	-	-	-	-		
Yes	−0.496	0.248	−0.129*	0.012	2.091	-	-	-	-		
Quality of life (EQ-VAS)	−0.016	0.006	−0.167*	0.024	2.056	-	-	-	-		
Cognitive (FACT-Cog total score)	−0.054	0.008	−0.103***	0.159	1.998	−0.037	0.009	−0.269***	1.368		
Depression (PHQ-9)	0.142	0.019	0.44***	0.19	2.016	0.097	0.024	0.294***	1.628		

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$ using Chi-square test or *t*-test (or other tests) when appropriate
Adjusted model was applied using a stepwise linear regression, wherein all statistically significant correlates from the unadjusted model were added.
β, standardized regression coefficients; *B*, regression coefficient;
FACT-Cog, functional assessment of cancer therapy-cognitive; PHQ-9, Patient Health Questionnaire-9; SE, standard error; VIF, variance inflation factor; DW, Durbin-Watson test

Table 4. Association factors of posttraumatic stress symptom in patient with lung cancer stratified by chemotherapy, surgery and cancer stage

Stratified	Variable	*B*	SE	β	R^2	DW
Surgery						
Received surgery (*n* = 102)	Education: Senior high school or higher	1.016	0.385	0.266*	0.338	1.882
	Cognitive (FACT-Cog total score)	−0.061	0.018	−0.348**		
	Depression (PHQ-9)	0.154	0.047	0.351**		
Without surgery (*n* = 137)	Education: Senior high school or higher	1.056	0.435	0.204*	0.369	1.976
	Depression (PHQ-9)	0.055	0.027	0.199*		
Chemotherapy						
Received chemotherapy (*n* = 134)	Education: Senior high school or higher	0.709	0.298	0.189*	0.34	1.882
	Psychiatric history	0.919	0.458	0.162*		
	Cognitive (FACT-Cog total score)	−0.039	0.012	−0.269**		
Without chemotherapy (*n* = 105)	Education: Senior high school or higher	0.698	0.346	0.220*	0.272	2.121
	Psychiatric history	1.095	0.473	0.202*		
	Cognitive (FACT-Cog total score)	−0.036	0.014	−0.283*		
	Depression (PHQ-9)	0.156	0.037	0.478***		
Stage						
Cancer stage I-II (*n* = 94)	Education: Senior high school or higher	1.150	0.364	0.304**	0.452	2.041
	Cognitive (FACT-Cog total score)	−0.061	0.018	−0.401**		
	Depression (PHQ-9)	0.187	0.044	0.426***		
Cancer stage III-IV (*n* = 145)	Psychiatric history	1.095	0.473	0.202*	0.237	1.836
	Cognitive (FACT-Cog total score)	−0.023	0.011	−0.182*		

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$ using Chi-square test or *t*-test (or other tests) when appropriate
Adjusted model was applied using a stepwise linear regression, wherein all statistically significant correlates from the unadjusted model were added.
β, standardized regression coefficients; *B*, regression coefficient;
FACT-Cog, functional assessment of cancer therapy-cognitive; PHQ-9, patient health questionnaire-9; SE, standard error, DW, Durbin-Watson test

function ($B = -0.023$, $\beta = -0.182$, $p < 0.05$) were significantly associated with PTSS score.

Discussion

In the present study (Table 3), we found that the predictive factors of PTSSs for lung cancer were significantly higher education level ($p < 0.05$), significantly more severe depressed mood ($p < 0.001$), and significantly poorer cognitive ability ($p < 0.001$). We further investigated the PTSS predictors through subgroup analysis; this may facilitate the creation of mental health promotion plans for patients. When investigating the risk factors in patients undergoing different treatments, high education level was the common risk factor for PTSS among all treatments (Table 4). Other risk factors for PTSS, including psychiatric history, poor cognitive function, and depressive symptoms, were comparable to risk factors generally observed in patients with lung cancer. When investigating the risk factors in different cancer stages, cognitive function was the common risk factor for PTSS in both early and late cancer stages (Table 4).

Studies showed that younger age, a history of smoking, a less sedentary lifestyle, more severe initial cancer symptoms, anxiety, and postoperative pain are potential predictors for PTSS among patients with lung cancer [8, 9]. Our study also supports the premise that poor cognitive ability and depressive symptoms can predict PTSS (Table 3). Patients with a history of depression before diagnosis of lung cancer may have already had poor mental health at the time of diagnosis [20, 21]. Worsening depressed mood after a cancer diagnosis results in reduced quality of life and distress among patients and thus increases their vulnerability to PTSSs [22]. Studies showed that poor quality of life and high symptom burden are risk factors lung cancer mortality [23, 24]. Early detection of PTSSs in patients with lung cancer is critical for care planning.

One noteworthy finding in our study (Table 3) is that a high education level predicted PTSSs in patients with lung cancer ($p < 0.05$). This finding is inconsistent with the results of a previous study investigating patients with breast cancer [25]. Studies have speculated that those with a lower level of education may have worse physical fitness and shorter life expectancies than those of patients with higher levels of education, and this is proposed to lead to vulnerability to PTSSs [26, 27]. In our study, we found that high education level was a common predictor for PTSSs in patients with lung cancer, even in most group analyzed (Table 4). One possible explanation is that patients with a high level of education may experience a more decrease in their physical and psychological health on diagnosis, and the diagnosis may considerably influence their quality of life.

In this study, we found that the predictors among patients who received surgery and those who did not receive surgery were negligibly different. For early-stage lung cancer, surgical resection is the standard treatment, meaning that the patients in the nonsurgery group have a more advanced stage of the disease and possibly poorer physical and psychological health [28]. This finding may suggest that, whether the prognosis is good or not, the lung cancer diagnosis itself makes patients more vulnerable to PTSSs. Pain-induced somatic, cognitive,

emotional, and behavioral responses are similar to the features of the reaction to traumatic stress [29]. Jeantieu et al. [9] also expressed that preoperative anxiety and postoperative pain are strong predictors for PTSSs. However, we did not observe the same finding in our study (Table 4).

The analysis of the chemotherapy and nonchemotherapy subgroups revealed common predictors, including high education level, psychiatric history, and poor cognitive function; these were similar to the overall PTSS predictors for patients with lung cancer (Table 4). The only difference between the chemotherapy group and nonchemotherapy groups was the association of depressive symptoms with PTSS for patients not undergoing chemotherapy; this association was not evident for patients receiving chemotherapy (Table 4). The condition of patients receiving chemotherapy is likely to vary. Patients not receiving chemotherapy may have either early-stage disease or poor physical conditions that make chemotherapy inappropriate [30]. We infer that patients who have a poor physical condition and who cannot tolerate chemotherapy may have a higher burden of life-threatening stress, which leads them to develop depressive symptoms. Nonchemotherapy patients who have depressive symptoms were vulnerable to PTSSs; this may be caused by the fear of death. It may be that patients with depression have poor interactions and communication with their medical provider, resulting in poor clinical outcomes in patients with lung cancer [31-33]. Another factor may be that patients with unresectable lung cancer who must receive chemotherapy often delay and reduce chemotherapy regimens because of depression and fear of suffering from severe cancer-related symptoms when undergoing chemotherapy [34-36]. The vulnerability to PTSSs may be caused by a lower overall survival rate resulting from treatment adherence [37]. Therefore, we should pay more attention to people with mental health problems before the administration of chemotherapy. Patients with lung cancer receiving chemotherapy should not only consider their physical condition but also their mental health and the prevention of PTSSs.

When investigating PTSS predictors in different cancer stages, the PTSS predictors in the early-stage disease group were similar to those of general patients with lung cancer (Table 4). This result suggests that the mental health of patients with lung cancer should continue to be monitored even if their physical condition and prognosis are both good. History of psychiatric disorder in our study (Table 4) was significantly associated with PTSSs for only patients with advanced-stage lung cancer ($p < 0.05$). Psychiatric disorders such as depression have been associated with smoking; the comorbid symptoms of smoking, such as cough and shortness of breath, may mask lung cancer-specific symptoms and thus delay diagnosis and result in poor prognosis [38]. Therefore, in addition to physical improvement programs, mental health promotion programs should be offered to patients with advanced-stage lung cancer.

Study limitations

The readers are advised not to over-interpret our study results because this study has eight limitations:

- Causal inference was limited because this study was cross-sectional. Detection of possible predictors was limited by the small sample size (although it was larger than those in previous studies) [8, 10].
- We did not include all of the possible psychological correlations and characteristics of PTSSs that have been reported in the literature [3].
- Because of differences in the overall survival rate and treatment strategies, a subgroup analysis of patients with non-small-cell and small-cell lung cancer should be considered.
- The PTSD Checklist (PCL) was used in the literature, whereas SPAN-C was used in our study. One study suggested that PCL (area under the curve [AUC] = 0.882) is the preferred screening tool (significant difference in overall diagnostic ability), whereas SPAN-C (AUC = 0.837) is easier toadminister [39].
- In addition to the risks of PTSSs for the patients with cancer reported in this study, a reverse-risk association may exist. One systemic review reported no positive significant associations between psychological trauma and lung cancer [40]. In addition, Cohn et al. [41] conducted a study with a large-nest cohort in the United Kingdom to identify additional risks for future cancer diagnosis for patients with PTSD. Among four types of cancer (lung, colorectal, breast, and prostate), no significant association was observed between PTSD diagnosis and cancer diagnosis. This result suggests that PTSD cannot predict cancer risk. But that the study was sampled the population of the United Kingdom. Studies should be done for other populations, such as those of Asia.
- The average age of our study was 63.75 ± 9.75. Although chemotherapy may also affect cognitive function, age-associated cognitive function decline was also to be considered. Further study of young and elderly patients should be warranted.
- Considering the high comorbidity between lung cancer and major depression [42], we excluded patients with major psychiatric disorder history except for major depression. But patients with depression and PTSD may share some overlapping symptoms [43] which may result in different treatment strategies. Sub-analysis of PTSS in lung cancer patients without major depression should be conducted in future research.

Summary

Our study revealed that higher education level, more severe depressive symptoms, and poorer cognitive function are particularly noteworthy risk factors for PTSSs. Patients with a history of psychiatric disorders should also be aware of their risk of PTSS, especially patients with advanced-stage cancer and those undergoing chemotherapy. Psychological burden screening, cognitive function examination, and rehabilitation should be considered in the clinical practice of oncology.

Financial Support and Sponsorship

This study was supported by grants from the Chang Gung Memorial Hospital, Chiayi, Taiwan (grant numbers = CORPG6G0101-103, CORPG6G0131-133).

Conflicts of Interest

Prof. Vincent Chin-Hung Chen, an editorial board member at *Taiwanese Journal of Psychiatry* (Taipei), had no rôle in the peer review process of or decision to publish this article. The other authors declared no conflicts of interest in writing this paper.

References

1. Lee MJ, Huang CW, Lee CP, et al.: Investigation of anxiety and depressive disorders and psychiatric medication use before and after cancer diagnosis. *Psychooncology* 2021; 30: 919-27.
2. Alter CL, Pelcovitz D, Axelrod A, et al.: Identification of PTSD in cancer survivors. *Psychosomatics* 1996; 37: 137-43.
3. Kangas M, Henry JL, Bryant RA: Posttraumatic stress disorder following cancer. a conceptual and empirical review. *Clin Psychol Rev* 2002; 22: 499-524.
4. Bryant RA, Harvey AG: Psychological impairment following motor vehicle accidents. *Aust J Public Health* 1995; 19: 185-8.
5. Koopman C, Classen C, Spiegel D: Predictors of posttraumatic stress symptoms among survivors of the Oakland/Berkeley, Calif., firestorm. *Am J Psychiatry* 1994; 151: 888-94.
6. McFarlane AC, Papay P: Multiple diagnoses in posttraumatic stress disorder in the victims of a natural disaster. *J Nerv Ment Dis* 1992; 180: 498-504.
7. World Health Organization: *Cancer*. Geneva, Swilzerland: World Health Organization. 2021.
8. Ni J, Feng J, Denehy L, et al.: Symptoms of posttraumatic stress disorder and associated risk factors in patients with lung cancer: a longitudinal observational study. *Integr Cancer Ther* 2018; 17: 1195-203.
9. Jeantieu M, Gaillat F, Antonini F, et al.: Postoperative pain and subsequent PTSD-related symptoms in patients undergoing lung resection for suspected cancer. *J Thorac Oncol* 2014; 9: 362-9.
10. Dougall AL, Swanson J, Kyutoku Y, et al.: Posttraumatic symptoms, quality of life, and survival among lung cancer patients. *J Appl Biobehav Res* 2017; 22: e12065.
11. Abbey G, Thompson SB, Hickish T, et al.: A meta-analysis of prevalence rates and moderating factors for cancer-related post-traumatic stress disorder. *Psychooncology* 2015; 24: 371-81.
12. Redd WH, DuHamel KN, Vickberg SM, et al.: Long-term adjustment in cancer survivors: Integration of classical-conditioning and cognitive-processing models. In: Andersen BL, editor. *Psychosocial Interventions for Cancer*. Washington DC: American Psychological Association, 2001. p. 77-97.
13. Chen CH, Shen WW, Tan HK, et al.: The validation study and application of stratum-specific likelihood ratios in the Chinese version of SPAN. *Compr Psychiatry* 2003; 44: 78-81.
14. Kroenke K, Spitzer RL, Williams JB: The PHQ-9: Validity of a brief depression severity measure. *J Gen Intern Med* 2001; 16: 606-13.
15. Feng Y, Parkin D, Devlin NJ.: Assessing the performance of the EQ-VAS in the NHS PROMs programme. *Qual Life Res* 2014; 23: 977-89.
16. van Hout B, Janssen MF, Feng YS, et al.: Interim scoring for the EQ-5D-5L: Mapping the EQ-5D-5L to EQ-5D-3L value sets. *Value Health* 2012; 15: 708-15.
17. Cheung YT, Lim SR, Shwe M, et al.: Psychometric properties and measurement equivalence of the English and Chinese versions of the functional assessment of cancer therapy-cognitive in Asian patients with breast cancer. *Value Health* 2013; 16: 1001-13.
18. Carlsson AM: Assessment of chronic pain. I. Aspects of the reliability and validity of the visual analogue scale. *Pain* 1983; 16: 87-101.
19. O'brien RM: A caution regarding rules of thumb for variance inflation factors. *Qual Q* 2007; 41: 673-90.
20. Wang YH, Li JQ, Shi JF, et al.: Depression and anxiety in relation to cancer incidence and mortality: a systematic review and meta-analysis of cohort studies. *Mol Psychiatry* 2020; 25: 1487-99.
21. Jia Y, Li F, Liu YF, et al: Depression and cancer risk: a systematic review and meta-analysis. *Public Health* 2017; 149: 138-48.
22. Tishelman C, Degner LF, Rudman A, et al.: Symptoms in patients with lung carcinoma: Distinguishing distress from intensity. *Cancer* 2005; 104: 2013-21.
23. Tishelman C, Petersson LM, Degner LF, et al.: Symptom prevalence, intensity, and distress in patients with inoperable lung cancer in relation to time of death. *J Clin Oncol* 2007; 25: 5381-9.
24. Cheville AL, Novotny PJ, Sloan JA, et al.: The value of a symptom cluster of fatigue, dyspnea, and cough in predicting clinical outcomes in lung cancer survivors. *J Pain Symptom Manage* 2011; 42: 213-21.
25. Jacobsen PB, Widows MR, Hann DM, et al.: Posttraumatic stress disorder symptoms after bone marrow transplantation for breast cancer. *Psychosom Med* 1998; 60: 366-71.
26. Herndon JE 2nd, Kornblith AB, Holland JC, et al.: Patient education level as a predictor of survival in lung cancer clinical trials. *J Clin Oncol* 2008; 26: 4116-23.
27. Di Maio M, Signoriello S, Morabito A, et al.: Prognostic impact of education level of patients with advanced non-small cell lung cancer enrolled in clinical trials. *Lung Cancer* 2012; 76: 457-64.
28. Howington JA, Blum MG, Chang AC, et al.: Treatment of stage I and II non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American college of chest physicians evidence-based clinical practice guidelines. *Chest* 2013; 143: S278-313.
29. Kleiman V, Clarke H, Katz J: Sensitivity to pain traumatization: A higher-order factor underlying pain-related anxiety, pain catastrophizing and anxiety sensitivity among patients scheduled for major surgery. *Pain Res Manag* 2011; 16: 169-77.
30. Nasim F, Sabath BF, Eapen GA: Lung cancer. *Med Clin North Am* 2019; 103: 463-73.
31. Lin J, McGlynn KA, Carter CA, et al.: The impact of preexisting mental health disorders on the diagnosis, treatment, and survival among lung cancer patients in the U.S. military health system. *Cancer Epidemiol Biomarkers Prev* 2016; 25: 1564-71.
32. Lin JJ, Lake J, Wall MM, et al. Association of patient-provider communication domains with lung cancer treatment. *J Thorac Oncol* 2014; 9: 1249-54.
33. Dalton AF, Bunton AJ, Cykert S, et al.: Patient characteristics associated with favorable perceptions of patient-provider communication in early-stage lung cancer treatment. *J Health Commun* 2014; 19: 532-44.
34. Akechi T, Okamura H, Nishiwaki Y, et al.: Psychiatric disorders and associated and predictive factors in patients with unresectable nonsmall cell lung carcinoma: A longitudinal study. *Cancer* 2001; 92: 2609-22.
35. Tchekmedyian NS, Kallich J, McDermott A, et al.: The relationship between psychologic distress and cancer-related fatigue. *Cancer* 2003; 98: 198-203.
36. Thuné-Boyle IC, Myers LB, Newman SP. The role of illness beliefs, treatment beliefs, and perceived severity of symptoms in explaining distress in cancer patients during chemotherapy treatment. *Behav Med* 2006; 32: 19-29.
37. Greer JA, Pirl WF, Park ER, et al.: Behavioral and psychological predictors of chemotherapy adherence in patients with advanced non-small cell lung cancer. *J Psychosom Res* 2008; 65: 549-52.
38. Iachina M, Brønserud MM, Jakobsen E, et al.: History of depression in lung cancer patients: impact of delay. *Clin Oncol (R Coll Radiol)* 2017; 29: 585-92.
39. Yeager DE, Magruder KM, Knapp RG, et al.: Performance characteristics of the posttraumatic stress disorder checklist and SPAN in veterans affairs primary care settings. *Gen Hosp Psychiatry* 2007; 29: 294-301.
40. Pereira MA, Araújo A, Simões M, et al.: Influence of psychological factors in breast and lung cancer risk – a systematic review. *Front Psychol* 2021; 12: 769394.
41. Cohn E, Lurie I, Yang YX, et al.: Posttraumatic stress disorder and cancer risk: A nested case-control study. *J Trauma Stress* 2018; 31: 919-26.
42. Walker J, Hansen CH, Martin P, et al.: Prevalence, associations, and adequacy of treatment of major depression in patients with cancer: A cross-sectional analysis of routinely collected clinical data. *Lancet Psychiatry* 2014; 1: 343-50.
43. Flory JD, Yehuda R: Comorbidity between post-traumatic stress disorder and major depressive disorder: alternative explanations and treatment considerations. *Dialogues Clin Neurosci* 2015; 17: 141-50.