Symptom Experience Following Lung Cancer Surgery

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Abstract

Background: Annually over 225,000 individuals are diagnosed with lung cancer and over 80,000 undergo surgery with many experiencing concurrent post-operative symptoms. **Objectives:** The purposes of this study were to: 1) describe the symptom experience during the first year following lung cancer surgery, 2) explore relationships between symptoms, influencing factors and functional performance, and 3) compare responses in patients with and without PTPS. **Methods:** This descriptive, cross-sectional, correlational study was guided by the Theory of Unpleasant Symptoms (TOUS). Patients were recruited over 28 months from a university medical center and subsequently completed the following six self-report instruments: the Symptom Distress Scale, McGill Pain Questionnaire, Neuropathic Symptom Questionnaire, Hospital Anxiety and Depression Scale, the Health History Survey and Functional Assessment of Cancer Therapy-Lung; medical record reviews were conducted to corroborate responses. Spearman's rho was used to measure relationships among variables. Comparisons between participants with and without PTPS were made using Chi-Square or Fisher's exact test. Significance was set at $p < .05$. **Results:** Patients were assessed on average 6 months after surgery, and were predominantly diagnosed at cancer Stage I, elderly, female, Caucasian, educated at the high school level with mild to moderate psychiatric distress, and at least five comorbid conditions. The majority reported distress associated with concurrent symptoms.

Patients with more psychiatric distress reported more symptom distress and patients with higher symptom distress reported lower functional performance. Patients who were younger, had some mood disorder and decreased functionality were significantly more likely to report PTPS. **Conclusions:** Patients reported distress associated with a wide range of concurrent post-operative symptoms, including PTPS. The TOUS may assist clinicians to explore relationships that are important for the assessment and management of symptoms after surgery for lung cancer.

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PREFACE

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1.0 INTRODUCTION

Globally, lung cancer claims more lives each year than colon, prostate, ovarian, lymph, and breast cancer combined (American Cancer Society, 2014). Although often diagnosed late, expected survival following the diagnosis of Stage I lung cancer is 52.9% at five years if confined to the primary site (American Cancer Society, 2014). New innovative minimally invasive surgical techniques reduce the necessity of open chest thoracic surgery for lung cancer (Karasaki, et al. 2009; Keenan et al., 2004). Even with less invasive approaches, as many as 50% of patients continue to experience symptoms related to the surgical procedure for months or years (Karasaki, et al. 2009; Keenan et al., 2004).

A primary outcome, termed post-thoracotomy pain syndrome (PTPS), is defined as pain that recurs or persists along a thoracotomy incision at least two months after the surgical procedure (International Association for the Study of Pain, 2011; Merskey, 1986). PTPS has been attributed to rib or nerve damage from surgery or a chronic pain syndrome initiated by inadequate pain relief in the postoperative period (Chapman, 2011; Wildgaard et al., 2011). Typically described as aching, burning, or extreme sensitivity to touch at or near the scar or chest tube insertion site, the etiology of PTPS is thought to be distinct from acute post-operative pain, side effects of treatment, or cancer progression (American College of Chest Physicians, 2013; Wildgaard et al. 2011; American College of Chest Physicians, 2007).

In addition to pain, patients often experience multiple and concurrent symptoms after thoracotomy, including: dyspnea, fatigue, and depression (Sarna et al. 2010; Sarna et al. 2008). Anti-cancer treatments such as surgery, chemotherapy and radiation also influence the type and pattern of concurrent symptoms (American College of Chest Physicians, 2013). In spite of these possible explanations, patients often mistakenly worry that their post-surgical symptoms are due to cancer recurrence, a belief that creates anxiety and compromises Quality of Life (QOL) (Chapman, 2011)**.** Initiatives are needed to assist patients with lung cancer who are challenged by the physical and emotional impact of these troubling symptoms.

Historically, the majority of symptom research regarding lung cancer has been limited to patients with metastatic disease (Cleary et al, 2008; Dajczman, Gordon, Kresisman, & Wolkive, 1991) and complications following chemotherapy (Myers, 2009) and radiation (Pituskin et al., 2010). There continues to be little insight into managing symptoms experienced by patients who undergo potentially curative surgical treatment (Demmy, 2009; Landreneau et al., 1994). The paucity of information available makes identifying interventions to support patients during their surgical recovery a challenge (Sarna et al., 2010; Sarna et al., 2005).

1.1 PURPOSE

The purposes of this descriptive, cross-sectional, correlational study were to describe the symptoms experienced by patients in the first year following lung cancer surgery; explore the relationships between symptoms, the factors that influence them and the effect of symptoms on performance, and to compare these responses in patients with and without PTPS. Because the

symptom experience after surgery for lung cancer is complex and patients typically report multiple concurrent symptoms, the Theory of Unpleasant Symptoms (TOUS) (Lenz, Pugh, Milligan, Gift, & Suppe, 1997), a model that incorporates the multidimensionality of the symptom experience, was selected as the guiding framework for this study.

1.2 SPECIFIC AIMS

The aims of the study were to:

Aim 1. Describe the physiologic, psychologic and situational influencing factors, the symptoms, and performance outcomes.

Aim 2. Determine the strength of the associations between physiologic, psychologic situational factors and patients' symptom(s).

Aim 3. Determine the strength of the associations between symptom(s) and patients' performance.

Aim 4. Compare the symptom experience, the factors that influence the symptom experience and the impact of symptoms on performance between patients with and without PTPS after surgery for lung cancer.

2.0 BACKGROUND, SIGNIFIANCE, AND INNOVATION

2.1 BACKGROUND

The typical symptoms of lung cancer, cough, hemoptysis, and pain, commonly occur in advanced stages of the disease. Lung cancer at an earlier stage is often detected incidentally during a chest x-ray for pneumonia, following an accident, or other event (American Cancer Society, 2014). This finding triggers a referral to a thoracic surgeon who reviews the x-ray and clinical data to assess risk for a possible malignancy (National Comprehensive Cancer Network, 2012; Groome & Bolejack, 2007). If warranted, further diagnostic testing such as radiologic imaging, endobronchial ultrasound, or tissue biopsy using transthoracic needle aspiration or bronchoscopy are performed to determine cell type, stage, and guide clinical management (National Comprehensive Cancer Network, 2012; Memoli-Wang et al., 2011; Wiener, Schwartz, Woloshin, & Welch, 2011). Clinical staging is based upon the tumor size (T), the number and location of involved nodes (N) and number of metastatic sites (M) determined from pre-operative imaging and biopsy (National Comprehensive Cancer Network, 2012).

There are several cell types identified as lung cancer and, of these, adenocarcinoma and squamous cell cancer are the most common (American Cancer Society, 2014). Lung cancer is classified as non-small cell (NSCLC) (80%) and small cell (SCLC) (20%) (The National Lung Screening Trial Research Team, 2010). SCLC is typically more aggressive and often found in

later stages when it has metastasized to other sites (National Comprehensive Cancer Network, 2012). Therefore, surgery is typically not an option for treating SCLC.

Treatment for lung cancer depends upon tumor histology (cell type) and extent (stage) (Groome & Bolejack, 2007) and patient related factors (age, pulmonary function, comorbidity) (Keenan et al., 2004; Landreneau et al., 1994). Surgery offers the only curative option and therefore is the treatment of choice for those with localized non-small cell lung cancer NSCLC, (Stage I, II or possibly IIIa) (American Cancer Society, 2014) and enough cardio-pulmonary reserve to tolerate removal of the necessary amount of lung parenchyma. Approximately 30% of patients with lung cancer meet these criteria and undergo surgery (Wildgaard et al., 2011; Landreneau et al., 1994). The purpose of surgery is first to remove the tumor and examine the margins to ensure no cancer cells remain, and second to remove appropriate lymph nodes to investigate spread to the lymphatic system (Rodger & Duffy, 2000; Landreneau et al., 1994). The options for surgical approaches include a standard thoracotomy or a thorascopic procedure, also termed video assisted thoracic surgery (VATS) (National Comprehensive Cancer Network, 2012; Groome & Bolejack, 2007).

A thorascopic procedure is considered to be minimally invasive because the approach does not involve rib-spreading and only requires three small, one to five centimeter incisions or ports (Park et al., 2011; Rodger & Duffy, 2000). Figure 1. Incisions are typically in a triangular shaped array (Karasaki et al., 2009). These incisions are strategically placed to permit insertion of the fiber optic video camera (endoscope), instruments to inflate the chest cavity, and other holding and cutting surgical instruments (Rodger & Duffy, 2000). In some cases, a VATS procedure may need to be converted to a full thoracotomy if unexpected issues arise during the

surgery (e.g. more aggressive carcinoma) (Park et al., 2011; Boffa et al., 2008; Aoki, Tsuchida, Hashimoto, Saito, Koike, & Hayashi, 2007).

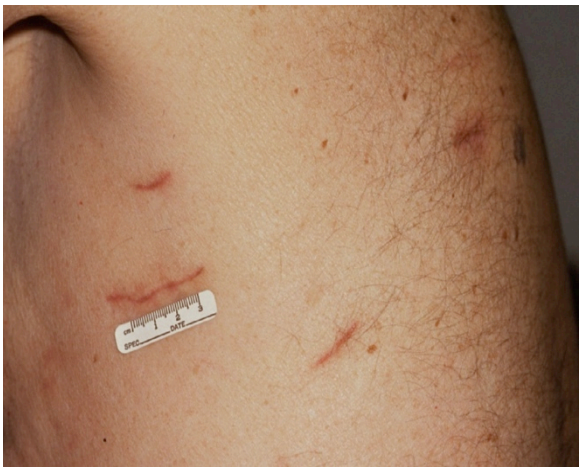

Figure 1. Illustration of scar location after thorascopic surgery (Photo courtesy of Dr. Rodney Landreneau)

Thoracotomy for lung cancer, the more common (Karasaki et al., 2009; Boffa et al., 2008) and invasive (Boffa et al., 2008; Keenan et al., 2004) approach, requires a larger surgical incision between the ribs that is typically six to 12 centimeters in length (Rogers & Duffy, 2000). After the incision, rib spreaders are used allowing a much larger entry into the chest wall and intercostal cavity. This procedure is known to cause injury to the costochondrial junction, ribs, cartilage, (Wildgaard et al., 2011), intercostal nerves (Wiener, Schwartz, Woloshin & Welch, 2011; Keenan et al., 2004), and latissimus dorsi muscle (Karasaki et al., 2009; Keenan et al., 2004) (Figure 2).

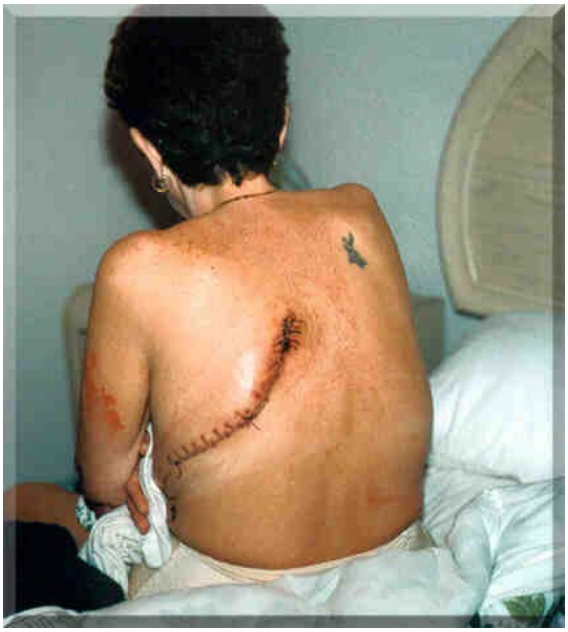

Figure 2. Illustration of scar location after a thoracotomy (Photo courtesy of Dr. Rodney Landreneau)

Regardless of the approach, surgery involves instrumentation that passes through major chest muscles, intercostal spaces, ribs, nerves, and pleural cavity (Park, 2011; Boffa et al., 2008). Surgical sequelae include atrophy of chest muscles (Boffa et al., 2008), chronic pain from injury to intercostal nerves (Pettunen, Tasmuth, & Kalso, 1999; Landreneau et al., 1994), and fractured and compressed ribs (Landreneau et al., 1994) to name a few (Rogers & Duffy, 2000). Upon healing, the only external visual reminders are the consequent scars. While some patients recover with no untoward consequences, others experience pain that recurs or persists along a thoracotomy incision at least two months after the surgical procedure, a condition known as PTPS (Wildgaard et al., 2011; Perttunen et al., 1999; Landreneau et al., 1994).

2.1.1 Post Thoracotomy Pain Syndrome (PTPS)

First described in 1944, PTPS received limited attention until 1991 when a seminal study surveyed 56 patients with lung cancer who were disease free up to five years after thoracotomy (Dajczman et al., 1991). Despite their long-term, disease free status, 54% of the sample reported PTPS (Dajczman et al., 1991). Other studies found PTPS to be present in 11–80% of patients, confirming that PTPS is a common complication (Corte, Mendola, Messina, & Cammarota, 2011; Duale et al., 2011; Sikorskii et al., 2007; Dajczman et al., 1991). Notably, although PTPS is common, not all patients who undergo lung cancer surgery develop PTPS suggesting different causative factors (Demmy, 2009; Karasaki et al., 2009; Shaw & Keefer 2008; Max et al., 2006).

Etiology of PTPS

The etiology of PTPS has been attributed to rib (Bayram, Ozcan, Kaya, & Gebitekin, 2011), nerve (Miyazaki et al., 2011; Benedetti et al., 1998), or muscle (Karasaki et al., 2009; Lia et al., 2003) damage from surgery or a chronic pain syndrome initiated by inadequate pain relief in the post-operative period (Wildgaard et al., 2012; Demmy, 2009). Other potential causative mechanisms include nerve or muscle damage related to the insertion of chest drainage mechanisms, e.g. chest tubes and Jackson Pratt (JP) tubing (Corte et al., 2011; Benedetti et al., 1998; Landreneau et al., 1998; Landreneau et al., 1994) and any instruments or drainage devices passing through the network of intercostal nerves that have the potential to cause nerve damage resulting in chronic neuropathic pain (Corte et al., 2011).

Prior to the advent of minimally invasive surgical techniques, PTPS was presumed to be attributed to the extent of the thoracotomy incision and the methods for pain relief achieved following surgery (Wildgaard, Ravn, & Kehlet, 2009). However, in one of the first reports

comparing outcomes following these surgeries, Landreneau and colleagues (1994) enrolled 343 consecutive patients undergoing a thoracotomy (n=165) or a thorascopic procedure (n=178) and found no significant difference in chronic pain levels between the two groups (Landreneau et al., 1994). Landreneau et al., used a scale of one (no pain) to ten (most severe pain ever) when comparing pain ratings. The design of this study did not involve matching between groups, a limitation of this study. More recently, Furrer and colleagues (1997) matched 15 thorascopic lobectomy patients with 15 patients who underwent a lobectomy with the more aggressive thoracotomy on age, gender and preoperative pulmonary function and found that 36% of the thorascopic and 33% of the thoracotomy group reported pain using a scale of one (no pain) to ten (most severe pain ever) (Furrer et al., 1997). Additional studies that examined potential mechanisms for PTPS and strategies for prevention have reported persistence of pain in patients who underwent either procedures (Wildgaard et al., 2012; Karasaki et al., 2009; Aoki et al., 2007; Furrrer et al., 1997). Findings of these studies provide additional evidence that PTPS is not solely related to the type of surgical procedure.

To further explore this syndrome, several studies have investigated muscle function following both surgical procedures. Frola and colleagues' study of 58 patients who underwent thoracotomy analyzed computed tomography (CT) scans taken before and after surgery. They reported that 40 participants had chest wall symmetry and atrophy in chest wall muscles simultaneously, 16 had no atrophy and 2 had atrophy in the serratus anterior muscle only (Frola et al., 1995). More recently, Karasaki and colleagues (2009) reported results of CT scans in 70 patients presenting with PTPS within 3 months after surgery. Of these, 53 had a thoracotomy and 17 had thoracoscopic surgery. Subjects reporting PTPS had an increase in muscle wall density. However, cross-sectional measurements of the latissimus dorsi muscle indicated that this muscle

was better preserved on the surgical side in patients who underwent a thorascopic procedure, compared to patients who underwent a standard thoracotomy (Karasaki et al., 2009). Although, this study concluded that thoracoscopic surgery may prevent atrophy, the sample was small and included a disproportionate number of participants with the two procedures (Karasaki et al., 2009).

PTPS literature is difficult to summarize due to methodological issues. In a recent review of PTPS mechanisms and strategies for prevention, Wildgaard et al. (2009) reported several inconsistencies in sampling methods and methods used to determine the presence of PTPS and related symptoms (Wildgaard et al., 2009). Some studies rated the presence and intensity of pain based upon a visual analog scale (VAS) whereas others retrospectively measured pain intensity based upon patients' consumption of analgesics (Demmy, 2009; Keskinbora, Pekel, & Aydinli, 2007). Other studies used descriptors such as aching, burning, tender and numbness (Maguire et al., 2006; Kalso et al., 1992). Some studies assessed preoperative anxiety and depression using researcher-developed questionnaires (Katz & Seltzer, 2009; Maguire et al., 2006). From their review, Wildgaard and colleagues (2009) concluded that intercostal nerve injury was the "most important pathologic factor responsible for the development of PTPS" (Wildgaard et al., 2009, p.172).

The most commonly cited definition of PTPS was first published by the International Association for the Study of Pain (IASP) in 1986 with little modification (International Association for the Study of Pain, 2011; Merskey, 1994; Merskey, 1986). Others have expanded this definition to include: "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (Patel, 2010, p.3). This expanded definition notes presence of a chronic and unpleasant sensory and emotional

experience after surgery not related to metastasis, inflammation, or other non-surgically related causes.

The search for physiologic explanations for PTPS has dominated the literature. Of interest, there has been limited attention paid to the potential influence of psychological or situational factors on this syndrome. In addition to the trauma of surgery, thoracic surgery patients may also experience physiological, psychological, and social changes due to their disease process (Gray, 2008; Williams, 2006; Landreneau et al., 1994). Sarna and colleagues (2010) noted pain related to PTPS often co-occurred with dyspnea (21%) and depression (29%) (Sarna et al., 2010). Co-morbidities involving pulmonary and cardiac disease are common in this population and these etiologies may be sources of pain. As a consequence, PTPS is difficult to diagnose, optimally manage and therefore is often under treated.

Assessment of PTPS

When patients present for follow-up post-surgical visits, a comprehensive assessment has been recommended to detect the presence of PTPS. During post-surgical clinic visits, surgeons and clinicians should inquire if patients continue to experience pain and, if so, ask them to rate their discomfort on a scale from one to ten (Wildgaard et al., 2011; Herr, 2004). The surgical area should be examined for inflammation of the chest muscles (Benedetti et al., 1998) and evidence of tissue, nerve, or muscle damage (Wildgaard et al., 2011; Benedetti et al., 1998). A full range of motion should be performed to detect any evidence of PTPS and documented in the medical record (Herr, 2004; Benedetti et al., 1998).

Rating PTPS (Pain or Neuropathy)

The early focus on pain as an explanation of the discomfort that occurs with PTPS, has more recently been expanded to other possible explanations. Findings of recent studies that

employ more comprehensive rating system; they focused on neuropathy and requires a physical exam that includes pricking patients with pointed instruments at the healing incision site, which was not allowed by the surgical group in this sample (Mongardon et al., 2011; Krause, & Backonja, 2003); Snaith, & Zigmond, 1994).Studies suggest that PTPS maybe neuropathic in origin, an outcome attributed to nerve damage caused by the instruments during the surgery, the percentage of patients reporting slight or mild pain and the patient's pain descriptors (Bayram et al., 2011; Miyazaki et al., 2011). The surgical origins of neuropathy are believed to occur when an axon is cut (nerve injury) and the distal portion forms a terminal swelling or end-bulb from which axonal buds or sprouts emerge. These sprouts can form a neuroma, a major source of ectopic impulse generation and therefore neuropathic pain (Herr, 2004; Gould et al., 2000). PTPS pain descriptors that resemble descriptors associated with neuropathic pain include numbness, tingling, and discomfort (Wildgaard et al., 2011; Herr, 2004). Therefore, ratings scales that attempt to capture symptoms caused by neuropathic pain are increasingly being included in measures of the discomfort from PTPS.

Pain ratings do not appear to differ depending on the type of surgical procedure. In the previously cited study, Furrer and colleagues (1997) reported that patients undergoing a thorascopic procedure and thoracotomy reported pain and neuropathic-like descriptors, e.g., pain that was "pleuritic or aching in nature" (Furrer et al., 1997, p. 1082). Postoperative ratings reflected mild pain (range 0.2 to 1.6 on a 10 point scale) and did not differ significantly with activities (Furrer et al., 1997). The prevalence of pain was similar to those reported by Dajczman and colleagues (1991) who asked 56 patients who underwent lung cancer surgery to rate their pain using a ten cm Visual Analog Scale (Dajczman et al., 1991). Dajczman and colleagues reported in 40%, 44.8%, and 37.5%,, of patients at one, two and three years after thoracotomy,

respectively (Dajczman et al., 1991). Gotoda and colleagues (2001) used a four point, Likert-type scale to assess post-thoracotomy pain within the first year, (i.e., none, slight, moderate, and severe), and found that 70.6 % of patients reported PTPS and 56.7%, rated their pain as slight, 23.3% as moderate, and 20% as severe (Gotoda et al., 2001). They further noted that respondents reported symptoms that indicated nerve impairment rather than simple muscle damage with this syndrome (Gotoda et al., 2001).

More extensive exploration has supported the presence of symptoms commonly associated with neuropathy and suggested a timeline for development. Duale and colleagues (2011) surveyed 73 post-operative pneumonectomy patients who were divided into two groups - those who did or did not receive perioperative ketamine (Duale et al., 2011). The patients' pain/sensitivity were assessed immediately post-operatively and again at week four and six, using a VAS (100 mm line) measuring sensitivity to the touch of the blunt end of a paintbrush. In addition, pain/sensitivity was measured at the scar area using an electronic algometer for mechanical threshold and Somedic Thermo test apparatus applied to measure thermal thresholds (Duale et al., 2011). Duale and colleagues (2011) concluded that neuropathy, at the second week, did not predict pain six weeks after surgery and "…thoracotomy often induced intercostal neuropathy that develops between the second and the sixth week after thoracotomy, with varying consequences" (Duale et al., 2011, p.252). Based on this work, Duale and colleagues (2011) concluded that both pain and neuropathic symptoms should be included in the definition of PTPS (Duale et al., 2011).

2.1.2 Theoretical Framework

Several theoretical frameworks focus on the symptom experience and opportunities to manage symptoms. Dodd's Symptom Management Conceptual Model, also known as the University of California-San Francisco School of Nursing Symptom Management Model (UCSF-SSM) is comprised of three interrelated dimensions: symptom experience, symptom management strategies and outcomes (Dodd et al., 2001). The UCSF model depicts symptoms in terms of three domains (person, environment, and health) and thus has been useful in identifying areas to target for management of symptoms (Peterson & Bredow, 2009). Although the UCSF model is multidimensional it does not reflect the presence and potential interaction of multiple concurrent symptoms, and thus may be less useful for studying the complex and multiplicative symptoms commonly reported among patients who have undergone surgery for lung cancer (Teel, Meek, McNamara, & Watson, 1997).

In the proposed research, determining an individual's interpretation of symptoms is critical to understanding the participant's symptom management decisions. Another model known as the Symptom Interpretation Model (SIM) was developed to facilitate the subjective understanding of symptoms from an intrapersonal perspective (Teel et al., 1997 To understand the participant's symptom experience, this model focuses on an individual's knowledge and the meaning of his or her symptoms. The symptom experience is viewed as multi-dimensional and includes sensory, affect, and cognitive elements. The SIM model has three major constructs: input, interpretation, and outcome (Teel et al., 1997). Input is the subject's recognition of the symptom. Interpretation is the participant's meaning attached to the symptom and outcome is the participant's decision-making result of the first two constructs. The SIM model is an expansion

of the UCSF-Single Symptom Model. However, it does not include an assessment of the impact of the patient's decisions and actions on performance.

The Theory of Unpleasant Symptoms (TOUS) includes three major concepts: concurrent unpleasant symptoms, the influencing factors that give rise to the nature of symptoms, and the impact of these symptoms on performance (Figure 3) (Lenz et al., 1997). Symptoms are described in terms of four dimensions: timing, distress, quality and intensity (Pituskin et al., 2010; Eaton & Tipton, 2009; Lenz et al., 1997). Influencing factors are the interrelated aspects that influence the symptom experience and include three domains: physiologic, psychologic, and situational factors. Symptoms, the central focus of the model, are defined as the "red flags" or a perceived indicator of change in a patient's normal functioning (Lenz et al., 1997; Lenz, Suppe, Gift, Pugh & Milligan, 1995; Hegyvarym, 1993). Performance refers to the consequences of the symptom experienced such as the impact on function, cognitive ability and QOL (Chapman, 2011; Lenz et al., 1997).

The TOUS was selected as the theoretical framework for this study over the aforementioned symptom models because the TOUS: 1) focuses on patients' subjective descriptors of unpleasant symptoms that occur alone or concurrently, 2) attends to the multidimensionality of symptoms, 3) makes the relationships between influencing factors, symptoms and performance explicit. Thus, the TOUS was ideally suited to guide this study because factors underlying development of PTPS are poorly understood, symptoms can co-occur, vary in onset, intensity and distress, and cause varying performance limitations.

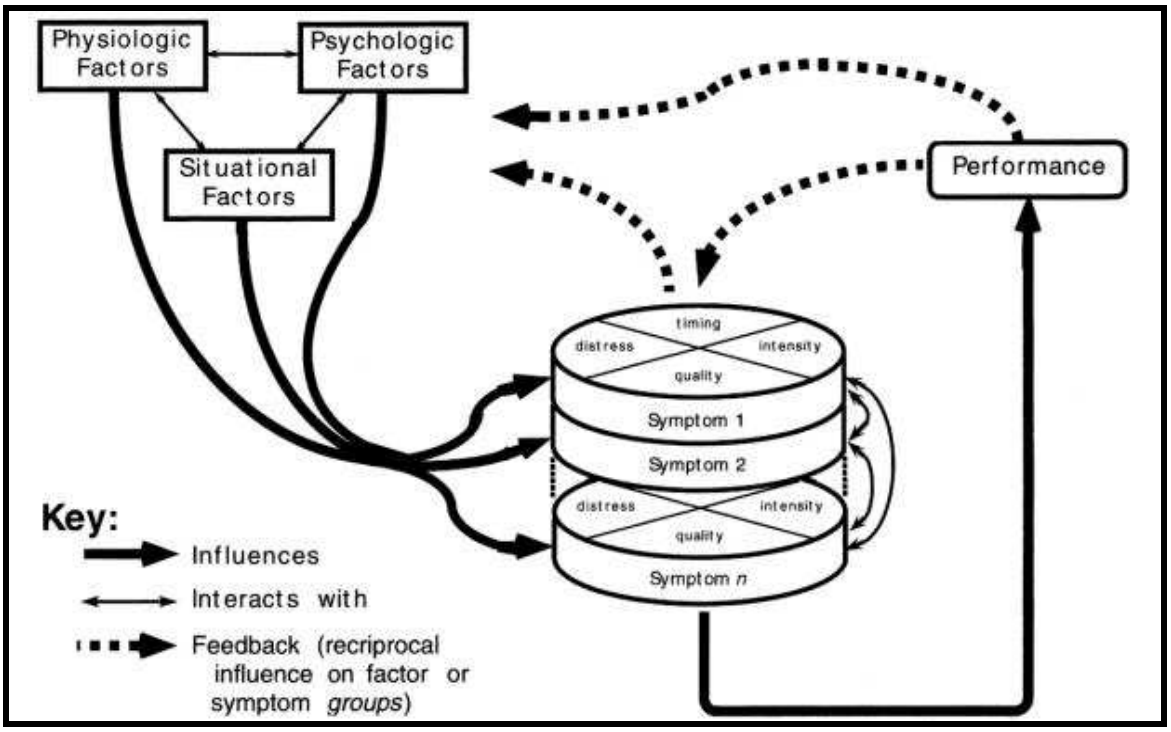

Figure 3. The Theory of Unpleasant Symptoms (TOUS) (Printed with permission from: Wolters Kluwer Health and RightsLink)

The following section organizes the literature related to symptoms after surgical treatment of lung cancer by concepts and relationships supported in the TOUS.

Symptoms

Symptoms reflect the individual's subjective and perceptual processes that assign meaning to the unpleasant experience or sensation (Brown, Cooley, Chernecky, & Sarna, 2011). Reviewing studies which reported multiple and concurrent symptoms, we noted the following. Lee et al. 2005 in a cross-sectional, correlational study of 125 women considered mood disturbances using the Linear Analogue Self-Assessment Scale for mood and Symptom

Experience Scale (SES) for symptoms. They reported that mood disturbance significantly accounted for the variance in symptom experience (< 0.001) (Lee, 2005).

Sarna and colleagues (2008) also reported this interrelationship in their survey of 94 patients 4 months after lung cancer surgery. This study noted multiple symptoms including fatigue (57%), dyspnea (49%), cough (29%), and pain (20%), were compounded in participants with significant mood distress (Sarna et al., 2008).

With respect to PTPS, prior studies (and the clinical experience of the Principal Investigator (PI), indicated that most patients do not mention pain from PTPS unless directly questioned (Demmy, 2009). When questioned, pain is typically described as aching (Chapman, 2011; Rogers & Duffy, 2000; Furrer et al. 1997) or burning (Merskey, 1986; Rogers & Duffy, 2000); that may be aggravated by touch (Wildgaard et al., 2012); or movements of the shoulder girdle (Karasaki et al., 2009; Perttunen et al., 1999; Frola et al., 1995); and rated as mild to moderate in severity (Dajczman et al., 2008; Rogers & Duffy, 2000; Perttunen et al., 1999). Neither muscle sparing surgery (Karasaki et al., 2009; Frola et al., 1995; Landreneau et al., 1994) nor VATS (Rogers & Duffy, 2000; Furrer et al., 1997; Landreneau et al., 1994) reduced the incidence of PTPS (Furrer et al., 1997; Landreneau et al., 1994). While important, a focus on aspects of the surgical procedure is likely inadequate in describing PTPS and other patient symptoms (Chapman, 2011; Landreneau et al., 1994). Lung cancer often occurs in older adults with a long history of smoking (American Lung Association, 2008). These cancer patients often bring additional psychological factors due to their personal history of smoking which may impact their perceptions of PTPS and other symptoms (American Cancer Society, 2014; Siegel, Ward, Brawley, & Jemal, 2011; Howlader et al., 2010; American Lung Association, 2008).

Sarna and colleagues (2008) surveyed 94 patients four months after lung cancer surgery. Symptoms noted in this sample included fatigue (57%), dyspnea (49%), cough (29%), and pain (20%).

Influencing Factors

Studies suggest an interrelationship (or feedback loop) between physiologic, psychologic and situational factors and symptoms.

Physiologic Influencing Factors

Comorbidities are common and likely contribute to PTPS, e.g. pain from arthritis, dyspnea due to cardiac or pulmonary dysfunction can increase one's sensitivity to PTPS (Chapman, 2011; Keenan et al., 2004). Two factors, inadequate acute pain relief (which may create a chronic pain state) (Demmy, 2009; Dodd et al., 2001; Rogers & Duffy, 2000, Teel et al., 1997) and nerve/rib damage from the surgical procedure (Rogers & Duffy, 2000; Landreneau et al., 1994), are most commonly cited as physiologic mechanisms responsible for PTPS (Wildgaard et al., 2009; Gould et al., 2000; Rogers & Duffy, 2000). Current protocols aggressively target pain; hence, recent studies report low pain ratings (Rogers & Duffy, 2000; Landreneau et al., 1994; Dajczman et al., 1991). Notably, PTPS pain descriptors resemble descriptors associated with neuropathic pain (International Association for the Study of Pain, 2011; Chapman, 2011; Merskey & Bogduk, 1994; Merskey, 1986). Nerve injury may be due to the laceration of an axon during surgery. This nerve injury is a possible source of ectopic impulse generation and therefore, neuropathic pain (Duale et al., 2011; Herr, 2004; Gould et al., 2000).

Psychologic Influencing Factors

Anxiety and depression are also thought to influence symptoms in persons who undergo surgery for lung cancer. When Sarna and colleagues (2010) expanded their study to 119 women who were disease free up to six years after lung cancer surgery, depressive symptoms remained common (29%) and influenced QOL ratings (Sarna et al., 2010). Several studies have explored interventions to minimize psychologic symptoms (Myers, 2009; Jamsen et al., 2008; Sarna et al., 2008; Sikorskii et al., 2007; Prasertisri et. al., 2011; Gift et al., 2004). Myers (2009) reported variable effects of chemotherapy-related changes in cognitive function that often increases anxiety in patients diagnosed with cancer (Myers, 2009). Myers' review of the literature, reported that the TOUS as an appropriate model for describing the symptom experience related to mild to moderate changes in both cognitive impairment and the potential resulting increases in anxiety as described by both Aoki, Tsuhida, and colleagues (2007) and Prasertsri and colleagues (2011) (Prasertisri et. al., 2011; Aoki et al., 2007).

Situational Influencing Factors

Race and socioeconomic status appear to be a social determinants of pain and survival in lung cancer patients, with a large national study of (n = 248,741) lung cancer patients, reportedAfrican American, American Indian and Alaskan native, and Hawaiian natives having higher levels of pain and lower survival rates (Clegg et al., 2002). Asian Americans and Non-Hispanic Caucasians were typically diagnosed at a later age than other ethnic groups or racial groups (Clegg et al., 2002). Similarly Fogel and Fogel (2003) reported that factors, such as marital status, employment status and income may also affect symptoms (Fogel & Fogel 2003).

Performance

Effective management of unpleasant symptoms aims to reduce symptom severity and frequency in order to improve outcomes such as functional performance and enhanced quality of life. Merskey and Portenoy were two of the first researchers to measure the influence of pain on performance and QOL in cancer patients QOL(McGill, 2009; Portenoy & Kanner, 1997; Portenoy, 1990; Merskey, 1986). Other researchers examined the influence of symptoms on performance and QOL (Sarna et al., 2010; Sarna et al., 2005) and found that depressed mood, comorbidities, and dyspnea were related to poorer physical and emotional QOL (Sarna et al., 2010). Chapman (2011) noted that chronic pain had a significant effect on a cancer survivors' QOL.

In summary, while important, a focus on aspects of the surgical procedure is likely inadequate in describing patient symptoms after surgery, including PTPS (Chapman, 2011; Landreneau et al., 1994). No prior studies were identified that comprehensively explored the symptom experience of persons who underwent surgery for lung cancer, the factors that influence the experience, or the relationships between symptoms and performance.

2.2 SIGNIFICANCE

Symptom assessment and managements targeted to improve post-operative recovery following lung cancer surgery tend to be intensive in regard to the use of resources and personnel (Cleary et al., 2008; American College of Chest 2007; Sikorskii et al., 2007; Logue, 2006; Herr, 2004), thus limiting translation into clinical practice. With patient encounters becoming increasingly brief (Sikorskii et al., 2007; Herr, 2004; Huang et al., 2003), there is an urgent need to ensure

consistent and optimal symptom assessment and management for patients recovering from lung cancer surgery. In the clinic where data were collected for this study, the average time patients with lung cancer spend in a clinic visit is ten minutes, a finding that mirrors national averages and suggests tremendous potential for patient centered educational tools to be developed based on findings from this study (Murray, Burns, See, Lai, & Nazareth, 2005; Fogel & Fogel, 2003).

The TOUS provides a comprehensive framework to guide exploration of the symptom experience of patients who undergo early stage lung cancer surgery and the complex and challenging problem of both concurrent symptoms and PTPS. This framework was used to explore patient reported symptoms, influencing factors and outcomes with the goal of understanding the impact of surgical treatment on symptoms, patient functioning and well-being and guide the development of future interventions.

Thoracic surgery, clinicians have historically viewed PTPS as a "pain" only symptom with an unknown orgin, managed using traditional opioid modalities for relief, and morphine as the "gold standard" (International Association for the Stidu of Pain, 2011; Demmy, 2009; Perttunnen, Tasmuth, & Kalso, 1999). Historically, opioids have not provided adaquate releif (Wildgaard et al., 2011; Williams, 2006) and unconrolled pain is a known risk factor for PTPS. Today, in addition to opiods both antidepressants and GABA analog medications are now available and being prescribed for these patients (Ballantyne, 2010; Keskinbora, Pekel, & Aydinli, 2007; Mattia, Paoletti, Coluzzi, & Boanelli, 2002). Views are changing and clinicians are beginning to view PTPS as a complex syndrome which includes concurrent symptoms influenced by a variety of factors (Chapman, 2011; Wildgarrd et al, 2011; Herr, 2004). Thus, clinicians are beginning to expand the treatment of PTPS to include non-opioid based interventions and the impact of these new interventnions are just beginning to be known

(Keskinbora et al., 2007; Mattia et al., 2002; Lickiss, 2001). A comprehensive approach to studying this phenomena which includes not only concurrent symptoms but also their influencing factors, has the potential to expand understanding of PTPS, and inform the development of strategies to better manage it.

This study addresses the research priorities of the National Comprehensive Cancer and Oncology Nursing Society to develop an in-depth understanding of cancer-related symptoms and side effects, including causal pathways, patient outcomes, and nursing interventions to ameliorate symptoms (National Comprehensive Cancer Network, 2012; Eaton & Tipton, 2009). Optimally, findings of this study will assist clinicians to address three challenges: limited understanding of the patients' full symptom experience, limited time to intervene in the clinical setting, and the need to identify innovative ways to improve the symptom experience.

2.3 INNOVATION

This study is thought to be the first to comprehensively examine the symptom experience following potentially curative surgical resection of lung cancer, including the experience of patients with and without PTPS. Since the 1990's, few studies have examined the symptom experience of patients diagnosed with early stage lung cancer and hence, little is known about the types of symptoms patients experience, their influencing factors, or impact on performance after surgery.

Tools to guide the assessment and management of symptoms after surgical treatment of lung cancer are lacking. The TOUS was used to guide this study with the promise of offering

clinical utility to reduce the impact of symptoms for persons who undergo surgery for lung cancer.

3.0 METHODS

3.1 SETTING

The study recruited patients over a 28 month period, between August 2010 and December 2012. Patients were recruited from the clinics of eight thoracic surgeons in one surgical practice. This surgical practice is affiliated with the University of Pittsburgh Medical Center (UPMC) Cancer Centers with locations at: Presbyterian Hospital, Hillman Cancer Center, Shadyside Hospital and Medical Center.

3.2 SAMPLE

A total of 1140 patients attended clinic and were screened, resulting in 112 potentially eligible subjects. Two patients were not enrolled due to refusal. Of the 110 patients who provided informed consent, 13 did not complete the study for the following reasons: 5 did not return instruments, 5 died, and 3 were no longer eligible due to new metastatic disease. The sample therefore consisted of 97 of 110 (88.1%) potential participants. All 97 were included in the PTPS Manuscript (Section 5). One subject of the 97, did not complete the symptoms instrument, and therefore was not included in the TOUS Manuscript (n=96) (Section 4).

3.3 RECRUITMENT

Screening was based on the study's inclusion and exclusion criteria. Prior to screening, all clinical staff were educated about the study and given screening cards to use as tools in introducing the study to potential participants. A member of the surgical team introduced the study to potential participants. If the patient agreed, the PI then approached the potential subject, confirmed that the potential subject met study inclusion criteria and, if eligible, obtained informed consent. During recruitment, the PI was present in the clinical suite and answered all study questions, from the staff, potential participants, and participants.

Inclusion criteria. 1) managed surgically for Stage I, II, or IIIa lung cancer without evidence of metastasis (Siegel et al., 2011; American Lung Association, 2008; American College of Chest, 2007); 2) between two and 12 months post–surgery (conforms to definition of PTPS and other chronic symptoms) (International Association for the Study of Pain, 2011; Eaton & Tipton, 2009; Merskey & Bogduk, 1994; Merskey, 1986); 3) > 40 years of age (lung cancer was infrequent in those younger and if present likely atypical) (Howlader et al., 2010; American Lung Association, 2005; Parkin, Bray, Ferlay, & Pisani, 2005).

Exclusion criteria. 1) any other cancer diagnosis or metastatic disease, (to avoid confounding symptomatology); 2) inability to speak, read, or understand English (questionnaires were in English); and 3) presence of comorbidities such as dementia, or memory loss (limited ability to participate as informant).

After consent was obtained, participants were given the option of completing the instruments in the clinic suite or at home. If they chose the clinic suite, the PI verified the

instruments were completed. If completed at home, the participants were given a postage paid return envelope. The instruments were logged at the time of receipt.

3.4 MEASURES

3.4.1 Symptom Distress Scale (SDS)

The SDS is a 13-item, self-report instrument designed to assess the level of distress associated with 11 cancer related symptoms e.g. fatigue, pain, insomnia, cough, breathing using a Likert-type scale (one, least distress to five, most distress) (McCorkle, Cooley, & Shea, 1998; McCorkel & Young 1979). Ratings are summed to achieve a total symptom score ranging from 13 to 65; total scores of 25 to 32 indicate moderate distress and scores $\geq$ 33 indicate severe distress (McCorkle et al., 1998; Holmes, 1989).

In prior testing, the SDS was found to be internally consistent, with Cronbach's alpha coefficients ranging from 0.82 to 0.97 in populations including lung, breast, and other cancer patients (Chen, Lakshminarayanan, & Revicki, 2009; McCorkle et al., 1998; Holmes, 1989; McCorkel & Young 1979; Cronbach, 1951). The SDS was found to have acceptable construct validity based on the inverse relationship (r = -.58) found between the SDS and the Karnofsky Performance Status Scale (Sarna & Brecht 1997). The SDS was deemed internally consistent in this sample (Cronbach, 1951) with a Cronbach’s alpha of .852.

3.4.2 McGill Pain Questionnaire (MPQ)

The MPQ is a self-report instrument that measures pain intensity, quality, and distress using 80 descriptors in 21 pain categories (McGill, 2009; Wright, Asmudson, & McCreary, 2001). This instrument also includes a single pain intensity score, ranging from zero (none) to ten (severe) and a full body (front and back) figure on which respondents are asked to identify their pain and incisional sites by marking the specific body locations on this figure (McGill, 2009). Because prior studies of patients after chest surgery noted that, not just the surgical area, but also chest tube and drain sites were areas of pain, the instructions were modified to request that patients mark and rate their postsurgical pain at three locations: incision, drain, and chest tube sites. For this study an overall pain score was calculated based upon the incision pain score.

In prior testing, the MPQ was found to be internally consistent, with Cronbach's alpha coefficients ranging between 0.74–0.87 (McGill, 2009; Ljunggren, Strand, & Johnsen, 2007; Jensen, 2003; Wright et al., 2001; Cronbach, 1951). The McGill was considered a valid measure of pain based upon Spearman rank (ρ) correlations

3.4.3 Neuropathic Symptom Questionnaire (NSQ)

Mid-way during the study the PI realized that patients were complaining of several sensations (numbness and tingling) that were not included in the SDS or MPQ. After reviewing several pre-existing neuropathic pain instruments, none were deemed appropriate. The painDETECT (Freynhagen, Baron, Gockel, & Tolle, 2006), included items that overlapped with the McGill Pain Questionanire; the Neuropathic Pain Scale (Backonja & Krause, 2003) focused on pain and

included limited neuropathic descriptors that our participants reported such as numbness and tingling; other scales [LEEDS Assessment of Neuropathic symptoms, and the Neuropathic Pain Diagnostic Questionnaire (DN4)] focused on neuropathy and require a physical exam that includes a number of tests that entail testing that required specialized testing not judged feasible for this study. (Mongardon et al., 2011; Krause & Backonja, 2003; Snaith & Zigmond, 1994).

Therefore, the NSQ, a self-report instrument was developed by the PI to identify the intensity of neuropathic pain based upon six descriptors at the surgical site: discomfort, tingling pain, numbness, increased sensation due to touch, increased sensation due to movement, and discomfort affecting daily activities. Patients were asked to rate each item using a 0-10 visual analog scale (VAS) with anchors established previously (Backonja & Krause, 2003). Using a VAS scale with anchors, 0 indicated no neuropathic sensation and ten the worst neuropathic sensation possible. Since the NSQ was introduced after half of the sample had been recruited, data for the NSQ were available for only 47 patients. Validity and reliability of the NSQ were not determined.

3.4.4 Health History Survey (HHS)

The HHS is a 20-item self-report instrument that was designed by the investigator to assess patients' sociodemographic and medical characteristics. Selected items included age, smoking history (pack years), gender, race, and ethnicity. Medical information, provided by the participant and verified by the medical record included: location and tumor type (adenocarcinoma – other), cancer stage (Stage I – Stage II or IIIa), surgical approach (thoracotomy-thoracoscopic), surgical procedure (lobectomy-other) time since surgery (2 to 6 –

7 to 12 months) and tumor location by lobe (right upper lobe – others). Validity and reliability of the HHS were not determined.

3.4.5 Charlson Comorbidity Index (CCI)

The 16-item version of the CCI (Heller, Ahern, Pringle, & Brown, 2009) that was modified to eliminate overlapping items included in the original 19-item scale (Charlson, et al 1987) to reflect the extent of morbidity associated with chronic illness, including those with lung cancer (Heller et al., 2007; Wang et al., 2007; Hall, Ramachandran, Narayan, Jani, & Vijayakumar, 2004). Scores were calculated by applying a weighted value to each comorbid condition documented in the medical record for a possible range of scores from 0 to 24 with higher scores indicating higher comorbidity burden. Content validity for the CCI was strong for detecting comorbid illnesses in a sample of 30,535 U.S. elderly patients (Heller et al., 2007). CCI scores $\geq$ 5 have been found to predict 1-year mortality for patients with a range of conditions, e.g. heart disease, AIDS, lung cancer (Charlson, et al., 1987);

In the present study, each condition was verified with the medical record and coded as absent or present (Hall et al., 2006). Per scoring guidelines (Wang et al., 2007), a weight of one was assigned for coronary heart disease, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, peptic ulcer disease, mild liver disease, and diabetes. A weight of two was assigned for hemiplegia, moderate/severe renal disease, and moderate /severe diabetes with end organ damage. A weight of three was assigned for liver disease and a weight of six was assigned for participants with AIDS However, no participant in this study had hemiplegia or

items assigned weights greater than or equal to two and participants were excluded for dementia. The result was that only twelve of the 16 potential comorbid conditions were present in this population.

3.4.6 Hospital Anxiety and Depression Scale (HADS)

The HADS is a 14-item questionnaire, designed to screen for mood disorders (Snaith, 2003). The HADS includes an anxiety and depression subscale; each subscale contains seven Likert-response items scored zero to three for a possible subscale range of 0-21 (Snaith, 2003). Based on prior studies, scores $\leq$ seven are considered normal; scores 8-10 are suggestive of a mood disorder; scores $\geq$ 11 indicate probable presence of a mood disorder (Snaith, 2003; Zigmong & Snaith 1983).

The HADs has been used widely (Bjelland et al 2002; Zigmond, & Snaith, 1983) and has been shown to be internally consistent with Cronbach's alpha coefficients of .81, .90, and .87 for the anxiety, depression and total HADS scores, respectively (Zigmond and Snaith 1983). A review of studies that employed the HADS reaffirmed the construct validity of the HADs (Bjellend, Dahl, Haug, & Neckelmann, 2002; Snaith, & Zigmond, 1994). In the present study, The HADS was deemed internally consistent in this sample with a Cronbach's alpha of .89, .88, and .93, for anxiety, depression and total HADS scores, respectively.

3.4.7 Functional Assessment of Cancer Therapy-Lung (FACT-L)

The FACT-L is a 44-item, self-report instrument with 5 subscales designed to measure five dimensions of quality of life (e.g. physical, social, functional, emotional) and a cumulative total score (Myers, 2009; Cella et al., 2002). The 44 Likert response items were scored using the established Administration and Scoring Guidelines (Cella et al., 2002). The sub-scores were summed and averaged to obtain a total score; higher scores indicate higher levels of functional performance. Likert scale (zero equals not at all, to a four which equals very much) and is considered a QOL measure (Cella et al., 1995).

The FACT-L was developed as a revised version of the FACT-G, with additional lung cancer focused questions. Cella (1995), validated internal consistency between the historical FACT-G and the FACT-L, by administering the FACT-L lung questions with the FACT-G questionnaire to 116 patients with lung cancer; the internal consistency (Cronbach's alpha) was 0.68. Soni and colleagues (2002), verified content validity using a comprehensive literature review and deemed the FACT-L to be one of three most comprehensive lung cancer-specific QOL measures. In more recent studies of patients with lung cancer, the FACT-L was found to be reliable with alpha coefficients $\geq$ .81 for the total and each of the subscale scores (Browning, Ferketich, Otterson, Reynolds, & Wewers, 2009); strong criterion validity was found between the FACT-L and the Lung Cancer Symptom Scale (Browning et al., 2011). In this sample Cronbach's alpha for the total FACT-L and its subscales ranged between .57 and .82.

3.5 HUMAN SUBJECTS PROTECTION

3.5.1 Data Sources

Data sources included self-report questionnaires and abstraction of data from medical records. Screening was based on the study's inclusion and exclusion criteria (Section 3.2).

3.5.2 Potential Risks and Protection Against Risks

The major risks were fatigue, distress from recall of the surgical experience, or breach of confidentiality. If patients complained of fatigue or distress, they were given an opportunity to rest and continue participation later. To reduce the likelihood of a breach of confidentiality, questionnaires were assigned a code number and stored in a locked file cabinet separate from the file containing identifiable information of participants.

Two study instruments measured symptoms that could reflect a level of distress requiring notification of clinic staff. For the SDS, clinic staff was notified of scores ≥ 33 (severe distress). Per protocol, the clinical staff were notified within 24 hours of the high SDS scores for 10 participants; and the staff confirmed that all participants were currently receiving treatment for conditions related to their scores. For the HADS, scores ≥ 11 (probable presence of mood disorder), were reported to clinic staff within 24 hours. Of the 97 patients enrolled in this study, the clinical staff were notified of high HADS scores for two participants who confirmed that all participants were currently receiving treatment for these conditions.

3.5.3 Informed Consent

Participants were informed about the study by the surgical team either during a clinic visit (using an IRB clinician recruitment script) or by an IRB formatted letter mailed to their homes. If interested in participating, both methods informed potential participants how they could contact the PI. This contact was typically done by phone or during the participant's next clinic visit. Those participants who chose to contact the PI by phone or in the office were screened using an IRB-approved script. If participants elected not to participate or were not eligible, all data obtained from the screening interview was destroyed. Participants were informed that their participation in this study was completely voluntary, they could refuse to take part in it or withdraw at any time, even after signing informed consent and their decision to not participate in the study did not affect their relationship with or the care received from the UPMC Cancer Centers or UPMC.

3.5.4 Potential Benefits

Participants were not likely to experience any direct benefit from this study, although some found the opportunity to share their experiences of dealing with lung cancer gratifying. It was hoped that study data would provide findings that would be used to improve care for future patients.

3.5.5 Importance of Knowledge to be Gained

It was hoped that, the knowledge gained from this study will improve outcomes of patients diagnosed with early stage lung cancer by providing information that was disseminated through publications and presentations and used to design future interventions.

3.5.6 Data Safety Monitoring Plan

Data and safety monitoring were conducted during monthly meetings with the Sponsor and Co – Sponsor during which data acquisition, management and any adverse events arising from the study were reviewed. Study procedures required that evidence of these reviews be provided to the IRB at the time of the yearly renewal. No unanticipated adverse events occurred.

3.5.7 Inclusion of Woman, Minorities, and Children

At the time of the study, patient demographic composition at the UPMC Cancer Center were 49% female; 1% Hispanic, 99% Non-Hispanic with a Non-Hispanic population composition of: 0% American Indian/Alaskan Native and Native Hawaiian/Pacific Islander, 5% Asian, 20% African American and 75% Caucasian.

Based on American Cancer Society 2008 statistics, the annual incidence of lung cancer per 100,000 people in minorities was 154.1 for blacks, 140.9 for whites, 68.9 for American Indians/Alaska Natives (AI/ANs), 122.6 for Asian/Pacific Islanders, and 22.3 for Hispanics (American Lung Association, 2008). Slightly more men than women were diagnosed with lung

cancer; however the incidence in men has been relatively stable whereas the incidence in women steadily increased until 2010 (American Cancer Society, 2014; American Lung Association, 2008).

The present study incorporated several measures to ensure ability to meet minority and gender recruitment goals. Dr. Rosenzweig (Committee Member) had been conducting research involving African American women with breast cancer. She and her team, which included several minority participants, provided advisement on ways to insure that the final sample reached the desired minority and gender participation goals, including publicizing the study through literature placed in the clinic and creating an atmosphere that encouraged participation. Gender and race of participants enrolled in this study were consistent with UPMC-wide patient demographics and slightly lower than the national averages.

3.6 METHODS SPECIFIC TO STUDY I: A DESCRIPTION OF THE SYMPTOM EXPERIENCE AFTER SURGERY FOR LUNG CANCER BASED ON THE THEORY OF UNPLEASANT SYMPTOMS (TOUS)

3.6.1 Purpose

The purposes of Study I: TOUS (Chapter 4) were: to describe the symptom experience of lung cancer patients within their first year after thoracic surgery and to determine the clinical utility of the TOUS for monitoring and managing symptom distress. The specific aims of the Study I were to: describe the symptoms experienced by patients in the first year following lung cancer

surgery, determine the associations between physiologic, psychologic and situational factors that influence patients' symptom(s), and determine the associations between symptom(s) on patients' performance.

3.6.2 Design

A cross-sectional, correlational design was used to describe the symptom experience and examine the relationships supported by the TOUS.

3.6.3 Data Analysis

Using SPSS Version 21 (2013, Armonk, New York), data were inspected for accuracy, missing values, and normality of distributions (Pallant, 2007; Tabachnick & Fidell, 2007). Data were inspected for accuracy, missing values, and normality of distributions (Pallant, 2007; Tabachnick & Fidell, 2007). Descriptive statistics were used to calculate percentages, frequencies, means, and standard deviations. When indicated, due to distribution of the data, variables were dichotomized. Scores obtained from the instruments used for this study were not normally distributed. Therefore, Spearman's rho ($p < .05$), was used to determine correlations between measures of symptom distress, influencing factors, and performance. The anxiety and depression subscales were highly correlated ($rho = .752$, $p < .01$); therefore, the HADS total score was used in the analysis. Statistical significance was set at $p \leq 0.05$ for all variables.

3.7 METHODS SPECIFIC TO STUDY II: POST THORACOTOMY PAIN SYNDROME (PTPS) FOLLOWING SURGERY FOR LUNG CANCER: PREVALENCE, CHARACTERISTICS AND IMPACT ON QUALITY OF LIFE

3.7.1 Purpose

The purpose of Study II (PTPS) (Chapter 5) was to compare the prevalence, characteristics, symptom experience, and impact of symptoms on quality of life in patients with and without PTPS.

3.7.2 Design

A between group comparison was used to describe the symptom experience of patients with and without PTPS.

3.7.3 Data Analysis

Using SPSS Version 21 (2013, Armonk, New York), data were inspected for accuracy, missing values, and normality of distributions and proportions (Pallant, 2007; Tabachnick & Fidell, 2007). Chi-Square or Fisher's exact test were used to determine differences between participants with and without PTPS (Pallant, 2007; Tabachnick & Fidell, 2007). Mann Whitney test was used to test for statistical significance between groups not normally distributed (Pallant, 2007; Tabachnick & Fidell, 2007). When significant differences were found, post-hoc comparisons

(Kruskal-Wallis) were performed to detect the point of difference (Tabachnick & Fidell, 2007). Significance was set at alpha ≤ 0.05.

3.8 SUMMARY OF FINDINGS

3.8.1 Study I: TOUS

There were six major findings in this study: 1) patients with no evidence of metastatic disease 2-12 months following surgery for lung cancer reported frequent symptoms; 2) although symptoms were frequent and often concurrent, most symptoms were associated with mild to moderate distress; 3) influencing factors were predominantly psychologic; 4) younger and earlier stage lung cancer patients reported more symptom distress; 5) greater symptom distress was associated with a greater impact on performance; and 6) greater psychological distress was associated with increased symptom distress and lower performance.

3.8.2 Study II: PTPS

The major findings in this study were: 1) patients who underwent a thoracotomy or thoracoscopic procedure using current surgical techniques were equally likely to report symptoms consistent with PTPS; 2) patients who experienced PTPS had discomfort at varied locations (incision, shoulder, chest tube and drain insertion sites), 3) Younger patients were more likely to report PTPS; 4)PTPS discomfort manifested as pain only, neuropathic symptoms only,

or as combination of both; and 5) symptom distress and quality of life differed significantly between patients with and without PTPS.

3.8.3 Plan for Publication of Findings

A summary of these findings are presented in the format of two manuscripts to be submitted for publication; Study I: TOUS in Chapter 4 and Study II: PTPS in Chapter 5.

3.9 SUMMARY OF GLOBAL IMPLICATIONS

3.9.1 Study I: TOUS

In 2008, the World Health Organization (WHO) recognized cancer as a leading cause of death with an estimated 7.6 million deaths worldwide, a number that is expected to increase to over 13 million deaths in 2030. Lung cancer was noted as a common cause of cancer death, accounting for 1.37 million (71%) of these deaths (Globocan, 2010). Hence, management of the care of patients who acquire lung cancer is an important aspect of nursing practice and, in particular, the practice of clinicians whose practice focuses on oncology. These findings can be used globally to improve the care of patients diagnosed with lung cancer. In particular, this study provides support for the TOUS as a conceptual framework with clinical utility assisting oncology clinicians in both explaining and identifying: the interaction of symptoms, influencing factors and their impact on performance in patient with cancer.

3.9.2 STUDY II. PTPS

In 2008, the WHO and the International Agency for Research on Cancer (IARC) collaborated with worldwide partners in the development and implementation of a Cancer Control: Knowledge into Action Plan designed to increase palliative care interventions for more effective management of symptoms resulting from cancer (World Health Organization, 2008). Pain and, in particular PTPS, is a concern for those involved in cancer care (Chapman, 2011; Pituskin et al., 2010; Montazeri et al., 1998). Findings of this study enhance understanding of symptoms associated with PTPS and, in particular, its neuropathic origins.

4.0 STUDY I: A DESCRIPTION OF THE SYMPTOM EXPERIENCE AFTER SURGERY FOR LUNG CANCER BASED ON THE THEORY OF UNPLEASANT SYMPTOMS (TOUS)

Abstract

Purposes: Although therapies have increased survival rates for lung cancer, symptom assessment and management of symptoms after lung cancer surgery remain a significant problem. The purpose of this study were to describe the symptom experience of lung cancer patients within their first year after thoracic surgery using the concepts and relationships of the Theory of Unpleasant Symptoms (TOUS) and to determine whether the TOUS has clinical utility for the monitoring and managing of symptoms.

Design: Descriptive, cross sectional, correlational study

Setting: Surgical oncology clinics of a large, academic medical center in the Mid-Atlantic Region of the United States

Sample: Convenience sample of 96 patients with no evidence of metastases who were between two months and 12 months after surgery for Stage I, II, or IIIa lung cancer

Methods: Patients who met eligibility criteria completed six self-report instruments during a regularly scheduled clinic visit. Data regarding clinical characteristics and comorbidities were abstracted from the medical record. Descriptive statistics were used to summarize results. Due to non-normality, Spearman's rho ($p \leq .05$) was used to determine correlations between symptom distress, influencing factors, and performance.

Main Research Variables and Measures: The TOUS includes three major concepts: symptoms, influencing factors (physiologic, psychologic, or situational), and performance. The Symptom Distress Scale (SDS) was used to measure symptom distress. Physiologic factors (age, gender, race, cancer stage, comorbidities and surgical approach) were measured using items of the Health History Survey (HHS) and the Charlson Comorbidity Index (CCI). Psychologic factors were measured using the Hospital Anxiety and Depression Scale (HADS) which includes subscales for anxiety and depression. Situational factors (educational level, marital status, and residential area) were measured using items of the Health History Survey (HHS). The Functional Well-Being Subscale of the Functional Assessment of Cancer Therapy-Lung (FACT-L) was used to measure functional performance.

Findings: The mean age of the sample was 67 years. Mean time since surgery was 6 months (SD = 2.9). The majority were white (92%) and married or with a steady partner (65%). On average, patients had 5.2 comorbid conditions (range 2-10). The median number of symptoms was 3, with 91% of patients reporting the presence of 2 or more concurrent symptoms. The majority of patients (97%) reported some level of symptom distress. Statistically significant negative correlations were found between age (rho = -.279, $p < .01$) and cancer stage (rho = -.228, $p < .05$)

and higher levels of symptom distress; those younger in age and later in stage reported more symptom distress. Statistically significant negative correlations were also found between level of symptom distress and performance (FACT-L functional subscale) (rho =-.684, p <.01); those with more symptom distress had less functional performance. Statistically significant positive correlations were found between psychologic factors (total HADS score) and level of symptom distress (rho =.763, p <.01) and poorer functional performance (rho = -676, p <.01). No additional physiologic factors (gender, surgical approach or CCI scores) or any of the situational factors (education, marital status, or place of residence) were significantly correlated with symptom distress.

Conclusion: Patients with early-stage lung cancer and no evidence of metastasis reported a wide range of post-operative symptoms. The majority of these symptoms occurred concurrently and were, for some, associated with severe distress. Consistent with the TOUS, the extent of symptom distress was found to influence functional performance. Greater psychologic distress (anxiety and depressive symptoms) was associated with increased levels of symptom distress and poorer functional performance. Some, but not all, physiologic influencing factors were associated with higher levels of distress; no situational influencing factors were significantly associated with symptom distress.

Implications for Nursing/Interpretation: The majority of patients reported multiple symptoms and some degree of symptom distress. Psychologic distress was found to be the strongest influence on level of symptom distress and reduced functional performance. A comprehensive approach to assessing and managing symptoms after surgery for lung cancer is needed. Oncology nurses can use the TOUS as a guide to assess an individual's symptoms, the factors that may be influencing

symptom distress and the impact of symptoms on performance in order to tailor symptom management strategies to the individual's experience.

Knowledge Translation: The TOUS provides clinical utility for nurses, as it reinforces the need to assess the presence of symptoms, degree of distress associated with the symptoms, factors that influence these symptoms, and impact of symptoms on performance.

4.1 INTRODUCTION

Lung cancer claims more lives each year worldwide than colon, prostate, ovarian, lymph, and breast cancer combined (American Cancer Society, 2013). Although new surgical techniques and combination therapies have increased survival rates (American Cancer Society, 2013), symptom assessment and management remain a significant problem (Gift, Jablonski, Stommel, & Given, 2004; Sarna et al., 2008). Up to 77% of patients report multiple concurrent symptoms (Cheng & Lee, 2011; Gift et al., 2004). Even long-term lung cancer survivors are known to experience substantial symptom burden and impaired QOL years after surgery (Yang et al, 2012). Severe symptoms such as fatigue, dyspnea, cough, and pain often persist beyond the first two months post-operatively (Sarna et al., 2008). However, our understanding of the factors that influence symptoms after surgery for lung cancer and the impact of symptoms on performance is limited. Since the patients' symptom experiences after lung cancer surgery is complex, a comprehensive assessment is important for monitoring and managing symptoms.

The TOUS purports relationships between symptoms, influencing factors, and performance (Figure 3). Symptoms are considered "red flags" that indicate changes in the

patient's normal functioning (Hegyvary, 1993), are multidimensional, and often occur concurrently (Lenz, Pugh, Milligan, Gift, & Suppe, 1997). Influencing factors (physiologic, psychologic and situational) influence symptoms which, in turn, impact functional performance and account for the distress, reduced QOL and other negative consequences of the symptom experience. The TOUS captures the complexity of the symptom experience (Lenz et al., 1997), and therefore, may serve as a useful framework for monitoring and managing symptoms.

The purposes of this study were to use the TOUS to describe the symptom experience of lung cancer patients within their first year after thoracic surgery and determine if the TOUS has clinical utility for monitoring and managing symptom distress.

4.2 METHODS

4.2.1 Design

A cross-sectional, correlational design was used to describe the symptom experience based upon the relationships supported in the TOUS. The study was approved by the Institutional Review Board, and patients provided written informed consent.

4.2.2 Sample Screening and Recruitment

Convenience sampling was used to recruit a cross-sectional cohort of patients treated by eight surgeons in three of the 14 university-based surgical oncology clinics of a large academic medical system between August 2010 and December 2012. Inclusion criteria were: 1) managed

surgically for Stage I, II, or IIIa lung cancer without evidence of metastasis (American College of Chest, 2007); 2) between two and 12 months post surgery for lung cancer (conforms to definition of chronic post-thoracotomy pain syndrome) (International Association for the Study of Pain, 2011); and 3) > 40 and < 86 years of age (lung cancer is infrequent at a younger age, and if present, likely atypical; older individuals are unlikely to be surgical candidates) (American Lung Association, 2008; Howlader et al., 2010). Exclusion criteria were: 1) any other cancer diagnosis or metastatic disease (to avoid confounding symptoms); 2) inability to speak, read, or understand English (instruments were in English); and 3) dementia or memory loss (limited ability to participate as informant).

To facilitate recruitment, clinic staff were educated about the study and given cards describing the inclusion and exclusion criteria to aid in identifying potential study participants. Clinic staff prescreened potential participants for eligibility, introduced the study, and referred interested patients to the principal investigator, who reconfirmed eligibility, obtained written informed consent and collected data.

4.2.3 Measures by Concepts of the TOUS

Symptoms

Symptoms were measured using the Symptom Distress Scale (SDS). The SDS is a 13-item, self-report instrument for patients to rate their distress due to cancer-related symptoms using Likert-scale responses (1 = No distress; 5 = Most distress). The total SDS distress score is calculated by summing distress ratings for all symptoms; possible scores range from 13 (no symptom distress) to 65 (highest level of distress) (McCorkle, Cooley, & Shea, 1998). Based on prior breast cancer

studies, total SDS scores of 25 to 32 represent moderate levels of distress, and scores greater than 32 represent severe distress (McCorkle et al., 1998). In addition to determining the overall level of symptom distress and distress for each symptom, the SDS was used to describe the number, type and presence of concurrent symptoms. The SDS has established reliability with Cronbach's alpha coefficients ranging from .82 to .97 in cancer populations, including persons with lung cancer, (McCorkle et al., 1998) and .85 in this sample. The SDS was found to have acceptable construct validity based on the inverse relationship found between the SDS and the Karnofsky Performance Status Scale (Sarna & Brecht 1997).

Physiologic Influencing Factors

The Health History Survey (HHS), an investigator-designed instrument, was used to assess the socio-demographic and clinical characteristics of the sample including age, gender, race, cancer stage and surgical approach. The 16-item version of the Charlson Comorbidity Index (CCI) (Heller, Ahern, Pringle, & Brown, 2009) was used to identify the number and severity of comorbidities. Scores were calculated by applying a weighted value to each comorbid condition documented in the medical record for a possible range of scores from 0 to 24 (Heller, Ahern, Pringle, & Brown, 2009) Higher scores indicate higher comorbidity burden. The original 19-item version CCI has well established validity with higher scores associated with increased mortality (X^2 = 165; p <.0001) (Charlson, et al 1987). Modification from the 19-item version to the 16-item version was made to eliminate overlapping items (Heller et al., 2009).

Psychologic Influencing Factors

The Hospital Anxiety and Depression Scale (HADS), a 14-item, self-report instrument, was administered to assess the presence of distressing mood (Snaith, 2003). The HADS includes an anxiety and depression subscale; each subscale includes seven Likert-scale items scored from

0 to 3, with some scores reversed so that higher scores indicate worse mood (Snaith, 2003). Items are summed for a possible range of 0-42 for the total HADS score and 0-21 for each subscale. Based on previously established thresholds for psychologic distress (Snaith, 2003), subscale scores between 0 and 7 are considered normal; subscale scores between 8 and 10 are suggestive of a mood disorder; and subscale scores ≥ 11 indicate the probable presence of a mood disorder. Initially developed in 1983, the HADs was shown to be internally consistent and reliable with Cronbach's alpha coefficients of .81, .90, and .87 for the anxiety, depression and total HADS scores, respectively (Zigmond and Snaith 1983) The HADS has since been used in over 740 studies (Bjelland et al 2002). A review of these studies reaffirmed the construct validity of the HADs. In the present study, Cronbach's alpha coefficients were .89 .88, and .93, for anxiety, depression and total HADS scores, respectively.

Situational Influencing Factors

Additional items of the Health History Survey (HHS) were used to assess situational factors. These were defined as the highest level of education, marital status and residential area (rural or urban).

Performance

The FACT-L includes five subscales measuring physical, social, emotional and functional well-being and an additional subscale for lung. Higher scores indicate a more positive assessment of quality of life. The TOUS model measures performance, rather than quality of life and, recently, researchers have noted that functional status is a more appropriate measure of performance, rather than QOL (Cheng & Lee, 2011). Therefore, the 7-item Functional Well-Being subscale of the FACT-L (Cella et al., 2002) was used to measure physical performance. Higher scores indicated higher levels of functional performance.

In studies of patients with lung cancer, the FACT-L was found to be reliable with alpha coefficients $\geq$ .81 for the total and each of the subscale scores (Browning, Ferketich, Otterson, Reynolds, & Wewers, 2009); strong criterion validity was found between the FACT-L and the Lung Cancer Symptom Scale (Browning et al., 2011). Cronbach's alpha for the functional subscale in this sample was .90.

4.2.4 Data Analysis

Analyses were conducted using SPSS Version 21 (2013, Armonk, New York). Data were inspected for accuracy, missing values, and normality of distributions (Pallant, 2007; Tabachnick & Fidell, 2007). Descriptive statistics were used to calculate percentages, frequencies, means, and standard deviations. Due to a disproportionate number of cases in the original groupings, both physiological (gender, cancer stage, surgical approach) and situational influencing factors (education, marital status, and residential area) were dichotomized. Due to limited variation in the sample, race was not included in the final analysis. None of the continuous scores (CCI, SDS, HADS, FACT-L) were normally distributed, therefore, Spearman's rho ($p < .05$), was used to determine correlations between measures of symptom distress, influencing factors, and performance. The anxiety and depression subscales were highly correlated (rho = .752, $p < .01$); therefore, the HADS total score was used in the analysis.

4.3 **RESULTS**

Of the 112 patients deemed eligible, 110 agreed to participate, yielding a 98% acceptance rate. Fourteen subjects were lost to attrition, resulting in final sample of 96 subjects (Figure 4) .

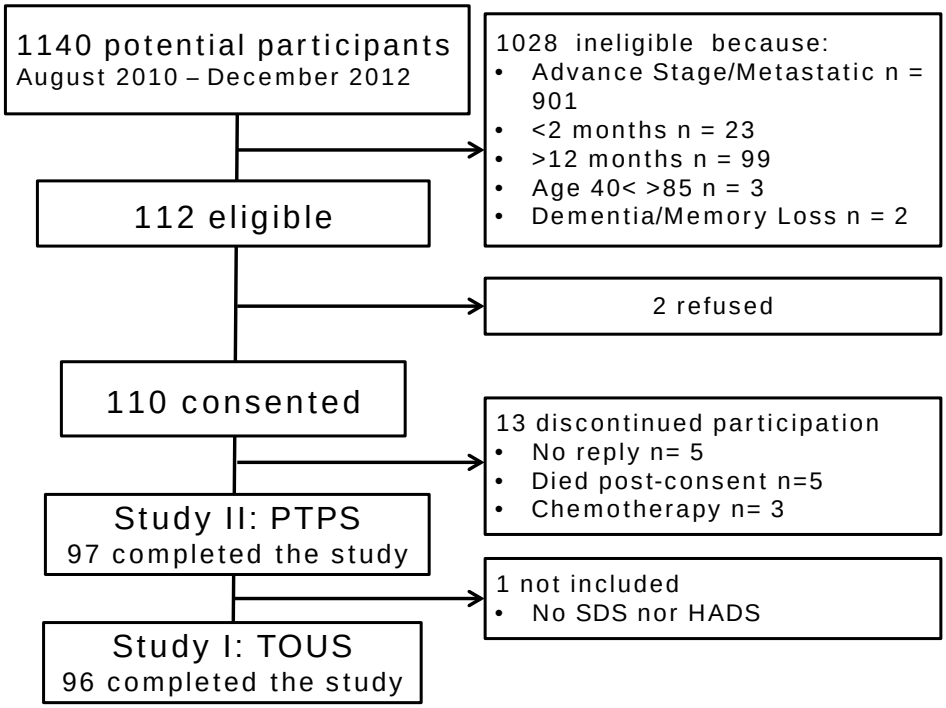

Figure 4. Flowchart of study recruitment and retention

4.3.1 Sample Characteristics

Characterstics of the sample, including scores on the instruments, are presented in Table 1 and discussed below, according to the concepts of the TOUS.

Table 1. Characteristics of the TOUS concepts (n=96)

	N	%	Mean	SD	Range
Symptoms					
Symptom Distress Scale (Total Score)			22.4	7.4	(13-49)
Physiologic Influencing Factors					
Time since surgery, months			6.0	2.9	(2-12)
Age, years			67.2	9.7	(45-84)
Gender, Male	46	47.9			
Race, White	88	91.7			
Cancer Stage					
Stage I	53	55.2			
Stage II	31	32.3			
Stage IIIa	12	12.5			
Surgical Approach					
Thoracotomy	51	53.1			
Thorascopic	45	46.9			
Charlson Comorbidity Index			5.2	1.5	(3-10)
Psychologic Influencing Factor					
Hospital Anxiety and Depression Scale					
Anxiety Subscale-score			4.3	3.9	(0-15)
Depression Subscale-score			3.6	3.6	(0-16)
Total HADS Score			7.9	7.1	(0-26)
Situational Influencing Factors					
Highest Level of Education					
Elementary	9	9.3			
High School/GED	39	40.6			
Technical School/Some College	28	29.2			
College Graduate	20	20.8			
Marital Status					
Divorced	16	16.7			
Single	4	4.2			
Widowed	14	14.6			
Married or in a steady partnership	62	64.6			
Residential Area					
Rural	50	52.1			
Urban	46	47.9			
Performance [a]					
FACT-L					
Functional Performance Subscale-score			20.3	7.0	(0-28)

[a] n=95

Symptoms

Total SDS scores ranged from 13 to 49 with a mean (SD) of 22.4 (7.4) (Table 1). The distribution of total SDS scores with the line of threshold ≥ 33 indicating severe distress (McCorkle et al., 1998; Holmes, 1989) are presented in Figure 5.The number of patients endorsing each symptom and the level of reported distress per symptom is shown in Figure 6. The number of symptoms reported per patient ranged from 0 - 13 (mode = 3). The majority (91%) reported the presence of concurrent symptoms (≥ 2 symptoms) (Figures 5 & 6).

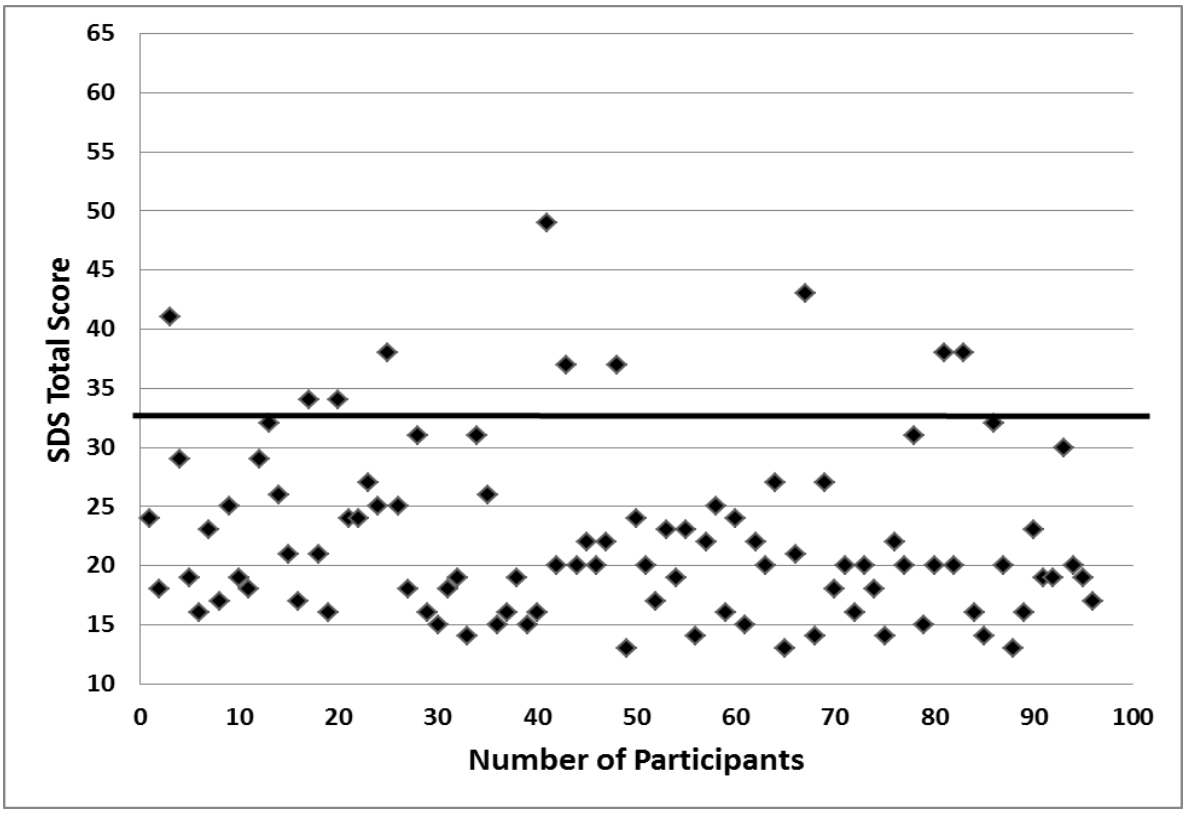

Figure 5. Distribution of SDS total scores

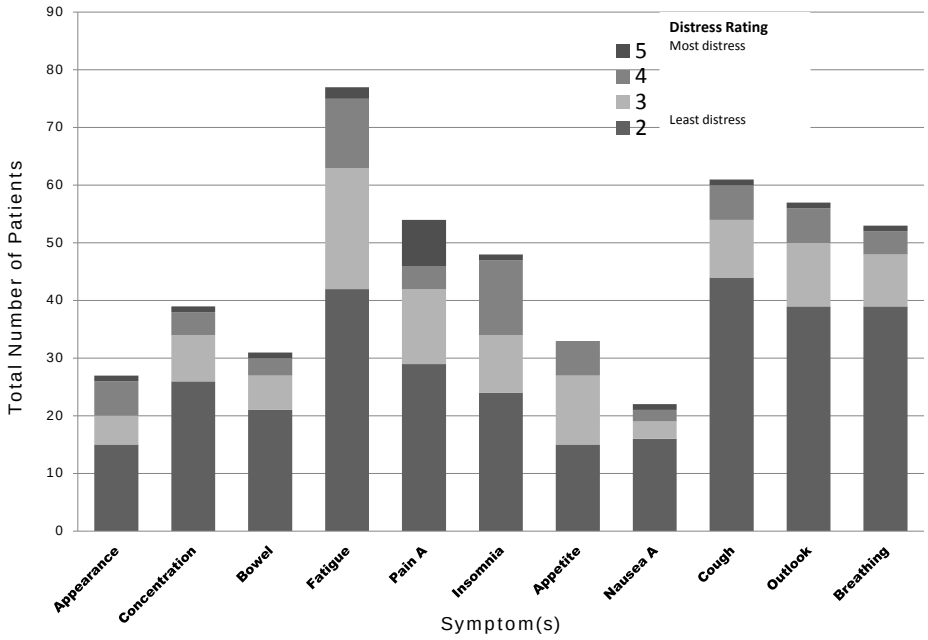

Figure 6. Symptom distress ratings

Physiologic Influencing Factors

Age ranged from 45 to 84 with a mean of 67 years (Table 1). The majority was white (92%). Approximately half were female (52%), underwent a thoracotomy (53%), and had Stage 1 lung cancer (55%). The number of comorbid conditions ranged from 3-10 with a mean CCI score of 5.2 (1.5), median of 5.

Psychologic Influencing Factors

The total HADS score ranged from 0 to 26 with a mean of 7.9 (7.1). Mean anxiety and depression subscale scores were 4.3 and 3.6, respectively. Six patients (6.2%) reported sub-

scores $\geq$ 11 for either anxiety or depression, the threshold for a reportable mood disorder. These findings were reported to the clinical staff and all patients were found to be currently receiving treatment for their psychologic distress.

Situational Influencing Factors

The majority of the sample was married or with a steady partner (62%). Nearly half were educated beyond high school (49%) and more than half resided in a rural area (52%).

Performance

The mean FACT-L functional subscale score for the sample was 20.3 (7.0), with a median of 22. Scores ranged from 0 to 28.

4.3.2 Correlational Analysis

The correlation coefficients (Spearman's rho) between symptoms, influencing factors and performance are shown in Table 2. Statistically significant negative correlations were found between symptom distress and two physiologic influencing factors (age and cancer stage I) (rho = -.279, $p<.01$ and rho = -.228, $p<.01$, respectively), and between level of symptom distress and performance (rho = -.684, $p<.01$). Statistically significant positive correlations were found between symptom distress and psychologic influencing factors (total HADS score) and level of symptom distress (rho=.763, $p<.01$).

Two physiologic influencing factors, age and gender, demonstrated significant negative correlations with the psychologic influencing factors (total HADS score), (rho = -.308, $p<.01$ and rho = -.263, $p<.01$, respectively). Cancer stage I was positively correlated with performance (rho

=.205, p <.05). In addition, the psychologic influencing factors (total HADS score) was negatively correlated with performance (rho = -.676, p<.01). No other physiologic influencing factors (gender, surgical approach, CCI scores) or situational influencing factors (education, marital status, place of residence) were significantly correlated with symptom distress, influencing factors or performance.

Table 2. Correlational comparisons (n=96)

	Symptoms	**Influencing Factors (Physiologic)**				**(Psychologic)**	**(Situational)**			**Performance**
	SDS Total Score	Age	Gender Male	Cancer Stage I	CCI Total Score	HADS Total Score	Education College	Marital status: Married/ steady partnership	Residence Urban	FACT-L [a] Functional Sub-Score
Symptoms SDS Total Score	-	-.279**	-.194	-.228*	.170	.763**	-.093	-.127	.034	-.684**
Influencing Factors (Physiologic) Age			.094	-.062	.097	-.308**	-.070	-.042	-.036	.130
Gender: Male				-089.	-.196	-.263**	.237*	.193	-.012	.025
Cancer Stage: I					-.041	-.112	.137	.028	.019	.205*
CCI Total Score						.135	-.146	-.133	-.002	-.109
Influencing Factors (Psychologic) HADS							-.179	-.160	.022	-.676**
Influencing Factors (Situational) Education: College								-.008	.010	.130
Marital Status: married/ steady partnership									.092	.007
Residence: Urban										-.163
Performance FACT-L [a] Functional Sub-Score										-

4.4 DISCUSSION

There were six major findings in this study: 1) patients with no evidence of metastatic disease 2-12 months following surgery for lung cancer reported frequent symptoms; 2) although symptoms were frequent and often concurrent, most were associated with mild to moderate distress; 3) influencing factors were predominately psychologic; 4) younger and earlier stage lung cancer patients reported more symptom distress; 5) greater symptom distress was associated with a greater impact on performance; and 6) greater psychological distress was associated with increased symptom distress and lower performance.

4.4.1 Symptoms

In the present study, the majority (96%) of patients with no evidence of metastatic disease following lung cancer surgery reported some level of symptom distress. In addition, most (91%) patients reported the presence of concurrent symptoms ($\geq$ 2 symptoms), with 14 (14.6%) patients reporting 3 concurrent symptoms and 12 (12.4%) patients reporting 5-7 concurrent symptoms. Although most scores reflected low to moderate distress, 10 patients (10%) presented with scores reflecting severe distress. Our findings support the need to comprehensively assess patients for symptom distress following the diagnosis of lung cancer, including those with early stage disease that who underwent surgery and those who are beyond the immediate postsurgical period.

Findings from the present study support that patients diagnosed with lung cancer experience multiple and common symptoms, regardless of the stage of the disease. The most frequently reported symptoms in this sample were fatigue (76%), cough (62%), breathing (54%) and pain (36%) were consistent with those previously reported (Gift, Jablonski, Stommel, & Given, 2004). Sarna et al., (2008) , reported the most commonly occurring symptoms as fatigue (57%), dyspnea (49%), cough (29%), and pain (20%), measured by the Lung Cancer Symptom Scale (Sarna et. al., 2008). Both studies report symptoms similar to those reported by patients in the present study. Level of distress was difficult to compare owing to difference in instruments.

4.4.2 Influencing Factors

Physiologic influencing factors examined in this study, such as sociodemographics indicated that our sample was comparable to other lung cancer populations with regard to age and gender. Younger patients reported greater symptom distress, a finding contrary to prior studies. Earlier research in patients with lung cancer indicated that age (older) may be related to the type of symptoms reported and the level of distress associated with these symptoms (Gift et al., 2004). Although the mean age of our patients was typical of those with this diagnosis, there was a large range (45-84) that included patients notably younger than typical for this diagnosis, a potential explanatory factor.

Psychologic influencing factors measured in our sample reflected lower levels of anxiety and depression compared to a prior study of patients treated surgically for Stage I, II, or IIIa lung cancer (Sarna et al, 2010) but comparable to levels of distress among patients with non-small cell and small cell lung cancer, (Buchanan et al. (2010). In the present study, total HADS total scores indicated that

the typical subject had normal levels of psychologic distress with the exception of six subjects (6.2%) who were currently under treatment for these conditions. The reason for these differences are unclear but likely reflects differences in sample characteristics, measurement tools, and potentially time since surgery since our sample included patients 2-12 months post-surgery. With the exception of the percentage of our sample residing in rural areas, situational factors were similar to those reported previously for lung cancer populations.

4.4.3 Influencing Factors and Symptoms

As predicted by the TOUS, physiologic and psychologic influencing factors influenced symptom distress, as with previous studies, patients with higher levels of psychologic distress reported higher levels of symptom distress (Barsevick et al., 2006; Lee, 2005; Sarna et al., 2008). Of the five physiologic influencing factors (age, gender, cancer stage, surgical procedure, and comorbidities), only younger age and higher cancer stage were significantly related to symptom distress. Because HADS sub-scale scores for anxiety and depression were highly correlated ($r= .735$, $p=.01$), only the total score was used. Higher levels of anxiety and depressive symptoms were significantly associated with higher symptom distress ($rho = .763$, $p =.05$). No additional physiologic factors (gender, surgical approach or CCI scores) or any of the situational factors (education, marital status, or place of residence) were significantly correlated with symptom distress.

4.4.4 Symptoms and Performance

As predicted by the TOUS, and reported previously in studies of lung cancer, (Barsevick et al., 2006; Cheng & Lee, 2011; Dodd, Cho, Cooper, & Miaskowski, 2010; Gift et al 2008), patients with higher

levels of symptom distress experienced worse functional performance. This finding further highlights the need to explore symptoms experienced by patients with lung cancer and the impact on daily life activities (performance).

4.4.5 Interrelationships

In the present study, subjects reporting higher total scores on the HADS also reported lower functional performance (rho = -.676, p=.01). Contrary to expectations, age and gender were negatively associated with total HADS scores (rho = -.308, p <.01 and rho = -.263, p=.01, respectively) (Gift et al., 2004). Hence, younger and male subjects reported higher total HADS scores, reflecting greater anxiety and depressive symptoms.

Although significant relationships were found, it is important to note that the mean level of psychological distress in this sample was considered in the normal range (based on average HADs sub-scores < 8) and only 10% of patients in this sample were deemed to have clinically significant levels of anxiety or depression. Our sample may be healthier than those in other studies due to this study's inclusion criteria, which required that patients meet criteria for lung cancer surgery, which offers the potential of cure. Also, subjects were excluded if they were diagnosed with metastasis. Further, subjects were eligible for study entry 2-12 months after lung surgery.

4.4.6 Limitations

Subjects enrolled in this study were recruited from one university affiliated thoracic surgery practice with experienced operators that may not be representative of other centers. Also, subjects were predominantly white and therefore findings may not be generalizable to other non-white racial or ethnic groups. Subjects with metastasis who were not eligible for lung cancer surgery were excluded from this study. These patients may be more likely to experience higher cancer stages, lower survival rates, and therefore, more symptoms, psychological distress and lower functional performance.

4.5 NURSING IMPLICATIONS

Even up to one year after surgery, in patients with no evidence of metastatic disease, symptom distress was prevalent. Due to the presence of multiple symptoms, a comprehensive approach is needed in clinical practice to identify where to focus interventions. The TOUS may be a useful guide for oncology nurses because it considers the complexity of the symptom experience -- the potential for concurrent symptoms, the factors that influence them and their impact on performance. We concur with Lee (2005) and Myers (2009), who concluded that the TOUS had clinical utility for nurses to examine the relationships between symptoms, their influencing factors, and impact on performance to help identify opportunities for improving the symptom experience.

4.6 KNOWLEDGE TRANSLATION

Due to the complexity of lung cancer patients' symptom experiences, the TOUS may provide clinical utility for nurses, as it reinforces the need to assess the presence of symptoms, degree of distress associated with the symptoms, factors that influence these symptoms, and impact of symptoms on performance.

5.0 STUDY II: POST THORACOTOMY PAIN SYNDROME (PTPS) FOLLOWING SURGERY FOR LUNG CANCER: PREVALENCE, CHARACTERISTICS AND IMPACT ON QUALITY OF LIFE

Abstract

Purposes: Most prior studies examining persistent pain following surgery for lung cancer included few patients undergoing a minimally invasive approach. Several studies have proposed a neuropathic origin for this outcome. However, there has been limited exploration of this consequence using standardized instruments. We therefore compared the symptom experience and impact of symptoms on quality of life in patients with and without post-thoracotomy pain syndrome (PTPS). Methods: Patients completed questionnaires to assess presence of pain (McGill Pain Questionnaire), neuropathic symptoms (Neuropathic Symptom Questionnaire), symptom distress (McCorkle Symptom Distress Scale), anxiety and depression (Hospital Anxiety Depression Scale) and quality of life (Functional Assessment of Cancer Therapy-Lung). Results: The majority (54.6%) reported symptoms associated with PTPS, with no significant difference between surgical procedure groups (p=.398). Excepting younger age (p=.009), no demographic or surgical characteristic differentiated patients with and without PTPS. Patients with PTPS described their discomfort as pain only (15.1%), neuropathic symptoms only (30.2%) or pain and neuropathic symptoms (54.7%) at varied locations in combination

or singly (incision, chest tube and drain sites, shoulder). Scores on questionnaires differed between patients with and without PTPS for symptom distress ($p < .001$), anxiety and depression ($p < .001$), and quality of life ($p = .009$), with higher distress associated with PTPS. Discussion: Despite new surgical techniques, PTPS remains a common postsurgical complication and results in considerable distress. PTPS presents with varied symptoms, attributed to varied locations. A focused assessment is needed to identify all experiencing this condition, with referral to pain management specialists if symptoms persist.

5.1 INTRODUCTION

Post-thoracotomy pain syndrome (PTPS) has been defined as pain that recurs or persists along a thoracotomy incision at least 2 months after the surgical procedure (International Association for the Study of Pain, 2011; Merskey 1986). A variety of surgical procedures have been reported to cause chronic post-surgical pain, with an estimated incidence of 20% to 50% (International Association for the Study of Pain, 2011). For post thoracotomy patients, the estimated incidence ranges from 5-65% with 10% of patients reporting severe pain, defined as a > 5 rating on a 10-point scale (International Association for the Study of Pain, 2011). First reported as a consequence of “war wounds of the chest” (Blades & Dugan, 1944, p.301), PTPS received limited attention until a seminal study conducted by Dajczman et al. (1991) reported the presence of post-surgical pain in a series of 56 lung cancer patients who were disease free up to 5 years after thoracotomy.

Notably, not all patients who undergo lung cancer surgery develop PTPS. The pathology of PTPS has been attributed to rib (Bayram et al., 2011; Landreneau et al., 1994), nerve (Bayram et al., 2011; Miyazaki et al., 2011; Benedetti et al., 1998), or muscle (Karasaki et al., 2009; Frola et al., 1995) damage from surgery or a chronic pain syndrome initiated by inadequate pain relief in the postoperative period (Demmy, 2009; Duale et al., 2009); however, the true origin remains unclear. Other potential causative mechanisms include nerve or muscle damage related to the insertion of chest tubes and drains (Grosen, Petersen, Pfeiffer-Jensen, Hoejsgaar, & Pilegaard, 2012; Mongardon et al., 2011). More effective acute pain management has also not been successful in eliminating this condition (Wildgaard et al., 2011). As well, newer video-assisted surgical techniques do not appear to result in a reduction in incidence (Furrer et al., 1997).

Most prior studies of PTPS enrolled patients who underwent standard open thoracotomy and did not compare neoplasm location, cancer stage, or cell type, as potential factors influencing access and therefore injury to muscles, ribs, and costovertebral joints. Although it has been suggested that minimally invasive thoracoscopic procedures may result in less injury and therefore less risk for PTPS, most prior studies included few (Karasaki et al., 2009; Tsuchida, Hashimoto, Saito, Koike, & Hayashi, 2007; Furrer et al., 1997) or no (Grosen et al., 2012; Duale et al., 2011; Guastella et al., 2011; Mongardon et al., 2011; Pluijms, Steegers, Verhagen, Scheffer, & Wilder-Smith, 2006) patients managed using a minimally invasive approach.

Several prior studies have proposed a neuropathic origin for PTPS (Wildgaard et al., 2012; Duale et al., 2011; Magurie, Ravenscroft, Beggs, & Duffy, 2006; Pluijms et al., 2006). However, there has been limited exploration of this consequence using a battery of standardized instruments to rate pain intensity, symptom distress or impact on quality of life (Mongardon et al., 2011). The purpose of this

study was to compare the prevalence, characteristics, symptom experience, and impact of symptoms on quality of life in patients with and without PTPS. Our sample included 51 patients who underwent a standard thoracotomy and 46 who underwent a minimally invasive thoracoscopic procedure.

5.2 METHODS

The study was conducted between August 2010 and November 2012 at the University of Pittsburgh Medical Center Cancer Clinics. The study was approved by the University of Pittsburgh Institutional Review Board and all participants provided written informed consent.

5.2.1 Sample

Inclusion criteria: 1) managed surgically for Stage I, II, or IIIa lung cancer without evidence of metastasis; 2) between 2 and 12 months post–surgery (conforms to definition of PTPS); and 3) greater than 40 years of age (lung cancer is infrequent in those younger and if present likely atypical). Exclusion criteria: 1) any other cancer diagnosis or metastatic disease (to avoid confounding symptoms), 2) inability to speak, read, or understand English (questionnaires were in English), and 3) presence of comorbidities such as dementia, or memory loss (limited ability to participate as informant).

Study participants were selected from three of the fourteen hospitals in a university based surgical practice. A total of 1140 patients were screened, resulting in 112 potentially eligible subjects.

Two patients were not enrolled due to refusal. Of the 110 patients who provided informed consent, 13 did not complete the study for the following reasons: 5 did not return instruments, 5 died, and 3 were no longer eligible due to new metastatic disease. Thus, the final sample consisted of 97 of 110 (88.1%) participants.

5.2.2 Surgical Procedure

Choice of surgical procedure was at the discretion of the operating surgeon. Aside from surgeon preference, reasons for selecting the surgical procedure included tumor grade, location, lymphovascular invasion, histology type, pleural involvement, size and surgical margins (Detterbeck, Lewis, Diekemper, Addrizzo-Harris, & Albert, 2013). A complete surgical resection with curative intent was performed in all cases. No patient received preoperative radiation or chemotherapy.

5.2.3 Measures

Participants were given 6 self-report measures that took an average of 30 minutes to complete, with the option to complete the instruments in clinic or at home and return them in a pre-addressed mailing envelope. Study participants provided informed consent before completing study instruments.

McGill Pain Questionnaire (MPQ)

This self-report questionnaire was the primary tool used to identify pain resulting from PTPS. It was chosen because it assessed pain intensity (1-10 scale), rated quality and distress using 78 descriptors classified into 20 groups and included a figure used to identify this distress at specific body

locations (McGill, 2009). Of the descriptors, only two ("numb" and "tingling") were used to identify neuropathic symptoms in the present study. Because prior studies of patients after chest surgery noted that, not just the surgical area, but also chest tube and drain sites were areas of pain, the instructions were modified to request that patients mark and rate their postsurgical pain at three locations: incision, drain and chest tube sites. For this study an overall pain score was calculated based upon the incision pain score. Instrument reliability and validity have been established in prior testing (McGill, 2009; Graham, Bond, Gerkovich, & Cook, 1980).

Neuropathic Symptom Questionaire (NSQ)

Because the MPQ was deemed inadaquate to appropriately identify neuropathic symptom descriptors associated with PTPS, the NSQ was added after 51 subjects were recruited. The descriptors included in the NSQ were chosen based on the terminology used by patients during follow-up clinic visits and a literature review (Bousassira & Attal, 2011). When completing the NSQ, participants were asked to "describe their discomfort at the surgical site" and to rate the presence and severity of "tingling", "numbness", "increased sensation due to touch" and "increased sensation due to movement" using a numeric visual analog scale (VAS) with zero indicating no discomfort and 10 the worst discomfort possible. MPQ descriptors (numb and tingling) were used to identify participants with neuropathic symptoms for subjects enrolled prior to adding the NSQ.

McCorkle Symptom Distress Scale (SDS)

The SDS was a 13-item, self-report scale designed to assess the subjective distress associated with 11 cancer related symptoms e.g., fatigue, pain, insomnia, cough, breathing, using a Likert-type scale (1 = least distress to 5 = most distress) with a total score ranging from 13 to 65 (McCorkel & Young 1979). Higher scores indicate more distress. Ratings were summed to achieve a total symptom

score. McCorkle et al. (McCorkel & Young 1979) suggested that a total score of 25 to 32 indicate moderate distress and scores ≥ 33 indicate severe distress. This total score was the variable used in this study. Instrument reliability and validity of the SDS have been established in prior testing (McCorkle et al., 1998; McCorkel & Young 1979).

Health History Survey (HHS)

A researcher-designed self-report instrument was used to identify personal, social, and medical variations among patients. Personal information was provided by the participant and included age, gender, race, ethnicity and smoking history. Social information included marital and employment status. Information provided by medical record included tumor type, cancer stage, surgical approach, and surgical procedure.

Charlson Comorbidity Index (CCI)

The CCI was designed to assess the presence and type of 19 comorbid conditions (Charlson, et al., 1987). Each condition included in the medical history was assigned a weight (1-6 points) based on the strength of its association with mortality. No weight adjustments were made for age. Instrument reliability and validity have been established in prior testing (deGroot, Beckerman, Lankhorst, & Bouter, 2003; Charlson, et al., 1987).

Hospital Anxiety and Depression Scale (HADS)

This instrument was a 14-item questionnaire designed to screen for mood disorders (Snaith, 2003; Zigmong & Snaith 1983). The HADS was comprised of an anxiety and depression symptom subscale. Each of the subscales contained 7 Likert response items scored 0 to 3, with some scores reversed. The total possible score ranged from 0 to 42. The total possible score for two sub-scores

ranged from 0 to 21. Scores have been categorized as normal (range 0-7), suggestive of a mild mood disorder (range 8-10), and reportable presence of a reportable mood disorder (range 11-21). Prior studies have validated use of similar screening tools to evaluate distress in lung cancer patients (Buchanan, Milroy, Baker, Thompson, & Levack, 2010; Carlson, Groff, Maciejewski, & Bultz, 2010). Instrument reliability and validity have been established in prior testing (Snaith, 2003; Bjellend, Dahl, Haug, & Necklemann, 2002; Zigmong & Snaith 1983).

Functional Assessment of Cancer Therapy-Lung (FACT-L)

The FACT-L is a self-report, 44-item questionnaire designed to measure quality of life for lung cancer patients (Cella et al., 1995). The FACT-L is comprised of 5 subscales that measure lung-related symptoms and physical, social, functional, and emotional well-being. Scores for each of the five subscales range from 0 to 28, with higher scores implying higher quality of life. Subscale scores can be summed to calculate a total score (0 to 176) (Cella et al., 1995). Instrument reliability and validity have been established in prior testing (Cella et al., 2002; Soni et al., 2002; Soni & Cella, 2002; Cella et al., 1995).

5.2.4 Symptom Categories

Subjects were first divided into two categories consisting of patients with and without PTPS. No PTPS was defined as a MPQ score of 0 and no neuropathic descriptors. Next, patients with PTPS were divided into 3 subgroups to assist in exploring the neuropathic components of this condition. PTPS with pain only was defined as a MPQ score of greater than zero with no neuropathic descriptors. PTPS with neuropathic symptoms was defined as a MPQ score of 0 and one or more neuropathic descriptors.

PTPS with pain and neuropathic symptoms was defined as a MPQ score of greater than zero and one or more neuropathic descriptors.

5.2.5 Analytic Strategy

Data analysis was conducted using SPSS Version 21 (2013, Armonk, New York). Missing data were confined to one subject who did not return the SDS and HADS and a second subject who did not return the FACT-L. Comparisons between participants with and without PTPS were made using Chi-Square or Fisher's exact test, as indicated (Pallant, 2007; Tabachnick & Fidell, 2007). The Mann Whitney test was used to test for statistical significance between groups because responses were not normally distributed (Pallant, 2007; Tabachnick & Fidell, 2007). When significant differences were found, post-hoc comparisons (Kruskal-Wallis) were performed to detect the point of difference (Tabachnick & Fidell, 2007). Statistical significance was set at $p \leq 0.05$ for all variables.

5.3 RESULTS

5.3.1 Demographic and medical Characteristics

The sample included 97 patients (47 men, 50 women) who ranged in age from 45 to 84 years (mean 67.3 ± 9.7 years). The majority were Caucasian 89 (91.8%), married or living with a significant other

63 (64.9%), with half 49 (49.5%) having some college or technical training. A minority 23 (23.7%) worked either part or full time. Approximately half 46 (47.4%) lived in the city with the remainder in rural areas. These data are presented in Table 3. Only younger age showed a statistically significant difference between patients with and without PTPS (p=.009). Patients with PTPS were significantly younger than those without PTPS.

Of the 97 patients, 59 (60.8%) were between 2 and 6 post-operative months and 38 (39.2%) between 7 and 12 post-operative months. Approximately half 51 (52.6%) underwent a thoracotomy and the remainder 46 (47.4%) a thoracoscopic procedure for Stage I 64 (66.0%), II 19 (19.6%), or IIIa 14 (14.4%) lung cancer. Half of the patients 53 (54.6%) reported symptoms associated with PTPS, with no significant difference between those undergoing the two procedures (p=.398). All patients were disease free at follow-up interviews (2-12 months). Slightly more than half (57.3%) had a lobectomy and the remainder received either a wedge segmentectomy or sleeve lobectomy procedure. The sites most commonly resected were the right lung 51 (52.6%) and upper lobe 53 (54.6%). The majority were diagnosed with Stage I disease 64 (66.0%) and the most common neoplasm cell type was adenocarcinoma 60 (61.9%). There was no statistically significant difference between patients with and without PTPS for any examined medical characteristic.

Table 3. Between group comparisons (n=97)

Variable	No PTPS n=44	PTPS n=53	p-value
Age (Years) Mean (SD)	70.1 (9.0)	65.0 (9.8)	.009*
Smoking (Pack Years) Mean (SD)	46.6 (41.4)	41.1 (30.4)	.821
Charlson Comorbidity Score Mean (SD)	5.1 (1.6)	5.3 (1.3)	.371
Gender (Male)	50.0%	47.2%	.471
Race/Ethnicity (Caucasian)	95.5%	88.7%	.203
Married or steady partner	61.4%	67.9%	.528
Not employed	75.0%	77.4%	.4886
Some college or technical school	43.2%	54.7%	.177
Resident of rural area	56.8%	49.1%	.289
Time since surgery (2-6 months)	63.6%	58.5%	.380
Surgical Approach			-
Thoracotomy	50.0%	54.7%	.398
Thoracoscopic	50.0%	45.3%	
Surgical Procedure			-
Lobectomy	52.3%	60.4%	.275
Other Procedure	47.7%	39.6%	
Tumor Location			-
Right lung	54.5%	50.9%	.857
Upper lobe	54.5%	54.7%	.675
Cancer Stage (I a & b)	70.5%	62.3%	.149
Cancer Cell Type (Adenocarcinoma)	61.4%	62.3%	.087

PTPS: post thoracotomy pain syndrome

*Significant difference between patients with and without PTPS.

5.3.2 Impact of PTPS

Ratings of pain, symptom distress, anxiety, depression & quality of life in patients with (n=53) and without PTPS (n=44) are presented in Table 4. Patients with PTPS reported a relatively low rating of pain on the MPQ (3.3 ± 3.3). Although the majority 32 (60.4%) reported a pain score ≤ 3 (mild pain),

12 (22.6%) reported a score between 4 and 7 (moderate pain) and 9 (17.0%) reported a score > 7 (severe pain). Patients reporting moderate or severe pain were being managed using a variety of medications.

Table 4. Between group comparisons

Instrument	No PTPS n=44		PTPS n=53		p-value
	Mean	**SD**	**Mean**	**SD**	
SDS Total Score	18.3	3.7	25.9	8.1	.000*
HADS Total Score	5.4	5.4	10.1	7.6	.001*
Anxiety sub-score	3.1	3.2	5.4	4.3	.013*
Depression sub-score	2.2	2.6	5.0	3.9	.001*
FACT-L Total Score	112.3	15.5	92.1	24.5	.009*
Physical sub-score	26.0	1.9	20.6	6.1	.001*
Social sub-score	23.3	5.7	21.5	6.3	.100
Emotional sub-score	19.9	4.3	18.8	4.6	.321
Functional sub-score	22.2	7.1	18.5	7.1	.006*
Lung related symptoms	20.8	4.9	19.2	5.5	.114

PTPS: post thoracotomy pan syndrome; SDS: Symptom Distress Scale; HADS: Hospital Anxiety and Depression Scale; FACT-L: Functional Assessment of Cancer Therapy-Lung
* Significant differences between patients with and without PTPS.

Total SDS scores differed between patients with (25.9 ± 8.1) and without PTPS (18.3 ± 3.7), with patients with PTPS reporting significantly ($p < .0001$) more distress. Notably, both groups included patients who reported moderate distress (SDS score 25-32). These individuals included 4 (4.1%) patients who reported no symptoms associated with PTPS and 12 (12.4%) patients who reported symptoms associated with PTPS. Ten (10.3%) patients reported scores ≥ 33 (severe distress). All were diagnosed with PTPS and were offered treatment for this condition. These data are reported in Table 4.

Total HADS scores differed between patients with (10.1 ± 7.6) and without PTPS (5.4 ± 5.4); patients with PTPS reported higher total distress scores (p =.001) and higher sub-scores for anxiety (p=.013) and depression (p <. 001). Within the total group, 6 (6.2%) subjects reported at least one sub-score > 11 for anxiety or depression, which is a reportable level of distress. All were currently under treatment for their symptoms and all were in the group that reported PTPS.

FACT-L total scores differed between patients with (92.1 ± 24.5, range 43 to 136) and without PTPS (112.3 ± 15.5, range 66 to 135). Patients with PTPS reported lower ratings (p=.009) for quality of life. Scores for two of the five subscales were significantly different between groups. Patients with PTPS assigned lower ratings to sub-scores for physical (p=.001) and functional (p=.006), but not for social, emotional or lung related symptoms.

5.3.3 PTPS Symptom Characteristics

To further describe symptoms experienced by patients with PTPS, participants were divided into three subgroups – those reporting pain only (MPQ score), neuropathic symptoms only (NSQ score or MPQ descriptors “numb” or “tingling”) or pain and neuropathic symptoms (MPQ score + NSQ score). PTPS was reported by 53 (54.6%) participants. Of these, 8 (15.1%) reported pain only, 16 (30.2%) neuropathic symptoms only, and the remaining 29 (54.7%) both pain and neuropathic symptoms. With the exception of smoking pack years, there were no significant between group differences for any variable examined. These data are reported in Table 5.

Table 5. PTPS subgroup characteristics

Variable	Pain Only n=8	Neuropathic Symptoms Only n=16	Pain + Neuropathic Symptoms n=29	p-value
Age (Years) Mean (SD)	63.5 (8.4)	69.2 (9.2)	63.0 (9.9)	.110
Smoking (Pack Years) Mean (SD)	70.0 (37.7)	36.3 (24.6)	35.7 (27.5)	.027*
Charlson Comorbidity Score Mean (SD)	4.8 (1.8)	3.9 (1.1)	4.4 (1.2)	.404
Gender (Male)	50.0%	56.2%	41.4%	.623
Race/Ethnicity (Caucasian)	87.5%	93.7%	86.2%	.742
Married or steady Partner	75.0%	68.8%	65.5%	.875
Not employed	75.0%	75.0%	79.3%	.933
Some college/technical school	37.5%	68.8%	51.7%	.311
Resident of rural area	37.5%	56.3%	48.3%	.682
Time since Surgery (2 - 6 mos)	50.0%	68.8%	55.2%	.588
Location				.210
Right lung	37.5%	43.8%	58.6%	.485
Upper lobe	62.5%	43.8%	58.6%	
Cancer Stage (I a & b)	62.5%	50.0%	69.0%	.430
Cancer type (Adenocarcinoma)	50.0%	75.0%	58.6%	.131

PTPS: post thoracotomy pain syndrome

*Significant difference between patients with and without PTPS

5.3.4 Types of Surgery

In prior studies, surgical approach has often been implicated as a potential cause of PTPS. Equal numbers of patients who underwent a thoracotomy or thoracospic procedure reported pain only. Approximately equal numbers of patients reported neuropathic symptoms only or pain and neuropathic

symptoms. There were no statistically significant differences between the three groups related to type of surgery. These data are shown in Figure 7.

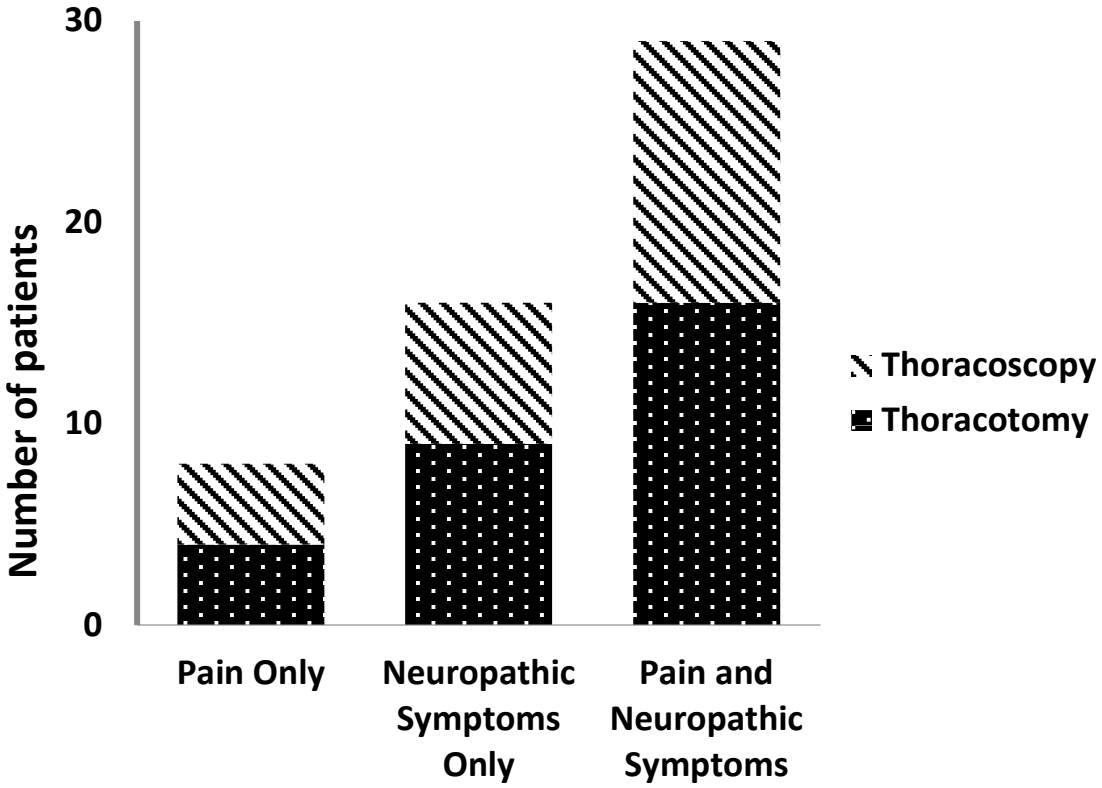

Figure 7. Surgical approach characteristics

Approximately equal numbers of patients, who underwent a thoracoscopic or thoracotomy procedure, reported either: pain only, neuropathic symptoms only, or pain and neuropathic symptoms. There were no statistically significant differences between subgroups.

5.3.5 Location of Discomfort

PTPS participants were also asked to report the location of their discomfort (incision, chest tube, drain, shoulder, or some combination of these sites) which could be described as pain, numbness, tingling and/or generalized discomfort. These data are reported in Figure 8. The 8 patients reporting pain only cited three locations, incision, chest tube, and drain site. There were 16 patients who reported neuropathic symptoms only. All reported discomfort located at the incision site. The 29 remaining participants reported both neuropathic symptoms and pain.

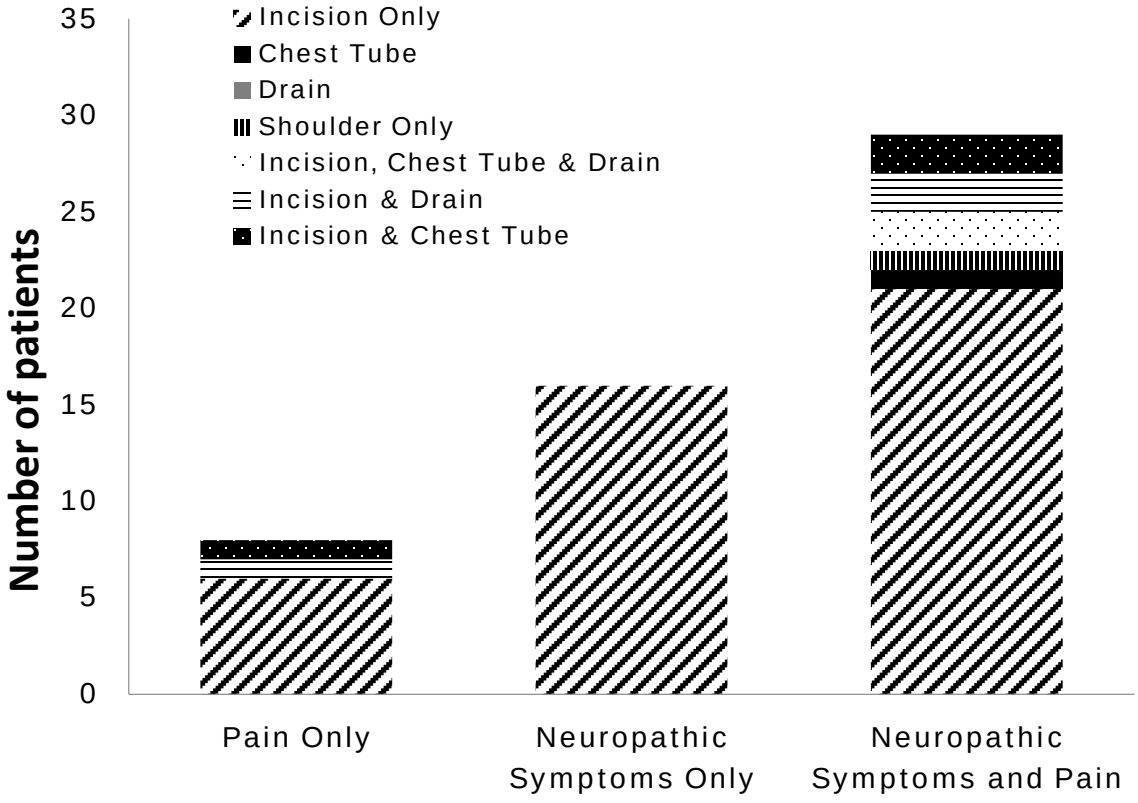

Figure 8. Discomfort location

Patients reporting pain only cited three locations - the incision, incision and chest tube, and incision and drain site. All patients who reported neuropathic symptoms only identified the incision site. The majority of patients reporting neuropathic symptoms and pain identified the incision site. Others identified the chest tube site, shoulder region, or a combination of these sites.

5.3.6 Subgroup Ratings of Anxiety, Depressive Symptoms, and Quality of Life

Because psychosocial experiences can influence PTPS (Buchanan et al., 2010; Carlson et al., 2010); we also explored the impact of anxiety and depression as determined by the HADS total score and subgroup scores in patients reporting pain only, neuropathic symptoms only and pain and neuropathic symptoms. The data are shown in Figure 9. Although those reporting pain tended to have higher HADS scores, there were no statistically significant differences between subgroup scores.

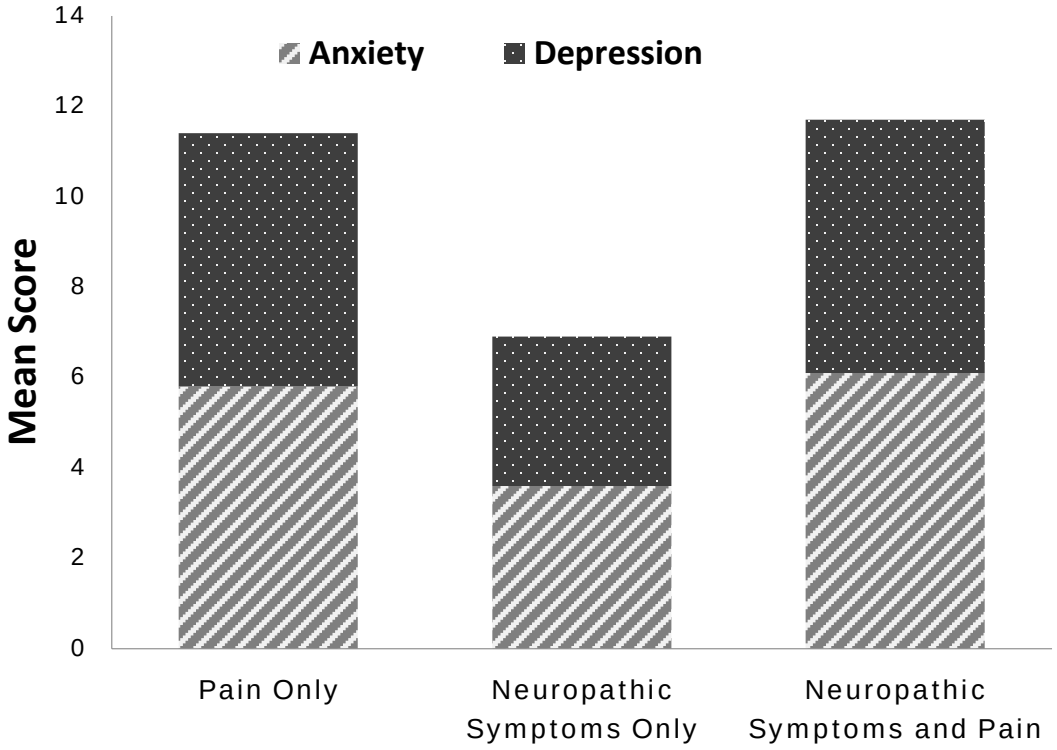

Figure 9. Anxiety and depression scores

HADS total scores did not differ significantly for patients who reported pain only (11.4 ± 6.9), neuropathic symptoms only (6.6 ± 6.4) or neuropathic symptoms and pain (11.8 ± 7.9). Also, there were no significant differences in sub-scores for anxiety and depression between the three groups.

Impact on quality of life was measured by the FACT-L. These data are presented in Figure 10. There were statistically significant differences between FACT-L total scores in patients who reported pain (84.5 ± 28.1, range 56 to 127), neuropathic symptoms (112.3.1 ± 16.8, range 79 to 136) or pain and neuropathic symptoms (95.9 ± 24.2, range 43 to 132). Those individuals who reported neuropathic

symptoms only reported higher well-being (p = .027) compared to those with pain only or both pain and neuropathic symptoms.

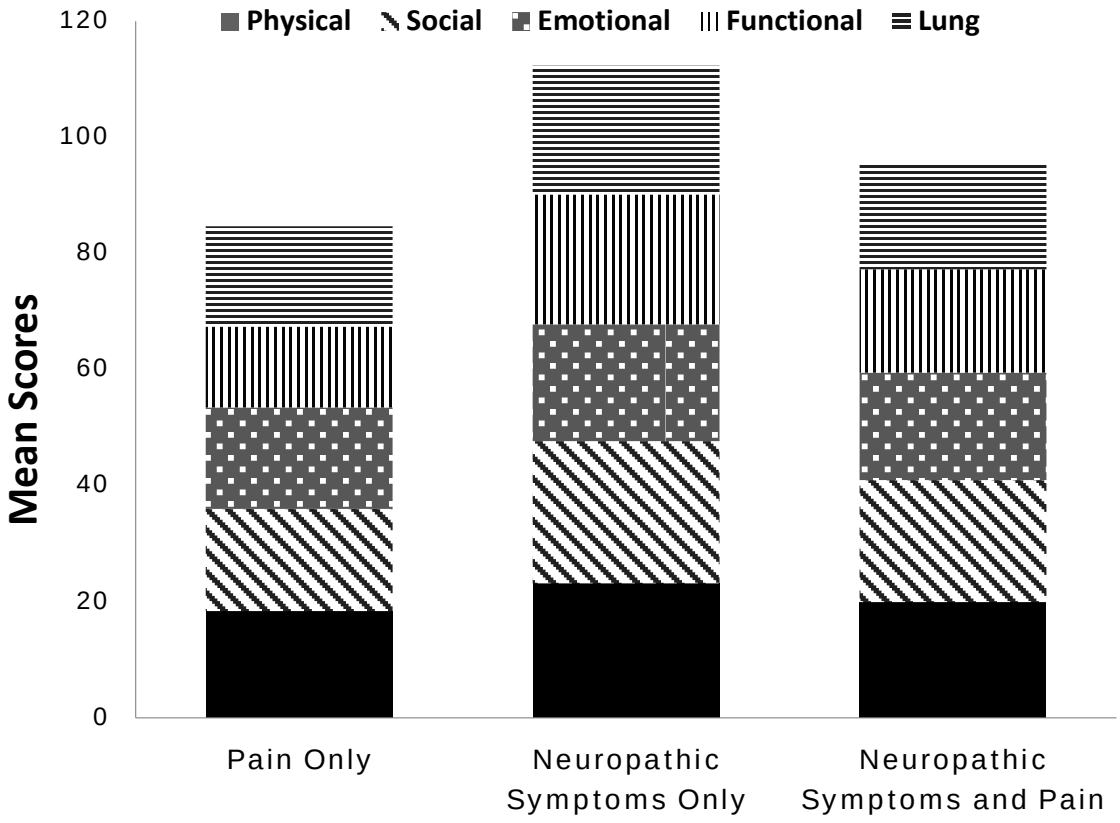

Figure 10. Quality of Life

There were statistically significant differences between FACT-L total scores in patients who reported pain only, neuropathic symptoms only, or pain and neuropathic symptoms. Those individuals who reported neuropathic symptoms only reported higher well-being (p = .027) compared to those with pain only or both pain and neuropathic symptoms.

5.4 MAJOR FINDINGS

There were four major findings in this study: 1) patients who underwent a thoracotomy or thoracospic procedure using current surgical techniques were equally likely to report symptoms consistent with PTPS; 2) patients who experienced PTPS had discomfort at varied locations (incision, shoulder, chest tube and drain insertion sites), 3) PTPS discomfort manifested as pain only, neuropathic symptoms only, or as combination of both; and 4) symptom distress and quality of life differed significantly in patients with and without PTPS.

5.4.1 Prevalence of PTPS

In the present study, which excluded patients with lung cancer metastasis, approximately half (54.6%) of the patients reported symptoms consistent with PTPS when the definition was expanded to include pain, neuropathic symptoms or both. There was no significant difference in report of symptoms related to the type of surgery (p=.398) or time since surgery (p=.380). In the 1990's, a survey of 343 patients managed at our Center reported no difference in pain 1-year following a thoracotomy or thoracoscopic procedure (Landreneau et al., 1994). Similar findings were reported by Furrer et al. 1997, from a matched study of 30 patients recruited during the same time period. In their study, 33% patients who underwent a thoracotomy and 36% of patients who underwent a thoracoscopic procedure reported pain or discomfort 3-18 months after surgery (Furrer et al., 1997). More recently, findings from two surveys (Wildgaard et al., 2011; Steegers et al. 2008) that included a total of 750 patients reported a similar prevalence of chronic pain following a thoracotomy (33%-40%) or thoracoscopic procedure (25%-

47%) at 22-23 months following surgery. To evaluate the contribution of intercostal nerve damage to the development of PTPS, Miyazaki et al. 2011 assessed nerve function using a series of stimuli (2000 Hz, 250 Hz and 5 Hz) for 24 weeks following surgery for lung cancer. Function of myelinated nerve fibers was significantly impaired following surgery that involved use of rib retractors but absent when these were not used, supporting the notion that these fibers are susceptible to damage by pressure or stretch (Miyazaki et al., 2011). Patients managed using video-assisted surgery without metal retractors reported no pain at 12 weeks following surgery. Conversely, approximately 70% of those undergoing video-assisted mini-thoracotomy with metal retractors and conventional thoracotomy reported pain. Although these findings hold promise as a means to reduce the prevalence of PTPS, there will likely continue to be extensive numbers of patients who experience this condition given the multiple factors that influence surgical decisions, including size of the lesion, ability to localize and remove the tumor, and surgeon preference.

5.4.2 Location of Symptoms

Consistent with prior findings, most patients reported pain or symptoms associated with neuropathy at the site of the incision. However, other sites were also mentioned, including chest tube and drain insertion sites and the shoulder. Mongardon et al. (Mongardon et al., 2011) reported that 21 (32%) of 65 thoracotomy patients noted more than one painful site, most frequently the incision and chest tube insertion site. Guastella et al. (Guastella et al., 2011) reported pain localization in an area entirely or largely distributed within the T5/T6 dermatomes on the operated side. Half of their patients described pain in the mammary or sub-mammary area and the remainder in a more diffuse area, including the

sternal/parasternal area and drain insertion point. Grosen et al. (Grosen et al., 2012) identified sites on the anterior, posterior and lateral chest wall. These findings are important, as they reinforce the need to inquire about pain and discomfort at various sites on the chest wall. In our study, two patients reported pain and neuropathic symptoms that were only present at the chest tube insertion site or shoulder region.

5.4.3 Symptom Presentation

PTPS can present as pain and neuropathic symptoms or both. We therefore categorized reports of discomfort into three categories - pain only, neuropathic symptoms only or the combination. In our study, most patients 29 (54.7%) identified a combination of symptoms. However, 8 (15.1%) identified pain only and 16 (30.2%) identified neuropathic symptoms only. Prior studies have reported a varying prevalence of neuropathic symptoms. Steegers et al. (Steegers et al., 2008) used a validated screening tool, the PainDETECT Questionnaire, to assess symptoms in 204 patients. At a median time of 23 months following surgery, 23% were described as having definite neuropathic pain and 30% probable neuropathic pain. Guastella et al. (Guastella et al., 2011) evaluated 54 patients 6 months after thoracotomy and identified 29% with neuropathic pain and 70% with chronic pain using a symptom grading system and the DN4, a screening tool for neuropathic pain. Mongardon et al. (Mongardon et al., 2011) reported chronic pain in 48% of patients, neuropathic symptoms in 12% and 40% with neither pain nor neuropathic symptoms. These findings appear similar to ours, although comparison is difficult due to the various methods used to detect presence of symptoms.

Several validated questionnaires are available for use in detecting the prevalence of neuropathic symptoms and describing related characteristics (Bousassira & Attal, 2011; Bennett et al., 2007; Freynhage et al., 2006). Serial monitoring using these instruments is strongly recommended to permit comparison between centers in regard to prevalence of PTPS, descriptors associated with its development, and response to treatment. In addition, there appear to be differences in ability to detect changes in tactile and thermal stimuli as well as side-to-side symmetry in patients with and without PTPS (Wildgaard et al., 2012). Further assessment of these differences may yield beneficial insights into causes of this syndrome.

5.4.4 Symptom Distress and Impact on Quality of Life

Although pain is a frequent complaint, the majority of patients identified their pain as mild with mean ratings in the range of 3.3 ± 3.3. However, a substantial minority reported moderate (22.6%) or severe (17.0%) pain, consistent with findings from prior studies (Grosen et al., 2012; Guastella et al., 2011; Wildgaard et al., 2011). Using standardized instruments, we also found significant between group differences in patients with and without PTPS in regard to symptom distress, presence of anxiety and depressive symptoms and quality of life. All instruments used in this study were brief and, in our experience, required approximately 20-30 minutes to complete if all were utilized. Serial monitoring of symptom distress using standardized instruments, including pre-surgical baseline measurement, is highly recommended to elicit objective data regarding the contribution of pre-existing risk factors and response to various therapeutic initiatives. Prior studies support high levels of symptom distress in patients diagnosed with cancer (Buchanan et al., 2010; Carson et al., 2010) that can be influenced by a

variety of factors, including time of surgery (Lehto, 2011), coping style (Prasertsri, Holden, Keefe, & Wilkie, 2011), and response to treatment (Shimizu et al., 2012). One large study of 1334 consecutively recruited lung cancer patients reported that 12.4% were classified with depressive symptoms based on HADS sub-scores (Shimizu et al., 2012). Hence, it is particularly important to assess symptom distress at baseline and serially over time.

5.5 LIMITATIONS

Our study used a cross sectional design that limited assessment of symptoms to a single time point. It is possible that symptoms may have differed over time. However, we found no difference in the number of patients reporting symptoms of PTPS based on time since surgery. The sample was recruited from a high volume academic service specializing in thoracic surgery. Results may not be generalizable to other practice settings. Approximately half of the subjects did not complete the NSQ, as it was added mid-study. MPQ descriptors ("numb", "tingling") were used prior to adding the NSQ. Patients with PTPS or subgroups may have been over or underestimated using this approach. Finally, we did not distinguish between muscle sparing and open thoracotomy nor did we distinguish between video assisted and robotic thoracoscopic surgeries.

5.6 CLINICAL IMPLICATIONS

Absent new innovations in surgical technique, the syndrome of PTPS appears unlikely to diminish in frequency. Clinicians managing the care of these patients need to be aware of the various ways symptoms can manifest, i.e., pain only, neuropathic symptoms only or a combination of these factors in various body locations and question patients specifically regarding their presence. Referral to specialists in pain management should be considered if initial interventions prove ineffective in obtaining symptom relief. Brief questionnaires are available to guide evaluation of response to therapy (Bousassira & Attal, 2011; McGill, 2009; Bennett et al., 2007; Freynhagen et al., 2006), impact on activities of daily living (Ringsted, Wildgaard, Kreiner & Kehlet 2013), and symptom distress (McCorkle et al., 1998; Holmes, 1989), including presence of anxiety and depression (Snaith, 2003; Bjellend et al., 2002; Zigmong & Snaith 1983). This approach has been beneficial in the management of other conditions, as it provides objective data that can be compared over time both to guide treatment and assess efficacy of various approaches. Future studies, should focus on identifying best treatment approaches to manage the complex and varying symptoms seen in this patient population.

APPENDIX A: IRB APPROVAL LETTERS AND CONSENT FORMS

University of Pittsburgh
Institutional Review Board

3500 Fifth Avenue
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)
http://www.irb.pitt.edu

Memorandum

To: Kathleen Hopkins RN MS
From: Christopher Ryan PHD, Vice Chair
Date: 6/2/2010
IRB#: PRO09110202
Subject: Management of pain following lung cancer surgery

The University of Pittsburgh Institutional Review Board reviewed and approved the above referenced study by the expedited review procedure authorized under 45 CFR 46.110. Your research study was approved under:
45 CFR 46.110.(5)
45 CFR 46.110.(7)

The advertisement(s) that was submitted for review has been approved as written. As a reminder, any changes to the wording of the approved advertisement would require IRB approval prior to distribution.

The waiver for the requirement to obtain a written informed consent for screening has been approved.

The IRB has approved a waiver of HIPAA authorization requirement for the sharing of contact information.

Approval Date: 5/28/2010
Expiration Date: 5/27/2011

For studies being conducted in UPMC facilities, no clinical activities can be undertaken by investigators until they have received approval from the UPMC Fiscal Review Office.

Please note that it is the investigator's responsibility to report to the IRB any unanticipated problems involving risks to subjects or others [see 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)]. The IRB Reference Manual (Chapter 3, Section 3.3) describes the reporting requirements for unanticipated problems which include, but are not limited to, adverse events. If you have any questions about this process, please contact the Adverse Events Coordinator at 412-383-1480.

The protocol and consent forms, along with a brief progress report must be resubmitted at least one month prior to the renewal date noted above as required by FWA00006790 (University of Pittsburgh), FWA00006735 (University of Pittsburgh Medical Center), FWA00000600 (Children's Hospital of Pittsburgh), FWA00003567 (Magee-Womens Health Corporation), FWA00003338 (University of Pittsburgh Medical Center Cancer Institute).

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

IN# 0023654

University of Pittsburgh
Institutional Review Board

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Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)
http://www.irb.pitt.edu

Memorandum

To: Kathleen Hopkins RN MS
From: Sue Beers PHD, Vice Chair
Date: 4/12/2011
IRB#: REN11030263 / PRO09110202
Subject: Management of symptoms following lung cancer surgery

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Your renewal for the above referenced research study has received expedited review and approval from the Institutional Review Board under:
45 CFR 46.110.(5)
45 CFR 46.110.(7)

Please note the following information:

Approval Date: 4/12/2011
Expiration Date: 4/11/2012

Please note that it is the investigator's responsibility to report to the IRB any unanticipated problems involving risks to subjects or others [see 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)]. The IRB Reference Manual (Chapter 3, Section 3.3) describes the reporting requirements for unanticipated problems which include, but are not limited to, adverse events. If you have any questions about this process, please contact the Adverse Events Coordinator at 412-383-1480.

The protocol and consent forms, along with a brief progress report must be resubmitted at least **one month** prior to the renewal date noted above as required by FWA00006790 (University of Pittsburgh), FWA00006735 (University of Pittsburgh Medical Center), FWA00000600 (Children's Hospital of Pittsburgh), FWA00003567 (Magee-Womens Health Corporation), FWA00003338 (University of Pittsburgh Medical Center Cancer Institute).

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

University of Pittsburgh
Institutional Review Board

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Pittsburgh, PA 15213
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(412) 383-1508 (fax)
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Memorandum

To: Kathleen Hopkins
From: Christopher Ryan Vice Chair
Date: 5/30/2012
IRB#: MOD09110202-06 / PRO09110202
Subject: Management of symptoms following lung cancer surgery

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The University of Pittsburgh Institutional Review Board reviewed and approved the requested modifications by expedited review procedure authorized under 45 CFR 46.110 and 21 CFR 56.110.

This study is supported by the following federal grant application:
1 F31 NR013114-01A1 Symptom Experience Following Lung Cancer Surgery

Modification Approval Date: 5/30/2012
Expiration Date: 3/4/2013

For studies being conducted in UPMC facilities, no clinical activities that are impacted by the modifications can be undertaken by investigators until they have received approval from the UPMC Fiscal Review Office.

Please note that it is the investigator's responsibility to report to the IRB any unanticipated problems involving risks to subjects or others [see 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)]. Refer to the IRB Policy and Procedure Manual regarding the reporting requirements for unanticipated problems which include, but are not limited to, adverse events. If you have any questions about this process, please contact the Adverse Events Coordinator at 412-383-1480.

The protocol and consent forms, along with a brief progress report must be resubmitted at least one month prior to the renewal date noted above as required by FWA00006790 (University of Pittsburgh), FWA00006735 (University of Pittsburgh Medical Center), FWA00000600 (Children's Hospital of Pittsburgh), FWA00003567 (Magee-Womens Health Corporation), FWA00003338 (University of Pittsburgh Medical Center Cancer Institute).

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

University of Pittsburgh
Institutional Review Board

3500 Fifth Avenue
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)
http://www.irb.pitt.edu

Memorandum

To: Kathleen Hopkins RN MS
From: Christopher Ryan PHD, Vice Chair
Date: 1/30/2014
IRB#: REN14010310 / PRO09110202
Subject: Management of symptoms following lung cancer surgery

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Your renewal for the above referenced research study has received expedited review and approval from the Institutional Review Board under:
45 CFR 46.110.(5)
45 CFR 46.110.(7)

Please note the following information:

Approval Date: 1/30/2014
Expiration Date: 1/29/2015

Please note that it is the investigator's responsibility to report to the IRB any unanticipated problems involving risks to subjects or others [see 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)]. Refer to the IRB Policy and Procedure Manual regarding the reporting requirements for unanticipated problems which include, but are not limited to, adverse events. If you have any questions about this process, please contact the Adverse Events Coordinator at 412-383-1480.

The protocol and consent forms, along with a brief progress report must be resubmitted at least **one month** prior to the renewal date noted above as required by FWA00006790 (University of Pittsburgh), FWA00006735 (University of Pittsburgh Medical Center), FWA00000600 (Children's Hospital of Pittsburgh), FWA00003567 (Magee-Womens Health Corporation), FWA00003338 (University of Pittsburgh Medical Center Cancer Institute).

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

CONSENT TO ACT AS A SUBJECT IN A RESEARCH STUDY

TITLE:	**Management of Pain Following Lung Cancer Surgery**
PRINCIPAL INVESTIGATOR:	Kathleen G. Hopkins, RN, MS University of Pittsburgh School of Nursing 336 Victoria Building Pittsburgh, PA 15213 Telephone: 412-334-2195
CO-INVESTIGATOR:	Peter Ferson, M.D., Professor of Surgery University of Pittsburgh Physicians Heart, Esophageal, and Thoracic Surgery Institute UPMC Presbyterian Hospital Suite C-800, 200 Lothrop Street Pittsburgh, PA 15213 Phone: 412-647-7556
CO- INVESTIGATOR:	Leslie Hoffman, RN, FAAN, Professor of Nursing University of Pittsburgh School of Nursing 336 Victoria Building Pittsburgh, PA 15213 Telephone: 412-334-2195
SOURCE OF SUPPORT:	No support

Why is this study being done?

The purpose of this study is to investigate the needs of post-surgical lung cancer patients with pain.

Who is being asked to take part in this study?

Approximately 50 men and women 45-80 years of age who had surgery for lung cancer will be asked to participate. Participant responses will be compared in regard to patients whose surgery was 2-4 months ago and 5-8 months ago.

What are the procedures of this study?
If you agree to participate in this research study, you will:

1. Authorize us to look at your medical records and record information related to the stage history of your lung cancer disease, your medications (especially for pain), comorbidities and the surgery you had to treat this disease.
2. Answer questions about your physical functioning, ability to do your job and routine household tasks, mood, and overall quality of life. We will audio-tape record your answers to help us

conduct the analysis. This interview will last about 30 minutes.

3. Answer a series of six questionnaires. Each of these questionnaires is expected to take an average of 5-10 minutes or a total of 30-60 minutes.

Responses of participants will be used to help us better understand how to best manage pain following lung cancer surgery. The interview and questionnaire completion will take place at the Hillman Cancer Center or the University of Pittsburgh School of Nursing.

To protect your privacy and confidentiality, we will label all of the information you give us and the information we record from your medical record with a code number. This information will not be labeled with your name or anything that would directly identify you.

What are the possible risks and discomforts of this study?

There is little risk involved in this study. No invasive procedures or medications are included. The common risk is that you may experience recollections of the surgical and post-surgical lung cancer experience with pain, but we will do everything possible to minimize the risk of this as a negative experience. To reduce the likelihood of a negative experience, we will stop the intervention at anytime if you have these feelings.

A second potential risk is a breach of confidentiality, but we will do everything possible to protect your privacy. To reduce the likelihood of a breach of confidentiality, we will use a code number to label all of the information we collect form your medical record, interview, and the questionnaires.

Will I benefit from taking part in this study?

You will receive no direct benefit from participating in this study.

Are there any costs to me if I participate in this study?

There are no costs to you for participating in this study.

How much will I be paid if I complete this study?

We will not pay you for each interview you complete. We will also not reimburse you for any parking fees while participating in this study.

Will anyone know that I am taking part in this study?

The study team will do everything possible to protect our subject's privacy. All records pertaining to your involvement in this study will be kept strictly confidential (private) and any data that includes your identity will be stored in locked files and kept for a minimum of six years. Your identity will not be revealed in any description or publications of this research.

There will be an ongoing monthly review of study procedures by members of the study team to ensure that privacy of research subjects and confidentiality of their research data have not been violated.

It is possible that authorized representatives from the University of Pittsburgh Research Conduct and Compliance Office may review your data for the purpose of monitoring the conduct of this study. In very unusual cases, your research records may be released in response to an order from a court of law.

Will this research study involve the use or disclosure of my identifiable medical information?

The research study will involve the recording of current and/or future identifiable medical information from your hospital and/or other (e.g. physician office) records. The information that will be recorded will be limited to information concerning (cancer stage, surgery, medications, and comorbidities). This information will be used for the purpose of verifying your postthoracic pain syndrome status and treatment.

How will the privacy of my medical record information be protected?

Several procedures have been put into place to protect the privacy of your medical record information. Only members of the study team and the Research Conduct and Compliance Office will have access to your identifiable medical record information, and these individuals will be required to sign a privacy agreement. However, just as with the use of your medical information for health care purposes, we cannot guarantee its privacy.

May I withdraw, at a future date, my permission for participation in this research study?

Yes. To do so, you must contact the investigators who are listed on the first page of this consent form. If you withdraw from this study, we will continue to use the information we have collected form your medical records and any of the phone interviews you have already completed.

At the end of the data analysis all master files and audio-taped files that have been assigned to this study will be destroyed.

Is my participation in this study voluntary?

Yes! Your participation in this study is completely voluntary. You may refuse to take part in it, or you may stop participating at any time, even after signing this form. Your decision will not affect your relationship with or the care you receive from the UPMC Cancer Centers, Presbyterian Hospital, Heart, Esophageal, and Thoracic Surgery Institute or the University of Pittsburgh.

As both your doctor and the research investigator, s/he is interested both in your medical care and the conduct of this research study. Before agreeing to participate in this research study, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are under no obligation to participate in any research study offered by your doctor.

How can I get more information about this study?

If you have any further questions about this research study, you may contact the investigators listed at the beginning of this consent form. If you have any questions about your rights as a research subject, please contact the Human Subjects Protection Advocate at the University of Pittsburgh IRB Office, 1-866-212-2668.

PARTICIPANT'S CERTIFICATION

- I have read the consent form for this study and any questions I had, including explanation of all terminology, have been answered to my satisfaction. A copy of this consent form will be provided to me.
- I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that those questions will be answered by the researchers listed on the first page of this form.
- I understand that my participation in this study is voluntary and that I am free to refuse to participate or to withdraw my consent and discontinue my participation in this study at any time without affecting my future relationship with this institution.
- I agree to participate in this study.

PARTICIPANT'S VOLUNTARY CONSENT

"The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any aspect of this research study during the course of this study, and that such future questions, concerns or complaints will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that occurred during my participation. By signing this form I agree to participate in this research study. A copy of this consent form will be given to me."

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Participant's Signature Date

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Printed Name of Participant

CERTIFICATION OF INFORMED CONSENT

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_____ _____

Printed Name of Person Obtaining Consent Principal Investigator

_____ _____

Signature of Person Obtaining Consent Date

CONSENT TO ACT AS A SUBJECT IN A RESEARCH STUDY

TITLE:	**Management of Symptoms Following Lung Cancer Surgery**
PRINCIPAL INVESTIGATOR:	Kathleen G. Hopkins, RN, MS University of Pittsburgh School of Nursing 336 Victoria Building Pittsburgh, PA 15213 Telephone: 412-334-2195
CO-INVESTIGATOR:	Peter Ferson, M.D., Professor of Surgery University of Pittsburgh Physicians Heart, Esophageal, and Thoracic Surgery Institute UPMC Presbyterian Hospital Suite C-800, 200 Lothrop Street Pittsburgh, PA 15213 Phone: 412-647-7556
CO- INVESTIGATOR:	Leslie Hoffman, RN, PhD, Professor of Nursing University of Pittsburgh School of Nursing 336 Victoria Building Pittsburgh, PA 15213 Telephone: 412-334-2195
SOURCE OF SUPPORT:	Pauline Thompson Clinical Nursing Research Award (Nursing Foundation of PA, PA Nurses Association) Small Grant Award (Oncology Nursing Association)

Why is this study being done?

The purpose of this study is to investigate the needs of post-surgical lung cancer patients.

Who is being asked to take part in this study?

Approximately 50 men and women 40-85 years of age who had surgery for lung cancer will be asked to participate.

What are the procedures of this study?
If you agree to participate in this research study, you will:

1. Authorize us to look at your medical records and record information related to the history of your lung cancer, your medications (especially for pain), other health problems and the surgery you had to treat this disease.

2. If you are selected for interview, answer questions about your physical functioning, ability to do your job and routine household tasks, mood, and overall quality of life. We will record the interview to better help us understand what you said. . This interview will last about 30 minutes.
3. Answer a series of six questionnaires. Each of these questionnaires is expected to take an average of 5-10 minutes or a total of 30 minutes.

Responses of participants will be used to help us better understand how to best manage pain and symptoms following lung cancer surgery. The interview and questionnaire completion will take place at the Hillman Cancer Center or the University of Pittsburgh School of Nursing.

To protect your privacy and confidentiality, we will label all of the information you give us and the information we record from your medical record with a code number. This information will not be labeled with your name or anything that would directly identify you.

What are the possible risks and discomforts of this study?

There is little risk involved in this study. No invasive procedures or medications are included. The common risk is that you may experience recollections of the surgical and post-surgical lung cancer experience with symptoms, but we will do everything possible to minimize the risk of this as a negative experience. To reduce the likelihood of a negative experience, we will stop the intervention at anytime if you have these feelings.

A second potential risk is a breach of confidentiality, but we will do everything possible to protect your privacy. To reduce the likelihood of a breach of confidentiality, we will use a code number to label all of the information we collect form your medical record, interview, and the questionnaires.

Will I benefit from taking part in this study?

You will receive no direct benefit from participating in this study.

Are there any costs to me if I participate in this study?

There are no costs to you for participating in this study.

How much will I be paid if I complete this study?

We will not pay you for each interview you complete. We will also not reimburse you for any parking fees while participating in this study.

Will anyone know that I am taking part in this study?

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Is my participation in this study voluntary?

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How can I get more information about this study?

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PARTICIPANT'S CERTIFICATION

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- I agree to participate in this study.

PARTICIPANT'S VOLUNTARY CONSENT

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Participant's Signature Date

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Printed Name of Participant

CERTIFICATION OF INFORMED CONSENT

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Printed Name of Person Obtaining Consent	Principal Investigator
Signature of Person Obtaining Consent	Date

CONSENT TO ACT AS A SUBJECT IN A RESEARCH STUDY

TITLE: **Management of Symptoms Following Lung Cancer Surgery**

PRINCIPAL INVESTIGATOR:
Kathleen G. Hopkins, RN, MS
University of Pittsburgh School of Nursing
336 Victoria Building
Pittsburgh, PA 15213
Telephone: 412-334-2195

CO-INVESTIGATOR:
Peter Ferson, M.D., Professor of Surgery
Neil Alexander Christie, M.D., FRCS(c)
Rodney Jerome Landreneau, M.D.
James D Luketich, M.D.
Manisha R Shende, M.D
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Heart, Esophageal, and Thoracic Surgery Institute
UPMC Presbyterian Hospital
Suite C-800, 200 Lothrop Street
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Phone: 412-647-7556

CO- INVESTIGATOR:
Leslie Hoffman, RN, PhD, Professor of Nursing
University of Pittsburgh School of Nursing
336 Victoria Building
Pittsburgh, PA 15213
Telephone: 412-334-2195

SOURCE OF SUPPORT:
Pauline Thompson Clinical Nursing Research Award (Nursing Foundation of PA, PA Nurses Association)
Small Grant Award (Oncology Nursing Association)
National Institute of Health (Ruth L. Kirschstein National Research Service F31 Award)

Why is this study being done?

The purpose of this study is to investigate the needs of post-surgical lung cancer patients.

Who is being asked to take part in this study?

Approximately 175 men and women 40-85 years of age who had surgery for lung cancer will be asked to

participate.

What are the procedures of this study?
If you agree to participate in this research study, you will:

1. Authorize us to look at your medical records and record information related to the history of your lung cancer, your medications (especially for pain), other health problems and the surgery you had to treat this disease.
2. If you are selected for interview, answer questions about your physical functioning, ability to do your job and routine household tasks, mood, and overall quality of life. We will record the interview to better help us understand what you said. This interview will last about 30 minutes.
3. Answer a series of seven questionnaires. Each of these questionnaires is expected to take an average of 5-10 minutes or a total of 30 minutes.

Responses of participants will be used to help us better understand how to best manage pain and symptoms following lung cancer surgery. The interview and questionnaire completion will take place at the Hillman Cancer Center or the University of Pittsburgh School of Nursing.

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Are there any costs to me if I participate in this study?

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Is my participation in this study voluntary?

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beginning of this consent form. If you have any questions about your rights as a research subject, please contact the Human Subjects Protection Advocate at the University of Pittsburgh IRB Office, 1-866-212-2668.

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Participant's Signature Date

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Printed Name of Participant

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Printed Name of Person Obtaining Consent	Principal Investigator
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CONSENT TO ACT AS A SUBJECT IN A RESEARCH STUDY

TITLE: **Management of Symptoms Following Lung Cancer Surgery**

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CO- INVESTIGATOR:
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- I agree to participate in this study.

PARTICIPANT'S VOLUNTARY CONSENT

"The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any aspect of this research study during the course of this study, and that such future questions, concerns or complaints will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that occurred during my participation. By signing this form I agree to participate in this research study. A copy of this consent form will be given to me."

_____ _____

Participant's Signature Date

_____

Printed Name of Participant

CERTIFICATION OF INFORMED CONSENT

I certify that I have explained the nature and purpose of this research study to the above-named individual, and I have discussed the potential benefits and possible risks of study participation. Any questions the individual has about this study have been answered, and we will always be available to address future questions as they arise.

Printed Name of Person Obtaining Consent	Principal Investigator
Signature of Person Obtaining Consent	Date

Participant's Initials _____

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Publisher:	Wolters Kluwer Health
Publication:	Advances in Nursing Science
Author:	Elizabeth R. Lenz, Linda C. Pugh, Renee A. Milligan, et al
Title:	The Middle-Range Theory of Unpleasant Symptoms: An Update
Quantity:	35000
Total Amt:	115.00 USD

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Priority: Normal
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Total: 115.00 USD

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Subject: Re: Symptom Distress Scale (SDS)
From: "McCorkle, Ruth" <ruth.mccorkle@yale.edu>
Date: Wed, June 20, 2012 7:33 am
To: "KGH6@pitt.edu" <KGH6@pitt.edu>
Priority: Normal
Options: View Full Header | View Printable Version | Download this as a file | Add to Address Book | View Message details

Yes
Best wishes
Ruth

SDS

Sent from my iPhone

On Jun 20, 2012, at 6:55 AM, "KGH6@pitt.edu " <KGH6@pitt.edu > wrote:

> Dear Professor Ruth McCorkle,
>
> I would like to continue to use your instrument I plan to increase my
> recruitment to 125 for my disertation work. May I have your permission?
>
> Regards,
> Kathy Hopkins
>
>> Dear Professor Ruth McCorkle,
>>
>> I am a PhD student at the University of Pittsburgh School of Nursing
>> requesting permission for the Symptom Distress Scale (SDS). My pilot study
>> population is 30-50 first year post-op (surgical) lung cancer patients.
>>
>> Kathleen Hopkins, RN
>> 421 Chelsea Court
>> Pittsburgh, PA 15241
>> cell 412-334-2195
>> e-mail kgh6@pitt.edu

>>
>>
>>
>
>

MPQ

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Subject: Your Registration Details
From: "registrations" <registrations@gl-assessment.co.uk>
Date: Wed, April 17, 2013 3:40 am
To: kgh6@pitt.edu
Priority: High
Read receipt: requested [Send read receipt now]
Options: View Full Header | View Printable Version | Download this as a file | Add to Address Book | View Message details | View as HTML

Please see attached your registration details

Many thanks

Mc Gill

Registrations

Customer Services

T: 0845 602 1937

F: 0845 601 5358

W: www.gl-assessment.co.uk <http://www.gl-assessment.co.uk/>

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E-mail: info@gl-assessment.co.uk
www.gl-assessment.co.uk

Welcome to GL-Assessment

Thank you for completing the GL-Assessment Registration Form
You have been entered onto our confidential registration list

To:	Kathleen Hopkins	Account No:	129400
From:	Customer Services	Qualification Code:	10230
Date:	19 April 2013	Reader No:	159068

Your Qualification Code is 10230

This code allows us to see which tests are available to you based on your qualifications.

We would be very grateful if you could quote both your **Account Number**, and **Qualification Code**, whenever you order from us. This will enable us to process your orders quickly and efficiently. Please notify us of any changes in your details so we can keep our records up-to-date.

If you have any enquiries, please contact

Customer Services on 0845 602 1937 opt 1
Alternatively, you can e-mail us at information@gl-assessment.co.uk

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Subject: Re: Charlson Comorbidity Scale Permission
From: "Mary E. Charlson, MD" <mecharl@med.cornell.edu>
Date: Fri, August 27, 2010 4:11 pm
To: KGH6@pitt.edu
Priority: Normal
Options: View Full Header | View Printable Version | Download this as a file | Add to Address Book | View Message details

You have my permission to use the scale.

CCI

Best,
Dr. Mary Charlson

At 12:01 PM 8/20/2010, you wrote:
> > Dear Dr. Mary E. Charlson,
> >
> > I am a PhD student at the University of Pittsburgh School of Nursing
> > requesting permission for the Charlson Comorbidity Scale. My pilot study
> > population is 30-50 first year post-op (surgical) lung cancer patients.
> >
> >
> > Kathleen Hopkins
> > 421 Chelsea Ct
> > Pittsburgh, PA 15241
> > kgh6@pitt.edu

> >
> >

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Message List | Delete | Forward | Forward as Attachment

Subject: RE: Hospital Anxiety and Depression Scale (HADS)
From: "Permissions" <permissions@gl-assessment.co.uk>
Date: Thu, August 12, 2010 6:55 am
To: kgh6@pitt.edu
Priority: Normal
Options: View Full Header | View Printable Version | Download this as a file | Add to Address Book | View Message details

Dear Ms Hopkins

Please find attached all the necessary forms and information you need to acquire a Licence to use HADS

Kind Regards
Permissions

-----Original Message-----
From: kgh6@pitt.edu
[mailto:kgh6@pitt.edu
]
Sent: 11 August 2010 17:52
To: Permissions
Cc: kgh6@pitt.edu

Subject: Hospital Anxiety and Depression Scale (HADS)

To whom it may consern,

I am a PhD student at the University of Pittsburgh School of Nursing requesting permission for the Hospital Anxiety and Depression Scale (HADS). My pilot study population is 30-50 first year post-op (surgical) lung cancer patients.

Kathleen Hopkins, RN
421 Chelsea Court
Pittsburgh, PA 15241
cell 412-334-2195
e-mail kgh6@pitt.edu

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Subject: RE: your facit.org information
From: "Jason Bredle" <jbredle@facit.org>
Date: Mon, April 7, 2014 10:26 am
To: "KGH6@pitt.edu" <KGH6@pitt.edu>
Priority: Normal
Options: View Full Header | View Printable Version | Download this as a file | Add to Address Book | View Message details

Hi Kathy,

Yes, that's fine. Non-commercial use of our questionnaires is free for anyone. Let me know if you have any other questions.

Kind regards,
Jason

Jason Bredle
FACIT.org
+1.773.807.9094

-----Original Message-----
From: KGH6@pitt.edu
[mailto:KGH6@pitt.edu
]
Sent: Monday, April 07, 2014 8:00 AM
To: Kathleen G Hopkins
Cc: Information
Subject: Re: your facit.org information

May I continue to use a total of 100 FACT-L instruments and the instructions.

Regards,
Kathy Hopkins

> I would like to order 50 FACT-L instruments and the instructions.
>
> regards,
> Kathy Hopkins
> kgh6@pitt.edu

> cell 412-334-2195
>
>
>

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APPENDIX C: COPIES OF STUDY MEASURES

Symptom Distress Scale

The following is a list of symptoms, each having five (5) different numbered statements. Think about what each statement says, then choose the one statement that most closely indicates how you have been feeling lately.

Note: the statements are ranked from 1 to 5, where 1 indicates no problems and 5 indicates the maximum amount of problems. Statements 2 through 4 indicate your feelings somewhere in between these two extremes.

PLEASE choose only one response for each symptom; do not skip any symptom.

1. Symptom: APPEARANCE

No Problems				The Most Problems
1	**2**	**3**	**4**	**5**
My appearance has basically not changed.	**My appearance has gotten a little worse.**	**My appearance is definitely worse than it used to be, and I am not greatly concerned about it.**	**My appearance is definitely worse than it used to be, and I am concerned about it.**	**My appearance has changed drastically from what it was.**

2. Symptom: CONCENTRATION

No Problems				The Most Problems
1	**2**	**3**	**4**	**5**
I have my normal ability to concentrate.	**I occasionally have trouble concentrating.**	**I often have trouble concentrating.**	**I usually have at least some difficulty concentrating.**	**I just cannot seem to concentrate at all.**

3. Symptom: BOWEL

No Problems				The Most Problems
1	**2**	**3**	**4**	**5**
I have my normal	**My bowel pattern occasionally**	**I frequently have discomfort from**	**I am usually in discomfort**	**My present bowel pattern has changes**

bowel pattern.	**causes me some concern and discomfort.**	**my present bowel pattern.**	**because of my present bowel pattern.**	**drastically from what was normal for me.**

4. Symptom: FATIGUE

No Problems				**The Most Problems**
1	**2**	**3**	**4**	**5**
I am usually not tired at all.	**I am occasionally rather tired.**	**There are frequently periods when I am quite tired.**	**I am usually very tired.**	**Most of the time I feel exhausted.**

5. Symptom: PAIN (A)

No Problems				**The Most Problems**
1	**2**	**3**	**4**	**5**
I almost never have pain.	**I have pain once in a while.**	**I frequently have pain -- several times a week.**	**I am usually in some degree of pain.**	**I am in some degree of pain almost constantly.**

6. Symptom: PAIN (B)

No Problems				**The Most Problems**
1	**2**	**3**	**4**	**5**
When I do have pain, it is very mild.	**When I do have pain, it is mildly distressing.**	**The pain I do have is usually fairly intense.**	**The pain I do is usually very intense.**	**The pain I have is almost unbearable.**

7. Symptom: INSOMNIA

No Problems				**The Most Problems**
1	**2**	**3**	**4**	**5**
I sleep as well as I always have.	**I have occasional spells of sleeplessness.**	**I frequently have trouble getting to sleep and staying asleep.**	**I have difficulty sleeping almost every night.**	**It is almost impossible for me to get a decent night's sleep.**

8. Symptom: APPETITE

No				**The Most**

Problems				Problems
1	2	3	4	5
I have my normal appetite.	My appetite is usually, but not always, pretty	I do not really enjoy my food like I use to.	I have to force myself to eat my food.	I cannot stand the thought of food.

9. Symptom: NAUSEA (A)

No Problems				The Most Problems
1	2	3	4	5
I seldom feel any nausea at all.	I am nauseous once in a while.	I am often nauseous.	I am usually nauseous.	I suffer from nausea almost constantly.

10. Symptom: NAUSEA (B)

No Problems				The Most Problems
1	2	3	4	5
When I do have nausea, it is very mild.	When I do have nausea, it is mildly distressing.	When I have nausea, I feel pretty sick.	When I have nausea, I feel very sick.	When I have nausea, I am as sick as I possibly could be.

11. Symptom: COUGH

No Problems				The Most Problems
1	2	3	4	5
I seldom cough.	I have an occasional cough.	I often cough.	I often cough and occasionally have severe coughing spells.	I often have persistent and severe coughing spells.

12. Symptom: OUTLOOK

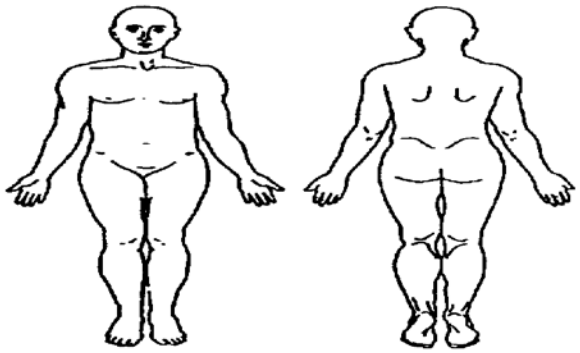
No Problems				The Most Problems
1	2	3	4	5
I am not fearful or worried.	I am a little worried about things.	I am quite worried but unafraid.	I am worried and a little frightened about things.	I am worried and scared about things.

13. Symptom: BREATHING

No Problems				The Most Problems
1	**2**	**3**	**4**	**5**
I usually breathe has basically normally.	**I occasionally have trouble breathing.**	**I often have trouble breathing.**	**I can hardly ever breathe as easily as I want.**	**I almost always have severe trouble with my breathing.**

McGill Pain Questionnaire

On the character mark the location of your surgical pain in "red" and your surgery scars in "black"



The words below describe pain. CHECK ONE word in each category if it best describes your present surgical pain. Leave out any group which does not apply.

1 Flickering ____
Quivering ____
Pulsing ____
Throbbing ____
Beating ____
Pounding ____

2 Jumping ____
Flashing ____
Shooting ____

3 Pricking ____
Boring ____
Drilling ____
Stabbing ____

4 Sharp ____
Cutting ____
Lancing ____

5 Pinching ____
Pressing ____
Gnawing ____
Cramping ____
Crushing ____

6 Tugging ____
Pulling ____
Wrenching ____

7 Hot ____
Burning ____
Scalding ____
Searing ____

8 Tingling ____
Itchy ____
Smarting ____
Stinging ____

9 Dull ____
Sore ____
Hurting ____
Aching ____
Heavy ____

10 Tender ____
Taut ____
Rasping ____
Splitting ____

11 Tiring ____
Exhausting ____

12 Sickening ____
Suffocating ____

13 Fearful ____
Frightful ____
Terrifying ____

14 Punishing ____
Grueling ____
Cruel ____
Vicious ____
Killing ____
Frightful ____
Terrifying ____

15 Wretched ____
Blinding ____

16 Annoying ____
Troublesome____

17 Spreading ____
Radiating ____
Penetrating____
Piercing ____

18 Tight ____
Numb ____
Drawing ____
Squeezing ____
Tearing ____

19 Cool ____
Cold ____
Freezing ____

20 Nagging ____
Nauseating ____
Agonizing ____
Dreadful ____
Torturing ____

21 Brief ____
Intermittent____
Continuous____

What is your level of surgical area pain on a scale of 0 to 10? ____
What is your level of chest tube pain on a scale of 0 to 10? ____
What is your level of drain pain on a scale of 0 to 10? ____

Neuropathic Pain Questionnaire

In order to assess your neuropathy problem, we need to thoroughly understand just exactly what type of neuropathy you have, and how it may or may not change over time. You may have only one site of neuropathy, or you may have more than one, and we can discuss each site.

1. How would you describe the discomfort at your surgical site on a scale from zero to ten?

0 _____10

No Discomfort Worst Discomfort Imaginable

2. How many sites feel this way?_____

3. Please indicate where this discomfort is. Note the location of each site._____

4. Do you feel any numbness or tingling at this (point or denote to a specific site) surgical site?

If yes for tingling

How would you describe your tingling on a scale from one (1) to ten (10)?

0 __ 1___2___3___4___5___6___7___8___9___10

No Tingling Worst Tingling Imaginable

If yes for numbness

How would you describe the numbness at your site on a scale from 1 to 10?

0 __ 1___2___3___4___5___6___7___8___9___10

No Numbness Worst Numbness

We are also interested in learning what circumstances cause change in these feelings. Please indicate the amount you experience each of the following in a scale from 0 to 10:

5. Increased sensation due to touch:

0 __ 1___2___3___4___5___6___7___8___9___10

No Increase Greatest Increase Imaginable

6. Increased sensation due to movement:

0 __ 1___2___3___4___5___6___7___8___9___10

No Increase Greatest Increase Imaginable

7. Discomfort affects my daily activities

0 __ 1___2___3___4___5___6___7___8___9___10

No Affect Cannot Perform Any Daily Activities

Repeat 4, 5, & 6 for each site with discomfort

Health History Survey

1. Please enter your age _____

2. What is your sex?
_____Male _____Female

3. Do you consider yourself of Hispanic or Latino decent; that is of Mexican, Puerto Rican, Cuban, or Latin American decent? _____Yes

4. Please choose one category that best applies to you?
_____Asian _____Black or African American

_____ Native Hawaiian or Other Pacific Islander

_____Native American Indian _____White

5. What education level did you complete?
_____ Elementary School _____High School or GRE
_____Technical School _____Some College
_____Associates Degree _____Bachelors Degree
_____Master's Degree _____MD or PhD

6. What best describes your current marital status?
_____Married _____Divorced _____Widowed
_____Separated _____Never been married
_____Member of an unmarried couple

7. What best describes your current employment status?
_____ Retired _____Working Full-time _____Homemaker
_____Student _____Working Part-time _____Unemployed

8. Please enter a yearly income _____

9. What state do you live in?
_____PA _____Ohio _____WV _____Other, please identify.

10. What type of area have you lived in for most of your life?

_____City (urban) _____Rural, farm

_____Suburb of a city _____Rural, nonfarm

Cancer HISTORY (Please list all cancers, the cancer stage at diagnosis and the date of diagnosis)**:**

Cancer type	**Cancer stage**	**Date**

Current lung cancer information:

TNM Classification: _____

Stage: _____

Tumor Type: Adenocarcinoma, Squamous Cell, Other (specify)_____

Tumor Location: Right Upper Lobe, Right Middle Lobe, Right Lower Lobe, Left Upper Lobe, Left Lower Lobe

SURGICAL HISTORY (Please list your known type of operations and dates for lung cancer for example. Thoracotomy – open chest, Wedge-long incision along ribs, VATS – several small incisions)**:**

Operation	**Date**

Prescribed medications:

Name of medication	Dose	Times per day	Rate Effectiveness (1=very effective 10=ineffective)

Home Remedies, Herbs

Name of medication	Dose	Times per day	Rate Effectiveness (1= very effective 10= ineffective)

Over the Counter Medications:

Name of medication	Dose	Times per day	Rate Effectiveness (1= very effective 10= ineffective)

Charlson Comorbidity Index

Age of the patient	☐ years	
Does the patient have?		
AIDS?	○ Yes	○ No
Cerebrovascular disease?	○ Yes	○ No
Chronic pulmonary disease?	○ Yes	○ No
Congestive heart failure?	○ Yes	○ No
Connective tissue disease?	○ Yes	○ No
Dementia?	○ Yes	○ No
Hemiplegia?	○ Yes	○ No
Leukemia?	○ Yes	○ No
Malignant lymphoma?	○ Yes	○ No
Myocardial infarction?	○ Yes	○ No
Peripheral vascular disease?	○ Yes	○ No
Ulcer disease?	○ Yes	○ No

Click the appropriate column for each condition (give only 1 answer per row)

	none	without end organ damage	with end organ damage	
Diabetes mellitus	○	○	○	
	none	mild	moderate	severe
Liver disease	○	○	○	○
Renal disease	○	○	○	○
	none	non-metastatic	metastatic	
Malignant solid tumor	○	○	○	

Hospital Anxiety and Depression Scale

Please choose one responses from the four selections; choosing an answer that best currently describes your feelings. You should give an immediate response and not thinking too long about their answers.

---

1. I feel tense or "wound up":

0	1	2	3
Not at All	From time to time	A Lot of the time	Most of the Time

2. I still enjoy the things I used to enjoy:

0	1	2	3
Definitely as much	Not quite so much	Only a little	Hardly at all

3. I get a sort of frightened feeling as if something awful is about to happen:

0	1	2	3
Not at all	A little, but it doesn't worry me	Yes, but not too badly	Very definitely and quite badly

4. I can laugh and see the funny side of things:

0	1	2	3
As much as I always could	Not quite so much now	Definitely not so much now	Not at All

5. Worrying thoughts go through my mind:

0	1	2	3
Only occasionally	From time to time, but not too often	A lot of the time	A great deal of the time

6. I feel cheerful:

0	1	2	3
Most of the time	Sometimes	Not often	Not at All

7. I can sit at ease and feel relaxed:

0	1	2	3
Definitely	Usually	Not often	Not at All

8. I feel as if I am slowed down:

0	1	2	3
Not at All	Sometimes	Very often	Nearly all the time

9. I get a sort of frightened feeling like 'butterflies' in the stomach:

0	1	2	3
Not at All	Occasionally	A Lot of the time	Most of the Time

10. I have lost interest in my appearance:

0	1	2	3
I take just as much care as ever	I may not take quite as much care	I don't take quite as much care as I should	Definitely

11. I feel restless as I have to be on the move:

0	1	2	3
Not at all	Not very much	Quite a lot	Very much indeed

12. I look forward with enjoyment to things:

0	1	2	3
As much as ever	Rather less than I use to	Definitely than than I use to	Hardly at all

13. I get sudden feelings of panic:

0	1	2	3
Not at All	Not very often	Quite often	Very often indeed

14. I can enjoy a good book or radio or TV program:

0	1	2	3
Often	Sometimes	Not often	Very seldom

Functional Assessment of Cancer Therapy – Lung (FACT-L Version 4)

Below is a list of statements that other people with your illness have said are important**. Please circle or mark one number per line to indicate your response as it applies to the past 7 days.**

PHYSICAL WELL-BEING

GP1 I have a lack of energy

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

GP2 I have nausea

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

GP3 Because of my physical condition, I have trouble meeting the needs of my family

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

GP4 I have pain

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

GP5 I am bothered by side effects of treatment

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

GP6 I feel ill

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

GP7 I am forced to spend time in bed

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

SOCIAL/FAMILY WELL-BEING

0-Not at all, 1-A little bit, 2-Somewhat, 3-Quite a bit, 4-Verymuch

GS1 I feel close to my friends

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

GS2 I get emotional support from my family

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

GS3 I get support from my friends

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

GS4 My family has accepted my illness

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

GS5 I am satisfied with family communication about my illness

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

GS6 I feel close to my partner (or the person who is my main support)

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

Q1 *Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please mark this box and go to the next section.*

GS7 I am satisfied with my sex life

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

EMOTIONAL WELL-BEING

0-Not at all, 1-A little bit, 2-Somewhat, 3-Quite a bit, 4-Verymuch

GE1 I feel sad

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

GE2 I am satisfied with how I am coping with my illness

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

GE3 I am losing hope in the fight against my illness

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

GE4 I feel nervous

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

GE5 I worry about dying

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

GE6 I worry that my condition will get worse

0	1	2	3	4
Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**

REFERENCES

American Cancer Society, ACS. (2014). Cancer facts and figures, Atlanta:Cancer Facts and Figures 2013. American Cancer Society. Atlanta, Georgia.

American College of Chest Physicians. (2007). Diagnosis and management of lung cancer executive summary. *Chest.* 132(3S), 1S-19S.

American College of Chest Physicians. (2013). Diagnosis and management of lung cancer, Third edition. *Chest*, 143(5S), 7S-37S. doi:10.1378/chest.12-2377. http://www.chestnet.org/Guidelines-and-Resources/Guidelines-and-Consensus-Statements/More-Guidelines/Lung-Cancer

American Lung Association, ALA. (2008). Trends in lung cancer morbidity and mortality. American Lung Association Epidemiology And Statistics Unit Research and Program Services Division. Retrieved July, 2011, from http://www.lungusa.org/finding-cures/our-research/trend-reports/lc-trend-report.pdf

Aoki, T., Tsuchida, M., Hashimoto, T., Saito, M., Koike, T., & Hayashi, J. (2007). Quality of life after lung cancer surgery: Video-assisted surgery versus thoratocomy. *Heart & Lung*, 16(2), 285-289.

Barsevick, A. M., Dudley, W. N., & Beck, S. L. (2006). Cancer-related fatigue, depressive symptoms, and functional status: A mediation model. *Nursing Research*, 55(5), 366-372.

Barlesi, F., Barrau, K., Loundou, A., Doddoli, C., Simeoni, M. C., Auquier, P., & Thomas, P. (2008). Impact of information on quality of life and satisfaction of non-small cell lung cancer patients: A randomized study of standardized versus individualized information before thoracic surgery. *Journal of Thoracic Oncology, 3*(10), 1146-1152.

Bayram, A. S., Ozcan, M., Kaya, F.N., & Gebitekin, C. (2011). Rib approximation without intercostal nerve compression reduces post-thoracotomy pain: A prospective randomized study. *European Journal of Cardiothoracic Surgery*, 39(4), 570-574. doi: 10.1016/j.ejcts.2010.08.003.

Belfer I. Nature and nurture of human pain. *Scientifica.* 2013: Article ID 415279, 19 pages.

Bennett, M. I., Attal, N., Backonja, M. M., Baron, R., Bouhassira, D., & Freynhagen, R. (2007). Using screening tools to identify neuropathic pain. *Pain*, 127(3), 199-208.

Benedetti, F., Vighetti, S., Ricco, C., Amanzio, M., Bergamasco, L., & Casadio, C. (1998). Neurophysiologic assessment of nerve impairment in posterolateral and muscle-sparing thoracotomy. *Journal of Thoracic & Cardiovascular Surgery*, 115(4), 841-847.

Bjellend, I., Dahl, A., Haug, T. T., & Neckelmann, D. (2002). The validity of the hospital anxiety and depression scale: An updated literature review. *Journal of Psychomatic Ressearch*, 52(2), 69-77.

Blades, B., & Dugan, D.J. (1944). Wounds of the chest observed at the Thoracic Surgery Center, Walter Reed General. *Journal of Thoracic Surgery,* 13(2), 294-306.

Boffa, D. J., Allen, M. S., Grab, J. D., Gaissert, H. A., Harpole, D. H., & Wright, C. D. (2008). The surgical management of primary lung tumors. *Journal of Thoracic and Cardiovascular Surgery, 135*(2), 247-254.

Bousassira, D., & Attal, N. Diagnosis and assessment of neuropathic pain: The saga of clinical tools. *Pain*, 152(3S), S74-S83. doi: 10.1016/j.pain.2010.11.027.

Bririm, O., Kappetein, A. P., & Bogers, A. J. (2005). Charlson comorbidity index as a predictor of long-term outcome after surgery for non small cell lung cancer. *European Journal of Cardiothoracic Surgery*, 28(6), 759-762.

Browning, K. K., Ferketich, A. K., Otterson, G. A., Reynolds, N. R., & Wewers, M. E. (2009). A psychometric analysis of quality of life tools in lung cancer patients who smoke. *Lung Cancer*, 66(1), 134-139.

Buchanan, D., Milroy, R., Baker, L., Thompson, A. M., & Levack, P. A. (2010). Perceptions of anxiety in lung cancer patients and their support network. *Support Care Cancer*, 18(1), 29-36.

Carlson, L. E., Groff, S. L., Maciejewski, O., & Bultz, B. D. (2010). Screening for distress in lung and breast cancer outpatients: A randomized controlled trial. *Journal of Clinical Oncology*, 28(33), 4884-4891.

Cella, D. F., Bonomi, A. E., Lloyd, S. R., Tulsky, D. S., Kaplan, E., & Bonomi, P. (1995). Reliability and validity of the functional assessment of cancer therapy-lung (FACT-L) quality of life instrument. *Lung Cancer*, 12(3), 199-220.

Cella, D., Eton, D. T., Fairclough, D. L., Donomi, P., Heyes, A. E., Silberman, C., & Johnson, D. H. (2002). What is a clinically meaningful change on the functional assessment of cancer therapy-lung (FACT-L) questionnaire? *Journal of Clinical Epidemiology*, 55(3), 285-295.

Charlson, M. E., Pompei, P., Ales, K. L., & MacKenzie, C. R. (1987). A new method of classifying prognostic comorbidity in longitudinal studies development and validation. *Journal of Chronic Dis*eases, 40(5), 373-383.

Chapman, S. (2011). Chronic pain syndromes in cancer survivors. *Nursing Standandards, 25*(21), 35-41.

Cheng, K. K. F., & Lee, D. T. F. (2011). Effects of pain, fatigue, insomnia, and mood disturbance on functional status and quality of life of elderly patients with cancer. *Critical Reviews in Oncology Hematology,* 78(2), 127-137. doi: 10.1016/j.critrevonc.2010.03.002.

Cleary, J. F., Dubenske, L. L., Buss, M. K., Carmack Taylor, C. L., Atwood, A., Traynor, A. M., & Gustafson, D. H. (2008). Impact of the Comprehensive Health Enhancement Support System (CHESS), an interactive computer support system (ICSS) on non small cell lung cancer (NSCLC) survival: A randomized study comparing CHESS with the internet. *Journal of Clinical Oncology,* 26(S15), 888.

Corte, F. D., Mendola, C., Messina, A., & Cammarota, G. (2011). Post Thoracotomy Pain Syndrome. [Technical Update]. Front Lines of Thoracic Surgery. International Association for the Study of Pain. pp.1-10

Cooley, M. E., Short, T. H., & Moriarty, H. J. (2002). Patterns of symptom distress in adults receiving treatment for lung cancer. *Journal of Palliative Care, 18*(3), 150-159.

Dajczman, E., Gordon, A., Kreisman, H., & Wolkove, N. (1991) Long-term postthoracotomy pain. *Chest*, 99(2), 270-274.

Demmy, T. L. (2009). Chest-tube delivered bupivacaine improves pain and decreases opioid use after thoracoscopy. *Annals of Thoracscic Surgery*, 87(4), 1040-1047.

Detterbeck, F. C., Lewis, S. Z., Diekemper, R., Addrizzo-Harris, D. J., & Alberts, W. M. (2013). Executive summary: Diagnosis and management of lung cancer. *Chest*, 143(S1), S7-S20.

deGroot, V., Beckerman, H., Lankhorst, G., & Bouter, L.M. (2013). How to measure comorbidity: a critical review of available methods. *Journal Clincal Epidemiology*, 56(3), 221-230.

Dodd, M. J., Cho, M. H., Cooper, B. A., & Miaskowski, C. (2010). The effect of symptom clusters on functional status and quality of life in women with breast cancer. *European Journal of Oncology Nursing,* 14(2), 101-110. doi: 10.1016/j.ejon.2009.09.005.

Duale´, C., Guastella, V., Morand, J. D., Cardot, J. M., Aublet-Cuvelier, B., & Mulliez, A. (2011). Characteristics of the neuropathy induced by thoracotomy a 4-month follow-up study with psychophysical examination. *Pain*, 108(5), 248-257.

Dualé, C., Sibaud, F., Guastella, V., Vallet, L., Gimbert, Y. A., & Taheri, H. (2009). Perioperative ketamine does not prevent chronic pain after thoracotomy. *European Journal of Pain,* 13(5), 497-505.

Fogel, J., & Fogel, J. (2003). Internet Use for Cancer Information Among Racial/Ethnic Populations and Low Literacy Groups. *Cancer Control* . 10 (5 Suppl), 45-51.

Forrest, L. F., Adams, J., Wareham, H., Rubin, G., White, M., & Mathers, C. D. (2013). Socioeconomic inequalities in lung cancer treatment: Systematic review and meta-analysis. *PLOS Medicine, 10,* 1371. doi:10.1371/journal.pmed.1001376.

Freynhagen, R., Baron, R., Gockel, U., & Tolle, T.R. (2006). PainDETECT: A new screening questionnaire to identify neuropathic components in patients with back pain. *Current Medical Research Opinion*, 22(10), 1911-1920.

Frola, C., Serrano, J., Cantoni, S., Turtulici, I., & Loria, F. C. T. (1995). Findings of atrophy of chest wall muscle after thoracotomy: Relationship between muscles involved and type of surgery. *American Journal of Res*earch, 164(3), 599-601.

Furrer, M., Rechsteiner, R., Eigenmann, V., Signer, C., Althaus, U., & Ris, H.B. (1997). Thoracotomy and thoracoscopy: postoperative pulmonary function, pain and chest wall complaints. *European Journal Cardiothorac Surg*ery, 12(1), 82-87.

Gift, A. G., Jablonski, A., Stommel, M., & Given, C. W. (2004). Symptom clusters in elderly patients with lung cancer. *Oncology Nursing Forum,* 31(2), 202-212.

Globocan, I. (2010). World Health Organization: Cancer Facts Sheet 2008. http://globocan.iarc.fr/Default.aspx. and http://www.who.int/mediacentre/factsheets/fs297/en.

Gould, H. J., Gould, T. N., England, J. D., Paul, D., Liu, Z. P., & Levinson, S. R. (2000). A possible role for nerve growth factor in the augmentation of sodium channels in models of chronic pain. *Brain Research, 854*(2), 19-29.

Graham, C., Bond, S. S., Gerkovich, M. M., & Cook, M. R. (1980). Use of the McGill pain questionnaire in the assessment of cancer pain: replicability and consistency. *Pain,* 8(3), 377-397.

Gray, P. (2008). Acute neuropathic pain: diagnosis and treatment. *Current Opinion Anaesthesiology, 21*, 590-595.

Groome, P. A., & Bolejack, V. (2007). NSLC Lung Cancer Staging Project: Validation of the proposals for revision of the T, N, and M descriptors and consequent stage groupings in the forthcoming (seventh) edition of the TNM classification of malignant tumors. *Journal of Thoracic Oncology,* 2(1), 694.

Grosen, K., Petersen, G. L., Pfeiffer-Jensen, M., Hoejsgaar, A., & Pilegaard, H. K. (2012). Persistent post-surgical pain following anterior thoracotomy for lung cancer: a cross-sectional study of

prevalence. characteristics and interference with functioning. *European Journal of Cardiothoracic Surg*ery, 43(1), 95-103.

Guastella, V., Mick, G., Soriano, C., Vallet, L., Escande, G., & Dubray, C. (2011). A prospective study of neuropathic pain induced by thoracotomy: incidence, clinical description, and diagnosis. *Pain*, 152(1), 74-81.

Hall, S. F. (2006). A user's guide to selecting a comorbidity index for clinical research. *Journal of Clinical Epidemiology*, 59(8), 849-855.

Hegyvary, S. T. (1993). Patient care outcomes related to management of symptoms. *Annual Review of Nursing Research*, 11(1), 145-168.

Heller, D. A., Ahern, F. M., Pringle, K. E., & Brown, T. V. (2009). Among older adults, the responsiveness of self-rated health to changes in charlson comorbidity was moderated by age and baseline comorbidity. *Journal of Clinical Epidemiology*, 62(2), 177-187. doi: 10.1016/j.jclinepi.2008.05.009.

Herr, K. (2004). Neuropathic pain: a guide to comprehensive assessment. *Pain Management Nursing*, *5*(S4), 9-18. doi: 10.1016/j.pmn.2004.10.004Holmes, S. (1989). Use of a modified symptom distress scale in assessment of the cancer patient. *International Journal of Nursing Studies*, 26(1), 69-79.

Howlader, N., Noone, A. M., Krapcho, M., Garshell, J., Neyman, N., Altekruse, S. F., Kosary, C. L., Yu, M., Ruhl, .J, Tatalovich, Z., Cho, H., Mariotto, A., Lewis, D. R., Chen, H. S., Feuer, E. J., & Cronin, K. A. (Editors). (2010). SEER cancer statistics review 1975-2008. Atlanta, Georga.

International Association for the Study of Pain. (2011). Chronic pain after surgery or injury. *Pain Clinical Updates*, 29(1), 1-5.

Kalso, E., Perttunen, K., & Kaasinen, S. (1992). Pain after thoracic surgery. *Acta Anaesthesiologica Scandinavica*, 36(1), 96-100.

Karasaki, T., Nakajima, J., Murakawa, T., Fukami, T., Yoshida, Y., & Kusakabe, M. (2009). Video-assisted thoracic surgery lobectomy preserves more latissimus dorsi muscle than conventional surgery. *Interact Cardiovascular Thoracic Surg*ery, 8(3), 316-320.

Katz, J., & Seltzer, Z. (2009). Transition from acute to chronic postsurgical pain: risk factors and protective factors. *Expert Review of Neurotherapeutics, 9(*5), 723-744.

Keenan, R. J., Landreneau, R. J., Maley, R. H., Singh, D., Macherey, R., Bartley, S., & Santucci, T. (2004). Segmental resection spares pulmonary function in patients with stage I lung cancer. *Annals of Thoracic Surgery, 78*(1), 228-233. doi: 10.1016/j.athoracsur.2004.01.024.

Kehlet, H. (2010). Persistent postsurgical pain: Pathway forward through better design of clinical studies. *Anesthesiology*, 112(3), 514-515.

Kehlet, H., Jensen, J. S., & Woolf, C. J. (2006). Persistent postsurgical pain: Risk factors and prevention. *Lancet*, 367(9522), 1618-1625.

Keskinbora, K., Pekel, A. F., & Aydinli, I. (2007). Gabapentin and an opioid combination versus opioid alone for the management of neuropathic cancer pain: A randomized open trial. *Journal of Pain Symptom Management, 34(2)*, 183-189.

Krause, S.J., & Backonja, M.M. (2003). Development of a Neuropathic Pain Questionnaire. *The Clinical Journal of Pain, 19*(5), 306–314.

Landreneau, R. J., Wiechmann, R. J., Hazelrigg, S. R., Mack, M. J., Keenan, R. J., & Ferson, P. F. (1998). Effect of minimally invasive thoracic surgical approaches on acute and chronic postoperative pain. *Chest Surgery Clinical North America, 8*(4), 891-907.

Landreneau, R. J., Mack, M. J., & Hazelrigg, S. R., (1994). Prevalence of chronic pain after pulmonary resection by thoracotomy or video-assisted thoracic surgery. *Journal of Thoracic & Cardiovascular Surgery*, 107(4), 1079-1085.

Lee, E. H. (2005). Relationships of mood disturbance, symptom experience, and attentional function in women with breast cancer based upon the theory of unpleasant symptoms. *Journal of Korean Academy of Nursing,* 35(4), 728-736.

Lehto, R. H. (2011). Identifying primary concerns in patients newly diagnosed with lung cancer. *Oncology Nursing Forum*, 38(4), 440-447.

Lenz, E. R., Pugh, L. C., Milligan, R. A., Gift, A., & Suppe, F. (1997). The middle-range theory of unpleasant symptoms: An update. *Advances in Nursing Science,* 19(3), 14-27.

Macrae, W. A., & Davies, H. T. O. (1999). Chronic postsurgical pain. In: Crombie IK, Linton S. Croft, P, Von Korff, M, LeResche L., Editors. Epidemiology of pain. Seattle: International Association for the Study of Pain (IASP) Press, p.125-142.

Maguire, M. F., Ravenscroft, A., Beggs, D., & Duffy, J. P. (2006). A questionnaire study investigating the prevalence of the neuropathic component of chronic pain after thoracic surgery. *European Journal of Cardiothorac Surg*ery, 29(5), 800-805.

Max, M. B., Wu, T., Atlas, S. J., Edwards, R. E., Haythornthwaite, J. A., Bollettino, A. F., . . . Belfer, I. (2006). A clinical genetic method to identify mechanisms by which pain causes depression and anxiety. *Molecular Pain, 2*(1), 1-15.

McCorkle, R., Cooley, M. E., & Shea, J. A. (1998). *A user's manual for the Symptom Distress Scale. Retreived November 5, 2013, from* http:// fhsson.mcmaster.ca/ apn/ images/ stories/pdfs/Symptom_Distress_Scale_user_manual.pdf.

McCorkle, R., & Young, K. (1978). Development of a symptom distress scale. *Cancer Nursing*, 1(5), 373-378.

Melzack, R. (1983). McGill Questionnaire. New York, NY, Raven Press. pp-25-90.

Memoli-Wang, J. S., El-Bayoumi, E., Pastis, N. J., Tannner, N. T., Gomez, M., Huggubs, J. T., Silvestri, G. A. (2011). Using endobronchial ultrasound features to predict lymph node metastasis in patients with lung cancer. *Chest*, 140(6), 1550-1556.

Merskey, H. (1986). Classification of chronic pain: Description of chronic pain syndromes and definition of pain terms. *Pain*, 3(S1), S138-S139.

Merskey, H. and H. Bogduk (1994). Classification of chronic pain. Seattle, WA:, IASP Press. pp.1-3.

Miyazaki, T., Sakai, T., Yamaski, N., Tagawa, T., Mine, M., & Shibata, Y. (2011). Assessment and follow-up of intercostal nerve damage after video-assisted thoracic surgery. *European Journal of Cardiothorac Surgery*, 39(6),1033-1039. doi: 10.1016/j.ejcts.2010.10.015.

McCorkle, R., M. E. Cooley, & Shea, J. A. (1998). A user's manual for the Symptom Distress Scale. http://fhsson.mcmaster.ca/apn/images/stories/pdfs/Symptom_Distress_Scale_user_manual.pdf, pp. 1-13,82.

McCorkle, R., & Young, K. (1978). Development of a symptom distress scale. *Cancer Nurs*ing, 1(5), 373-378.

McGill, R. (2009). McGill Pain Questionnaire. Accessed 11-20-2010. http://www.ama-cmeonline.com/pain_mgmt/pdf/mcgill.pdf.

Mongardon, N., Pinton-Gonnet, C., Szekely, B., Michel-Chequi, M., Dreyfus, J., & Fischler, M. (2011). Assessment of chronic pain after thoracotomy a 1-year prevalence study. *Clinical Journal of Pain*, 27(8), 677-81. doi: 10.1097/AJP.0b013e31821981a3

Murray, E., Burns, J., See, T.S., Lai, R., & Nazareth, I. (2005). Interactive Health Communication Applications for people with chronic disease. *Cochrane Database Systematic Review.* Oct 19; (4):CD004274.

Myers, J. S. (2009). A comparison of the theory of unpleasant symptoms and the conceptual model of chemotherapy-related changes in cognitive function. *Oncology Nursing Forum*, 36(1), E1-E10.

National Comprehensive Cancer Network. Practice Guidelines in Oncology Non-Small Cell Lung Cancer V.1.2012. http://www.tri-kobe.org/nccn/guideline/lung/english/non_small.pdf. Accessed 11-20-2012.

Park, J., Kim, H. K., Y.S., C., Kim, J., Shim, Y. M., & K., K. (2011). Unplanned conversion to thoracotomy during video-assisted thoracic surgery lobectomy does not compromise the surgical outcome. *World Journal of Surgery*, 35(3), 590-595. doi: 10.1007/s00268-010-0913-6.

Parkin, D. M., Bray, F., Ferlay, J., & Pisani, P. (2005). Global cancer statistics. *CA Cancer J Clin*, *55*(74), 74-108.

Pallant, J. (2007). SPSS Survival Manual: A step-by step guide to data analysis using SPSS version 15 (Third Edition). New York, NY: McGraw Hill. pp.1-145.

Patel, N. B. (2010). Physiology of Pain. In B. S. Kopf & D. Patel (Editors.), Guide to Pain Management in Low-Resource Setting. Seattle: International Association for the Study of Pain, IASP. pp. 370-371.

Perttunen, K., Tasmuth, T., & Kalso, E. (1999). Chronic pain after thoracic surgery: a follow-up study. *Acta Anaesthesiologica Scandinavica*, *43*(5), 563-567.

Pituskin, E., Fairchild, A., Dutka, J., Gagnon, L., Driga, A., Tachynski, P., Borschneck, J.A., & Ghosh, S. (2010). Multidisciplinary team contributions within a dedicated outpatient palliative

radiotherapy clinic: A prospective descriptive study. *International Journal of Radiation Oncology & Biological Physiology*, 78(2), 527-532.

Pluijms, W. A., Steegers, M. A., Verhagen, A. F., Scheffer, G. J., & Wilder-Smith, O. H. (2006). Chronic post-thoracotomy pain: a retrospective study. *Acta Anaesthesiologica Scandinavica*, 50(5), 804-808.

Prasertsri, N., Holden, J., Keefe, F. J., & Wilkie, D. J. (2011). Repressive coping style: Relationships with depression, pain, and pain coping strategies in lung cancer outpatients. *Lung Cancer*, 71(2), 235-240.

Ringsted, T. K., Wildgaard, K., Kreiner, S., & Kehlet, H. (2013). Pain-related impairment of daily activities after thoracic surgery; a questionnaire validation. *Clinical Journal of Pain*, 29(9), 791-799.

Rogers, M. L., & Duffy, J. P. (2000). Surgical aspects of chronic post-thoracotomy pain. *European Journal of Cardiothoracic Surgery*, 18(6), 711-716

Sarna, L. (1998). Effectiveness of structured nursing assessment of symptom distress in advanced lung cancer. *Oncology Nursing Forum, 25*(6), 1041-1048.

Sarna, L & Brecht, M. L. (1997). Dimensions of symptom distress in woman with advanced lung cancer: A factor analysis. *Heart & Lung*, 26(1), 23-30.

Sarna, L., Cooley, M. E., Brown, J. K., Chernecky, C., Elashoff, D., & Kotlerman, J. (2008). Symptom severity 1 to 4 months after thoracotomy for lung cancer. *American Journal of Critical Care*, 17(5), 455-467.

Sarna, L., Cooley, M. E., Brown, J. K., Chernecky, C., Padilla, G., Danao, L., Chernecky, C., & Elashoff, D. (2010). Woman with lung cancer: Quality of life after thoracotomy. *Cancer Nursing*, 33(2), 85-92.

Shaw, A., & Keefer, F. (2008). Genetic and environmental determinants of postthoracotomy pain syndrome. *Thoracic Anesthesia,* 21(1), 8-11. doi: 10.1097/ACO.0b013e3282f2daa2.

Shimizu, K., Nakaya, N., Saito-Nakaya, K., Akechi, T., Yamada, Y., & Fujimori, M. (2012). Clinical biopsychosocial risk factors for depression in lung cancer patients: a comprehensive analysis using data from the lung cancer database project. *Annals of Oncology,* 23(8), 1973-1979.

Siegel, R., Ward, E., Brawley, O., & Jemal, A. (2011). Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *CA Cancer, 61*(4), 212-236. doi: 10.3322/caac.20121.

Sikorskii, A., Given, C. W., Given, B., Jeon, S., Decker, V., Decker, D., & McCorkle, R. (2007). Symptom management for cancer patients: a trial comparing two multimodal interventions. *Journal of Pain Symptom Management, 34*(3), 253-264. doi: 10.1016/ j.jpainsymman.2006.11.018

Slatore, C. G., Gould, M. K., Au, D. H., Deffebach, M. E., & White, E. (2011). Lung cancer stage at diagnosis: individual associations in the prospective VITamins and lifestyle (VITAL) cohort. *BMC Cancer,* 11(3), 228. doi:10.1186/1471-2407-11-228.

Snaith, R. P. (2003). The hospital anxiety and depression Scale. *Health Quality of Life Outcomes*, 1(1), 29.

Snaith, R.P., & Zigmond, A.S. (1994). The hospital anxiety and depression scale with the irritable-depression-scale and the leeds situational anxiety scale manual. London, W4 4AL, UK: GL Windsor:NFER-Nelson. http://trove.nla.gov.au/work/81802490?q&versionId=95110147.

Soni, M. K., Cella, D., Masters, G. A., Burch, S. P., Heyes, A., & Silberman, C. (2002). The validity and clinical utility of symptom monitoring in advanced lung cancer: a literature review. *Clinical Lung Cancer*, 4(3), 153-60.

Soni, M. K., & Cella, D. (2002). Quality of life and symptom measures in oncology: An overview. *American Journal of Managed Care*, 8(18S), S560-S573.

Steegers, M. A., Snik, D. M., Verhagen, A. F., van der Drift, M. A., & Wilder-Smith, O. H. (2008). Only half of the chronic pain after thoracic surgery shows a neuropathic component. *Journal of Pain*, 9(10), 955-961.

Tabachnick, B. G., & Fidell, L. S. Using multivariate statistics (2007). (Fifth Edition). New York, NY: Allyn & Bacon. pp. 1-109, 78-92.

Turk, D. C., Rudy, T. E., & Salovey, P. (1985). The McGill pain questionnaire reconsidered: confirming the factor structure and examining appropriate uses. *Pain*, 21(4), 385-397.

Walker, M. S., Zona, D. M., & Fisher, E. B., (2006) Depressive symptoms after lung cancer surgery: their relation to coping style and social support. Psycho-Oncology, 15(8), 684–693. doi: 10.1002/pon.997.

Wiener, R. S., Schwartz, L. M., Woloshin, S., & Welch, H. G. (2011). Population-Based Risk for Complications After Transthoracic Needle Lung biopsy of a Pulmonary Nodule: An Analysis of Discharge Records. *Annals of Internal Medicine*, 155(3), 37-44.

Wildgaard, K., Ravn, J., & Kehlet, H. (2009). Chronic post-thoracotomy pain: a critical review of pathogenic mechanisms and strategies for prevention. *European Journal of Cardiothoracic Surgery, 36*, 170-180.

Wildgaard, K., Ravn, J., Nikolajsen, L., Jakobsen, E., Jensen, T. S, & Kehlet, H. (2011). Consequences of persistent pain after lung cancer surgery: A nationwide questionnaire study. *Acta Anaesthesiologica Scandinavica,* 55(1), 60-68. doi: 10.1111/j.1399-6576.2010.02357.x

Wildgaard, K., Ringsted, T. K., Aasvang, E. K., Ravn, J., Werner, M. U., & Kehlet, H. (2012). Neurophysiological characterization of persistent postthoracotomy pain. *Clinical Journal of Pain*, 28(2), 136-142. doi: 10.1097/AJP.0b013e3182261650.

Williams, H. (2006). Assessing, diagnosing, and managing neuropathic pain. *Nursing Times*, 102(1), 22-24. http://www.nursingtimes.net/nursing-practice/clinical-zones/pain-management/assessing-diagnosing-and-managing-neuropathic-pain/203272.article

World Health Organization, W. (2008). Cancer Control: Knowledge into Action. *WHO Guide for Effective Programs, Planning* (Module 1), 1-40.

Yorio, J. T., Yan, J., & Gerber, D. E. (2012). Socioeconomic disparities in lung cancer treatment and outcomes persist within a single academic medical center. *Clinical Lung Cancer*, 13(6), 448-457.

Zigmond, A. S. & Snaith, R. P. (1983). "The hospital anxiety and depression scale". *Acta Psychiatrica Scandinavica*, 67(6), 361–370.