Symptoms Burden in Lung Cancer Patients Undergoing Definitive Chemoradiotherapy: Insights from Electronic Patient-Reported Outcomes

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Background:

Lung cancer remains the leading cause of cancer-related morbidity and mortality in both men and women in China, accounting for 22.0% of new cases and 28.5% of cancer-related deaths in 2022[1]. For patients with locally advanced non-small cell lung cancer (NSCLC) and limited-stage small cell lung cancer (SCLC), definitive concurrent chemoradiotherapy (CRT) remains the standard of care. Despite offering substantial local control, radiotherapy (RT) can cause adverse events such as radiation pneumonitis, esophagitis, and dermatitis[2-4]. Radiation pneumonitis occurs in 10-30% of patients, typically 4-12 weeks post-RT, while acute radiation esophagitis often emerges within 2-3 weeks of treatment, significantly impairing patient quality of life.

In the era of extended survival and holistic health care, monitoring patient-reported symptoms during CRT is crucial. Traditional clinical assessments often fail to detect moderate-to-severe symptoms, particularly post-discharge. Therefore, a patient-centered, continuous symptom monitoring strategy is urgently needed.

Patient-reported outcomes (PROs) are direct reports from patients about their health status without interpretation by clinicians. These encompass symptoms, functional status, quality of life, treatment perceptions, and adherence[5]. Electronic PROs (ePROs), which leverage smartphones or computers, offer real-time, accurate, and scalable solutions for symptom monitoring.

In the West, ePROs are integrated into clinical trials, drug evaluations, and healthcare quality assessments. Studies show that ePROs enhance symptom detection, improve adherence, and prolong survival[6-9]. For example, Dr. Jennifer R. at Memorial Sloan Kettering Cancer Center analyzed ePROs from over 12,000 surgical cancer patients, establishing postoperative

symptom trajectories. Similarly, ePRO data in metastatic HR+/HER2- breast cancer patients on oral therapy showed a reduced risk of serious adverse events[10-12].

In China, research on ePROs is emerging. Professor Qiuling Shi's multicenter RCT implemented ePRO-based symptom monitoring in perioperative lung cancer patients, resulting in reduced complications and improved satisfaction[13]. However, no studies have yet focused on lung cancer patients receiving definitive CRT.

This study aims to evaluate symptom burden and clusters during and after CRT in lung cancer patients using validated ePRO instruments.

Objectives:

To longitudinally assess symptom burden and symptom clusters among lung cancer patients undergoing definitive CRT using ePROs and to compare patterns across clinical subgroups.

Significance:

Inform precise symptom management during and post-CRT.

Establish a PRO-driven framework for supportive care in lung cancer.

Study Design:

This is a prospective observational cohort study conducted from June 2024 to December 2025 in the Department of Thoracic Oncology, Tongji Hospital. Eligible participants will be recruited prior to CRT initiation and enrolled after informed consent.

Primary Outcomes:

Longitudinal trajectory of symptom burden over time based on M. D. Anderson Symptom Inventory-Lung Cancer (M. D. Anderson Symptom Inventory-Lung Cancer: Scale range 0–10, with higher scores indicating worse symptom burden)

Secondary Outcomes:

1. Questionnaire response rate
2. Trajectory of symptom interference over time based on M. D. Anderson Symptom Inventory-Lung Cancer (M. D. Anderson Symptom Inventory-Lung Cancer: scale range 0–10, with higher scores indicating worse interference)

3. Change of Quality of life over time (Quality of life will be assessed using the EuroQoL-5 Dimension Health Outcome Survey (EQ-5D) Questionnaire, Higher scores on the EQ-5D reflect better quality of life)
4. Associations between symptom severity and progression-free survival (PFS).
5. Identification of PRO-related risk factors; development of predictive models.

Eligibility Criteria:

Inclusion Criteria:

- Pathologically confirmed unresectable stage III NSCLC or limited-stage SCLC
- Age ≥ 18 years
- Receiving definitive concurrent chemoradiotherapy (CRT)
- Able and willing to complete electronic questionnaires
- Provided written informed consent

Exclusion Criteria:

- Severe comorbidities (heart, liver, kidney)
- Psychiatric illness or cognitive impairment
- Prior chest or mediastinal radiotherapy

Sample Size:

Using the rule-of-thumb for factor analysis (5-10 participants per variable), with 16 symptom items, the minimum sample size is estimated at 80 patients.

Study Procedures:

Participants will complete ePROs at baseline (1-2 days before CRT), weekly during CRT, and weekly for 12 weeks post-CRT.

Data Sources:

EMR: Demographics, tumor characteristics, comorbidities, treatment details, labs, and costs
Clinical research data platform: Survival tracking

ECOG, CTCAE v5.0: Clinical evaluations

PRO Tools:

MDASI-LC: 22 items (13 core symptoms, 3 lung-specific, 6 interference)

EQ-5D: 5 domains and visual analog scale

Data Collection Platform:

WeChat mini-program with automated reminders. Trained thoracic oncology clinicians will support data entry and follow-up.

Risk and Ethical Considerations:

As a non-interventional study, risks are minimal. No identifiable personal data will be collected. Study adheres to the Declaration of Helsinki.

Statistical Analysis:

Mixed-effects models to analyze symptom trajectories

Descriptive statistics for symptom frequency/severity

Cox models for associations with PFS and OS

PCA, EFA, and hierarchical clustering to identify symptom clusters

Multivariate regression and nomogram development for prediction modeling

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