Uncertainty and psychological adjustment in patients with lung cancer

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Abstract

Background: For many patients with lung cancer, disease progression occurs without notice or with vague symptoms, and unfortunately, most treatments are not curative. Given this unpredictability, we hypothesized the following: (1) poorer psychological adjustment (specifically, more depressive symptoms, higher perceptions of stress, and poorer emotional well-being) would be associated with higher intolerance for uncertainty, higher perceived illness-related ambiguity, and their interaction; and (2) greater avoidance would mediate associations between higher intolerance of uncertainty and poorer psychological adjustment.

Methods: Participants ($N = 49$) diagnosed with lung cancer at least 6 months prior to enrollment completed the Center for Epidemiologic Studies – Depression Scale, the Functional Assessment of Cancer Therapy – Lung Emotional Well-being subscale, the Perceived Stress scale, the Intolerance of Uncertainty scale, the Mishel Uncertainty in Illness Scale Ambiguity subscale, the Impact of Event – Revised Avoidance subscale, and the Short-scale Eysenck Personality Questionnaire – Revised Neuroticism subscale. Mean age was 64.2 years (standard deviation [SD] = 11.0), mean years of education was 15.6 (SD = 3.1), and 71.4% were female. Hypotheses were tested with regression analyses, adjusted for neuroticism.

Results: Higher perceptions of stress and poorer emotional well-being were associated with higher levels of intolerance of uncertainty and higher perceived illness-related ambiguity. Non-somatic depressive symptoms were associated with higher levels of intolerance of uncertainty. Avoidance was found to mediate relations of intolerance of uncertainty with non-somatic depressive symptoms and emotional well-being only.

Conclusions: Findings suggest that interventions to address avoidance and intolerance of uncertainty in individuals with lung cancer may help improve psychological adjustment.
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Introduction

Lung cancer is the second most frequently diagnosed cancer in the USA and the most common cause of cancer-related deaths [1]. Unfortunately, with its 16% 5-year survival rate, lung cancer is incurable for the majority of the over 400,000 individuals alive today who have the disease [1–3]. Thus, lung cancer survivorship often entails living with the knowledge that one is not fully cured. Because of the imminent risk of cancer recurrence or disease progression, patients are likely to view their futures as uncertain.

Both during and after treatment, individuals with lung cancer may experience a difficult disease course with higher levels of distress related to physical symptoms [4], greater challenges in psychological health and daily living [5], and higher levels of burden from their symptoms [6] than those with other types of cancer. Patients may experience nonspecific symptoms such as cough, pain, or fatigue that can indicate side effects of treatment, evidence of cancer growth, physical sequelae of stress, or conditions unrelated to disease [7,8]. They may not know whether these nonspecific symptoms signify progression of cancer, and as a result, survivorship can be fraught with ambiguity. Ambiguity has been positively associated with difficulties with psychological adjustment in patients with other cancers

[9–12]. To examine the contribution of ambiguity further, we also propose to study individuals' thresholds of tolerance for uncertainty.

If an individual who generally perceives uncertainty as unacceptable is faced with a situation that is highly ambiguous, excessive worrying may result [13]. One experimental study demonstrated that individuals who had a high intolerance of uncertainty, when presented with a condition with high situational uncertainty, worried more than those who had lower intolerance or a condition with lower uncertainty regarding health information [14]. Thus, individuals with a high intolerance of uncertainty, when faced with ambiguous symptoms, may experience increased psychological distress. Because symptoms of lung cancer, such as cough and fatigue, can either be minor and unrelated to cancer or signal a life-threatening progression of disease, symptom ambiguity is likely to be a challenge for some patients.

In this study, we hypothesized that higher levels of intolerance of uncertainty and illness-related ambiguity together would be independent predictors of more depressive symptoms, higher levels of perceived stress, and poorer emotional well-being compared with lower intolerance of uncertainty. In addition, we hypothesized that there would be a significant interaction such that individuals who have both a higher intolerance of uncertainty and higher perceived ambiguity

about their illness would have more difficulty adjusting than individuals who have lower levels of either or both. We adjusted statistically for neuroticism to distinguish intolerance of uncertainty from the potentially overlapping constructs of neuroticism [15,16].

We also sought to examine a possible mechanism for an association between intolerance of uncertainty and psychological adjustment. Cognitive models theorize that a high level of intolerance of uncertainty could manifest as the tendency to avoid uncertain situations [13]. For example, thought suppression, a dimension of cognitive avoidance, has been found to correlate positively with intolerance of uncertainty in one study in a non-clinical population [17]. Avoidance, a common reaction to traumatic events such as cancer diagnosis, can interfere or suppress effective processing of the events and hinder psychological adjustment [18,19]. Thus, avoidance of threatening images and thoughts may mediate the negative association between intolerance of uncertainty and psychological adjustment. We hypothesized that greater cancer-related avoidance would account for the relation between higher intolerance of uncertainty and more depressive symptoms, higher perceptions of stress, and poorer emotional well-being after adjusting for neuroticism.

Method

Participants and procedures

Participants were recruited from the University of California, Los Angeles (UCLA) Hematology/Oncology Clinics in Santa Monica and Los Angeles, California, between January 2009 and August 2011. Potential participants were eligible if they met the following inclusion criteria: (1) diagnosed for a minimum of 6 months with cancer of the lung with the exclusion of mesothelioma; (2) at least 18 years old; and (3) able to read and respond to questionnaires in English. Patients who had a diagnosis of melanoma or a non-skin-related cancer during the past 5 years were excluded. Of the 101 patients contacted, 7 were ineligible, and 11 declined participation because of unwillingness or expected difficulty in discussing their experiences, other priorities, and unknown reasons. Questionnaires were not returned by 34 patients who had initially agreed to participate because of death ($n = 3$), other pressing life events ($n = 2$), or unknown reasons. The remaining 49 participants (52% of those eligible) completed the study.

Mean age of participants was 64.2 years (SD = 11.0; range = 37–86). The sample was 71.4% female, 49.0% married or living as married, 24.3% widowed, and 18.4% divorced or separated. Ethnicity was 72.3% white, 19.1% Asian, 4.3% Latino, and 4.3% other. Mean years of education was 15.6 (SD = 3.1), and 33.3% were employed. Diagnoses were reported as 68.1% with non-small cell cancer (90.6% as Stage III or IV, 3.1% as Stage I or II, and 6.3% as unknown), 12.8% with small cell cancer (16.7% as limited and 83.3% as unknown), 12.8% with 'other lung cancer' (50% as Stage III or IV and 50% as unknown), and 6.4% who were unsure. Cancer treatments, either in the past or currently, included surgery (38.8%), chemotherapy (79.6%), radiation (53.1%), and at least one other mode of therapy such as biological therapy (53.2%). Average time elapsed since diagnosis was 29.0 months (SD = 35.9; range = 6–199). Only 6.7% of our sample reported that their tumor was now undetectable, 60.0% reported their tumor was getting smaller or had stopped growing, 28.9% reported their tumor was growing, and 4% reported they were unsure.

During their medical visit, potential participants were introduced to the study by the medical oncologist (E. B. G.), who was not aware of whether they ultimately elected participation. If they agreed to learn more, the researcher (K. K.) described the study, performed the eligibility screen, and if applicable, obtained informed consent. Questionnaires and pre-stamped return envelopes were provided. The study was approved by the UCLA Institutional Review Board.

Measures

Demographic and medical information

Age, sex, relationship status, ethnicity, years of education, employment status, treatment, stage of cancer at diagnosis, and time since diagnosis were obtained by questionnaire.

Intolerance of uncertainty

The Intolerance of Uncertainty Scale (IUS) measures emotional, cognitive, and behavioral reactions to uncertain situations [13,20]. Participants rated 27 items such as 'the smallest doubt can stop me from acting' and 'I must get away from all uncertain situations' on a scale from 1 (not at all characteristic of me) to 5 (entirely characteristic of me). The measure has excellent internal consistency, good test–retest reliability, and convergent and divergent validity [13]. Higher scores indicate higher intolerance of uncertainty. In this sample, internal reliability was $\alpha = 0.95$.

Perceived illness-related uncertainty

The Mishel Uncertainty in Illness Scale (MUIS) measures uncertainty related to a specific illness, including concepts of symptoms, diagnosis, treatment, relationships with caregivers, and planning for the future [21]. We used the 16-item ambiguity subscale of the two-factor, 28-item version of the MUIS to capture the degree to which participants perceive cues about their cancer to be vague and indistinct today. The items, such as 'I am unsure if my illness is getting better or worse' and 'it is not clear what is going to happen to me,' are rated on a scale from 1 (strongly disagree) to 5 (strongly agree) with higher scores indicating more perceived ambiguity. The scale has demonstrated high reliability and convergent validity [21]. Reliability for the illness-related ambiguity scale in our sample was $\alpha = 0.87$.

Avoidance

The Impact of Event Scale – Revised (IES-R) assesses the frequency of avoidance and other reactions to stressful life events within the last 7 days and is psychometrically sound [22,23]. Participants were asked to 'indicate how distressing each difficulty has been for you during the past 7 days with respect to your lung cancer' on a scale of 0 (not at all) to 4 (extremely). Participants completed the eight-item avoidance subscale, which had $\alpha = 0.84$.

Psychological adjustment

Three variables assessed positive psychological adjustment: fewer depressive symptoms, fewer symptoms of perceived stress, and better emotional well-being. The Center for Epidemiologic Studies – Depression Scale (CES-D) measures depressive symptomatology in a non-clinical population and has excellent reliability and validity [24]. The CES-D asks respondents to rate how often each item was felt during the past week on a scale of 0 (rarely or none of the time) to 3 (most or all of the time). Higher scores reflect more depressive symptoms, with a score of 16 or higher indicating a level of symptoms similar to those reported by individuals with diagnosable depression [25]. Because the CES-D includes four items that may measure the physical effects of cancer and its treatment, a modified non-somatic depressive symptoms scale was created that omits these somatic items: 'I did not feel like eating; my appetite was poor', 'I felt that everything I did was an effort', 'my sleep was restless', and 'I could not "get going"'. For both the full CES-D and the 16-item, non-somatic depressive symptoms scale, $\alpha = 0.86$.

The Perceived Stress Scale (PSS) measures the extent to which circumstances in one's life are perceived to be stressful [26]. The 14-item PSS asks respondents to rate how often they felt or thought a particular way during the last month on a scale from 0 (never) to 4 (very often). The scale has substantial reliability and validity [26]. Higher scores reflect a greater level of perceived stress. In our sample, $\alpha = 0.87$.

The Functional Assessment of Cancer Therapy – Lung (FACT-L), measuring quality of life for patients receiving cancer treatment with special emphasis on lung cancer symptomatology [27], is based on the Functional Assessment of Cancer Therapy – General and the lung cancer subscale, which has established reliability and validity [28]. We used the five items of the emotional well-being subscale from FACT-L (V3). Items are rated on a 0 (not at all) to 4 (very much) scale. Higher scores reflect a more positive quality of life. In our sample, $\alpha = 0.80$ for the emotional well-being subscale.

Neuroticism

Including neuroticism as a covariate provides discriminant validity with both perceived illness-related ambiguity and intolerance of uncertainty and allows for adjustment for anxiety symptoms that might also be associated with psychological adjustment. Participants completed the Short-scale Eysenck Personality Questionnaire – Revised (EPQ-R) neuroticism subscale [29]. The 12-item subscale asks respondents to provide dichotomous responses on questions about their moods and how they would characterize their feelings. Our sample's reliability was $\alpha = 0.82$ [29].

Statistical analysis

Correlations between demographic and medical variables (i.e., age, sex, living as married, years of education, employment status, surgery, chemotherapy, radiation, and time since diagnosis) and criterion variables were examined, in order to include significant correlates in analyses as covariates in addition to neuroticism. To examine the extent to which the main effects of intolerance of uncertainty and

perceived illness-related ambiguity and their interaction were related to depressive symptoms, perceived stress, and emotional well-being, hierarchical regression analyses were conducted for each criterion variable. Blocks of predictor variables were entered into regression models: the first block with covariates, the second block with the IUS and the MUIS ambiguity subscale, and the third block with the interaction term, which was the product of the centered scores of the IUS and the MUIS ambiguity subscale. This method allowed us to examine whether each block of predictor variables significantly contributed to explaining the variance in the criterion variable.

To test the extent to which avoidance mediated the relation between intolerance of uncertainty and psychological adjustment, a set of four regression equations was analyzed with the same covariates: (1) regressing avoidance on IUS (path a), (2) regressing each psychological adjustment criterion variable on avoidance as a direct effect (path b); (3) regressing each psychological adjustment criterion variable on IUS as a total effect without avoidance (path c); and (4) regressing each psychological adjustment criterion variable on IUS as a direct effect with avoidance (path c′). We tested whether there was a significant difference in path c and path c′ for indirect effects using bootstrapping, which is considered to be more powerful and less limiting than the Baron and Kenny [30] approach as the latter requires paths a, b, and c to be significant and distribution assumptions to be met, especially for smaller samples [31,32]. When the 95% confidence intervals (CIs) of the random sampling bootstrapping results did not include zero, we concluded that the indirect effect was significant [32].

Results

Table 1 describes the means and ranges of the criterion, predictor, and other relevant variables. Age, sex, living as married, years of education, employment status, surgery, chemotherapy, radiation, and time since diagnosis were not significantly correlated with the criterion variables. Thus, only neuroticism was statistically controlled in subsequent analyses. There were significant correlations between IUS and the MUIS ambiguity subscale ($r = 0.43$, $p = 0.004$) and each with neuroticism (with IUS, $r = 0.52$, $p < 0.001$; with the MUIS ambiguity subscale, $r = 0.44$, $p = 0.002$). Our sample reported levels of depressive symptoms that were higher than those reported in the literature by patients with cancer at other sites such as breast or prostate [33–35]. Our sample's reported mean level of depressive symptoms of 16 is similar to that reported in other studies of lung cancer patients [36], and 49.0% of our sample had scores of 16 or more, indicating about half of our sample was experiencing depressive symptoms similar to individuals diagnosed with depression. The sample also reported higher levels of perceived stress than men treated for prostate cancer [37].

Intolerance of uncertainty and illness-related ambiguity as predictors

Results of the regression analyses are described in Table 2. Higher intolerance of uncertainty was significantly associated with more non-somatic depressive symptoms, more

Table 1. Means and ranges of variables

	n	Mean (SD)	Possible range		Observed range	
			Min	Max	Min	Max
CES-D	49	16.1 (9.9)	0	60	1	39
Non-somatic CES-D[a]	49	11.9 (8.3)	0	48	0	33
PSS	47	23.3 (8.5)	0	56	5	42
Emotional Well-being subscale of FACT-L	49	13.2 (4.7)	0	20	0	20
IUS	46	50.6 (19.2)	27	135	27	102
Ambiguity subscale of MUIS	46	40.5 (11.4)	16	80	16	61
Neuroticism subscale of EPQ-R	47	3.9 (3.1)	0	12	0	12
Avoidance subscale of IES-R	48	8.8 (6.6)	0	32	0	25

CES-D, Center for Epidemiologic Studies – Depression Scale; PSS, Perceived Stress Scale; FACT-L, Functional Assessment of Cancer Therapy – Lung; IUS, Intolerance of Uncertainty Scale; MUIS, Mishel Uncertainty in Illness Scale; EPQ-R, Eysenck Personality Questionnaire – Revised; Min, minimum; Max, maximum.
[a]Non-somatic CES-D omits four somatic symptoms of depression.

perceived stress, and less emotional well-being, even after adjusting for neuroticism and illness-related ambiguity. Higher illness-related ambiguity was independently associated with more perceived stress and less emotional well-being. The interaction of intolerance of uncertainty and illness-related ambiguity was not associated with any of the psychological adjustment outcomes.

Avoidance as a mediator

The significant mediation models are described in Figure 1. There was evidence that avoidance completely mediated the effect of IUS on non-somatic depressive symptoms and emotional well-being (point estimate for path c – path $c' = 0.08$, 95% CIs: 0.004, 0.24; point estimate $= -0.06$, 95% CIs: -0.17, -0.02, respectively). An indirect effect was not found for avoidance between IUS and perceived stress (point estimate for path c – path $c' = 0.06$, 95% CIs: -0.004, 0.21).

Discussion

Findings demonstrate that attitudes and perceptions of uncertainty, along with neuroticism, explained a noteworthy proportion of the variance in poor psychological adjustment in this sample of individuals with lung cancer. Specifically, perceived stress and emotional well-being were explained by both general intolerance of uncertainty and the perceived ambiguity of the cancer. Intolerance of uncertainty also predicted non-somatic depressive symptoms. Although an association between intolerance of uncertainty and illness-related ambiguity was found, perhaps because both ask participants to evaluate perceptions and thresholds of ambiguous or uncertain situations, they each contributed independently and similarly to explaining the variance in perceived stress and emotional well-being.

Perhaps illness-related ambiguity was not associated with non-somatic depressive symptoms because the outcome measure excluded the very somatic symptoms that might have caused ambiguity. Indeed, a regression performed on our sample with the full-scale CES-D using the same predictors demonstrated that both main effects were significant ($p = 0.029$ for IUS and $p = 0.048$ for the MUIS ambiguity subscale).

Intolerance of uncertainty was positively associated with avoidance, suggesting that patients with a high intolerance of uncertainty may have found the unknown aspects of the illness difficult or unpleasant to consider or proactively manage. The majority of our participants agreed with statements such as 'I am unsure if my illness is getting better or worse' and 'It is difficult to determine how long it will be before I can care for myself.' These concerns may lead to avoidance behaviors as they cannot be easily addressed by patients with active disease. Concerns may be related to how or when the cancer may progress, not whether it recurs. Avoidance was associated with non-somatic depressive symptoms and poor emotional well-being, consistent with other studies that reveal an association between avoidance and distress [39]. Our findings of complete mediation by cancer-related avoidance indicate that no significant relations exist between intolerance of uncertainty and either non-somatic depressive symptoms or emotional well-being after accounting for avoidance and adjusting for neuroticism. No indirect effect of avoidance emerged on perceived stress, contrary to other studies with cancer patients that have demonstrated a relation [40]. One reason for our result may be that neuroticism was included in our models and was significantly associated with perceived stress. Removing neuroticism in the mediation models yielded a significant, positive relation between avoidance and perceived stress, as well as a significant indirect effect for avoidance.

One study limitation is the modest response rate, which raises the question of whether those who completed the study differed from those who did not. For example, our sample may have been better physically or mentally able to complete the self-report questionnaire or sufficiently comfortable responding to a range of items that may probe sensitive or vulnerable areas about their illness. This is a common challenge in studying a population that has advanced disease. The generalizability of these findings may also be limited because of the fact that data collection took place at only one oncology setting, which yielded a well-educated, primarily female, and therefore possibly skewed, sample. However, this sample may be typical of individuals who have had been living with a lung cancer diagnosis for some months, as those of higher socioeconomic status have lower cancer death rates than those of lower status and women diagnosed with lung cancer have better survival than men in the USA [1,41]. Additionally, the cross-sectional design raises questions about the direction of associations. For example, it is possible that patients' poor psychological adjustment influenced their levels of tolerance of uncertainty and perceptions of ambiguity,

Table 2. Results of regressing psychological adjustment on intolerance of uncertainty and illness-related uncertainty

Models[a]	Block 1				Blocks 1 and 2						Blocks 1, 2, and 3					
	Model R^2	Model Res df	Std. beta	p	Model R^2	Model Res df	p chg. model	Std. beta	p	Model R^2	Model Res df	p chg. model	Std. beta	p
Predicting non-somatic depressive symptoms	0.21	40			0.42	38	0.004			0.45	37	0.151		
Neuroticism								0.18	0.241				0.17	0.261
IUS			0.47	0.002				0.43	0.006				0.37	0.017
MUIS ambiguity								0.18	0.206				0.28	0.082
IUS × MUIS ambiguity[b]													0.20	0.151
Predicting perceived stress	0.41	39			0.60	37	0.001			0.60	36	0.825		
Neuroticism			0.64	0.000				0.34	0.012				0.34	0.013
IUS								0.28	0.038				0.28	0.041
MUIS ambiguity								0.34	0.008				0.33	0.018
IUS × MUIS ambiguity[b]													−0.03	0.825
Predicting emotional well-being	0.12	40			0.37	38	0.002			0.40	37	0.172		
Neuroticism			−0.35	0.022				−0.02	0.91				−0.01	0.959
IUS								−0.40	0.012				−0.35	0.032
MUIS ambiguity								−0.31	0.047				−0.40	0.018
IUS × MUIS ambiguity[b]													−0.20	0.172

IUS, Intolerance of Uncertainty Scale; MUIS, Mishel Uncertainty in Illness Scale.; Std. beta, standardized beta; Res df, residual degrees of freedom; p chg. model, p of the change in F of this model compared with the previous model.
[a]All models also include a constant term.
[b]The interaction term IUS × MUIS was the product of the two terms centered.
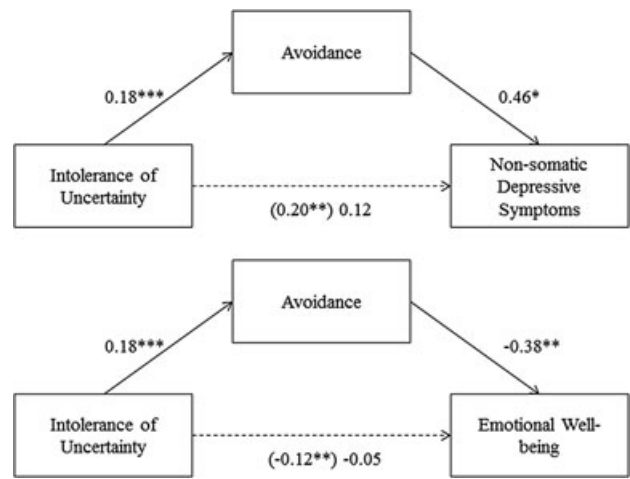
Figure 1. Relations among intolerance of uncertainty, avoidance, and psychological adjustment. Values presented are unstandardized regression coefficients as recommended by Preacher and Hayes [32,38]. Values in parentheses represent coefficients for unmediated paths. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

rather than adjustment being influenced by intolerance and perceived ambiguity as we had hypothesized.

Our study also has a number of strengths. We examined psychological adjustment in an under-studied population living with a lung cancer diagnosis for an average of over 2 years, whereas participants in other studies are closer to the point of diagnosis [36,42,43]. The 1-year relative survival rate is 42% [1], so our sample generally has a more favorable outcome than average, leading to results reflecting response to disease rather than unrelenting and progressive symptoms, which can be seen with this disease. Because cure is uncommon among individuals with lung cancer, quality of life is important as an objective of care but has been challenging to study [44].

Our findings may have therapeutic implications. Psychological adjustment may be influenced both by adopting alternative ways to process uncertainty cognitively and by addressing the factors that lead to perceived ambiguity. Applying cognitive skills and problem solving training and processing of traumatic material may improve adjustment. For example, promoting coping skills to manage the uncertainty about recurrence and metastatic disease has been demonstrated to be beneficial among long-term breast cancer survivors [45] and may be useful for survivors with lung cancer as well. A complementary approach is to address the specific characteristics of the cancer experience that induce the perception that the disease is ambiguous. For example, future research to identify the extent to which adequate patient–clinician communication, awareness and attitudes about current symptoms, and religious/spiritual beliefs influence perceptions may be valuable. These areas of further study warrant empirical examination as they may have a clinically significant impact on psychological adjustment and quality of life.

Acknowledgements

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