Postprint: Regional Differences in Clinical Characteristics and Basic Syndrome Distribution Among 2,340 Lung Cancer Patients Across China

Authors: Feng Zhenzhen, Liu Wenrui, Li Jiansheng, Guan Xutao, Jianfeng Quan, Gao Hong, Tian Jianhui, Rong Zhen, Hou Wei, Zhou Xun, Li Jiansheng

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Abstract

Background Traditional Chinese medicine theory holds that syndrome distribution is closely related to region; however, there is currently a lack of clinical studies on the differences in clinical characteristics and syndrome distribution among lung cancer patients from different regions.

Objective To analyze the differences in clinical characteristics and Traditional Chinese medicine syndrome distribution among lung cancer patients from different regions in China, so as to provide references for clinical syndrome differentiation.

Methods A cross-sectional survey was conducted. Questionnaires were distributed to lung cancer patients who visited outpatient clinics or were hospitalized at 11 hospitals—including the Affiliated Hospital of Liaoning University of Traditional Chinese Medicine, Guang' anmen Hospital of China Academy of Chinese Medical Sciences, Longhua Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Affiliated Hospital of Shandong University of Traditional Chinese Medicine, The First Affiliated Hospital of Henan University of Chinese Medicine, Henan Provincial Hospital of Traditional Chinese Medicine, Henan Cancer Hospital, The First Affiliated Hospital of Guangxi University of Chinese Medicine, The Second Affiliated Hospital of Guizhou University of Traditional Chinese Medicine, Affiliated Hospital of Chengdu University of Traditional Chinese Medicine, and Affiliated Hospital of Shaanxi University of Chinese Medicine—from June 2020 to June 2024. Based on regional distribution, patients were divided into seven regions: Northeast, North China, East China, South China, Central China, Northwest, and Southwest. General information including age, gender, ethnicity, tumor-node-metastasis (TNM) stage,

pathological type, treatment modality, as well as Traditional Chinese medicine syndromes such as lung qi deficiency syndrome, blood stasis syndrome, lung yin deficiency syndrome, etc., was collected. Differences in general information and Traditional Chinese medicine syndrome distribution among patients from the seven regions were compared.

Results A total of 2,400 questionnaires were distributed, with 2,340 validly recovered. Comparisons of age, gender, ethnicity, TNM stage, pathological type, treatment modality, smoking history, comorbid chronic respiratory diseases, family history of cancer, living environment, and patient self-assessment (pain, quality of life, functional status, physical condition, anxiety, depression scores) among patients from the seven regions all showed statistically significant differences ($P<0.05$). The frequency of common basic syndromes of lung cancer within the seven regions, from high to low, was lung qi deficiency syndrome, blood stasis syndrome, lung yin deficiency syndrome, spleen qi deficiency syndrome, phlegm-dampness syndrome, phlegm-heat syndrome, etc., with specific distribution showing regional differences ($P<0.05$). Specifically, the common basic syndromes in the Northeast region were, in order, lung qi deficiency syndrome (37.11%), lung yin deficiency syndrome (33.51%), phlegm-dampness syndrome (20.10%), etc.; North China region: lung qi deficiency syndrome (85.19%), blood stasis syndrome (72.84%), lung yin deficiency syndrome (44.44%), etc.; East China region: lung qi deficiency syndrome (69.15%), lung yin deficiency syndrome (44.47%), spleen qi deficiency syndrome (19.15%), blood stasis syndrome (19.15%), etc.; South China region: lung qi deficiency syndrome (58.50%), lung yin deficiency syndrome (37.00%), phlegm-dampness syndrome (21.00%), etc.; Central China region: lung qi deficiency syndrome (51.51%), blood stasis syndrome (35.92%), spleen qi deficiency syndrome (35.92%), etc.; Northwest region: lung qi deficiency syndrome (74.00%), spleen qi deficiency syndrome (58.00%), blood stasis syndrome (51.00%), etc.; Southwest region: blood stasis syndrome (31.34%), lung qi deficiency syndrome (28.26%), lung yin deficiency syndrome (18.41%), etc.

Conclusion Clinical characteristics and syndrome distribution differ among lung cancer patients from different regions; Traditional Chinese medicine syndrome differentiation and treatment should pay attention to adaptation based on both region and individual to improve clinical efficacy.

Full Text

Research on Regional Differences in Clinical Characteristics and Basic Syndrome Distribution Among 2,340 Lung Cancer Patients Across China

FENG Zhenzhen[1,2], **LIU Wenrui**[1,2], **LI Jiansheng**[1,2*], **GUAN Xutao**[3], **QUAN Jianfeng**[4], **GAO Hong**[5], **TIAN Jianhui**[6], **RONG Zhen**[7], **HOU Wei**[8], **ZHOU Xun**[9]

[1]National Regional Traditional Chinese Medicine (Lung Disease) Diagnosis and Treatment Center, the First Affiliated Hospital of Henan University of Chinese Medicine, Zhengzhou 450000, China
[2]Collaborative Innovation Center for Chinese Medicine and Respiratory Diseases Co-constructed by Henan Province & Ministry of Education/Henan Key Laboratory of Chinese Medicine for Respiratory Disease, Henan University of Chinese Medicine, Zhengzhou 450046, China
[3]Department of Hematology and Oncology, the First Affiliated Hospital of Henan University of Chinese Medicine, Zhengzhou 450000, China
[4]Department of Oncology, Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang 712000, China
[5]Department of Oncology, Affiliated Hospital of Liaoning University of Traditional Chinese Medicine, Shenyang 110000, China
[6]Department of Oncology, Shanghai Municipal Hospital of Traditional Chinese Medicine, Shanghai 200071, China
[7]Department of Oncology, the First Affiliated Hospital of Guangxi University of Traditional Chinese Medicine, Nanning 530023, China
[8]Department of Oncology, Guang' anmen Hospital, China Academy of Chinese Medical Sciences, Beijing 100053, China
[9]Department of Respiratory Medicine, the Second Affiliated Hospital of Guizhou University of Traditional Chinese Medicine, Guiyang 550003, China

Corresponding author: LI Jiansheng, Professor/Chief Physician/Doctoral Supervisor; E-mail: li_{js8}@163.com

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Abstract

Background: Traditional Chinese Medicine (TCM) theory posits a close relationship between syndrome distribution and geographical regions; however, clinical research investigating regional variations in clinical characteristics and TCM syndrome patterns among lung cancer patients remains insufficient.

Objective: To analyze regional differences in clinical characteristics and TCM syndrome distribution among lung cancer patients across China, providing evidence to support clinical syndrome differentiation.

Methods: A cross-sectional survey was conducted from June 2020 to June 2024. Questionnaires were distributed to lung cancer outpatients and inpatients at 11 hospitals: the Affiliated Hospital of Liaoning University of Traditional Chinese Medicine, Guang' anmen Hospital of China Academy of Chinese Medical Sciences, Longhua Hospital affiliated with Shanghai University of Traditional Chinese Medicine, the Affiliated Hospital of Shandong University of Traditional Chinese Medicine, the First Affiliated Hospital of Henan University of Traditional Chinese Medicine, Henan Provincial Hospital of Traditional Chinese Medicine, Henan Cancer Hospital, the First Affiliated Hospital of Guangxi University of Traditional Chinese Medicine, the Second Affiliated Hospital of

Guizhou University of Traditional Chinese Medicine, the Affiliated Hospital of Chengdu University of Traditional Chinese Medicine, and the Affiliated Hospital of Shaanxi University of Traditional Chinese Medicine. Patients were categorized into seven geographical regions: Northeast, North China, East China, South China, Central China, Northwest, and Southwest. Data collection included general information (age, gender, ethnicity, TNM staging, pathological type, treatment modality) and TCM syndromes (lung qi deficiency, blood stasis, lung yin deficiency, etc.). Regional differences in these parameters were compared across the seven regions.

Results: Of 2,400 questionnaires distributed, 2,340 valid responses were collected. Significant regional differences were observed in patient age, gender, ethnicity, TNM stage, pathological type, treatment modality, smoking history, chronic respiratory disease comorbidities, family history of cancer, living environment, and self-assessment scores (pain, quality of life, functional status, physical condition, anxiety, depression) ($P<0.05$). The overall frequency of basic lung cancer syndromes across all regions, from highest to lowest, was: lung qi deficiency, blood stasis, lung yin deficiency, spleen qi deficiency, phlegm-dampness, and phlegm-heat syndrome, with significant regional variations ($P<0.05$). Specifically, the predominant syndromes were: lung qi deficiency (37.11%), lung yin deficiency (33.51%), and phlegm-dampness (20.10%) in the Northeast; lung qi deficiency (85.19%), blood stasis (72.84%), and lung yin deficiency (44.44%) in North China; lung qi deficiency (69.15%), lung yin deficiency (44.47%), spleen qi deficiency (19.15%), and blood stasis (19.15%) in East China; lung qi deficiency (58.50%), lung yin deficiency (37.00%), and phlegm-dampness (21.00%) in South China; lung qi deficiency (51.51%), blood stasis (35.92%), and spleen qi deficiency (35.92%) in Central China; lung qi deficiency (74.00%), spleen qi deficiency (58.00%), and blood stasis (51.00%) in Northwest China; and blood stasis (31.34%), lung qi deficiency (28.26%), and lung yin deficiency (18.41%) in Southwest China.

Conclusion: Regional variations exist in the clinical characteristics and TCM syndrome distribution among lung cancer patients in China. TCM syndrome differentiation and treatment should consider both geographical and individual factors to enhance clinical efficacy.

Keywords: lung cancer; Traditional Chinese Medicine; syndrome; regional differences; clinical research

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Introduction

According to the latest global cancer statistics and data from the National Cancer Center, lung cancer ranks first in both mortality and incidence among malignant tumors in China and worldwide [1-2]. In 2022, approximately 1.06 million new lung cancer cases were reported in China, accounting for about 22% of all malignant tumors, with deaths reaching 733,300 cases, representing approximately 28.5% of all cancer-related deaths [2]. Traditional Chinese Medicine has demonstrated unique advantages in treating lung cancer at all stages [3]. Syndrome differentiation and holistic concepts represent the distinctive features of TCM diagnosis and treatment, emphasizing comprehensive consideration of patient pathogenesis and environmental factors to achieve individualized care [4]. TCM theory holds that syndromes are closely related to geographical regions [5]; however, relevant clinical research on regional differences in clinical characteristics and syndrome distribution among lung cancer patients remains lacking. This study analyzed data from 2,340 lung cancer patients across seven regions of China (Northeast, North China, East China, South China, Central China, Northwest, and Southwest) to explore differences in clinical characteristics and syndrome distribution, aiming to provide a reference for clinical diagnosis and treatment of lung cancer.

Methods

Study Design and Participants A cross-sectional survey was conducted using cluster sampling. The study population comprised 2,340 lung cancer outpatients and inpatients from June 2020 to June 2024 at 11 hospitals: the Affiliated Hospital of Liaoning University of Traditional Chinese Medicine, Guang' anmen Hospital of China Academy of Chinese Medical Sciences, Longhua Hospital affiliated with Shanghai University of Traditional Chinese Medicine, the Affiliated Hospital of Shandong University of Traditional Chinese Medicine, the First Affiliated Hospital of Henan University of Traditional Chinese Medicine, Henan Provincial Hospital of Traditional Chinese Medicine, Henan Cancer Hospital, the First Affiliated Hospital of Guangxi University of Traditional Chinese Medicine, the Second Affiliated Hospital of Guizhou University of Traditional Chinese Medicine, the Affiliated Hospital of Chengdu University of Traditional Chinese Medicine, and the Affiliated Hospital of Shaanxi University of Traditional Chinese Medicine. According to China' s administrative regional divisions, cases were categorized into seven regions: Northeast, North China, East China, Central China, South China, Southwest, and Northwest. This study was approved by the Ethics Committee of the First Affiliated Hospital of Henan University of Traditional Chinese Medicine (Ethics No.: 2020HL-083).

Inclusion criteria: (1) Patients meeting lung cancer diagnostic criteria; (2) Age $\geq$ 18 years; (3) Self-reported ability to communicate orally in Chinese; (4) Voluntary participation with signed informed consent.

Exclusion criteria: (1) Patients unsuitable for research participation, such as

pregnant/lactating women, critically ill/end-stage patients, or those with severe depression/anxiety or who refused participation; (2) Patients with cognitive or other impairments (e.g., vision, hearing, speech, physical) affecting self-report completion.

Diagnostic Criteria **Western medicine diagnostic criteria:** Referenced the "Chinese Medical Association Lung Cancer Clinical Diagnosis and Treatment Guidelines (2019 Edition)" [6], with diagnosis established through sputum cytology, lymph node or nodule biopsy, and other methods.

TCM syndrome diagnostic criteria: Based on "TCM Clinical Terminology: Syndromes: GB/T16751.2-1997" [7], "TCM Oncology Diagnosis and Treatment Guidelines: ZYYXH/T136~156-2008" [8], "TCM Internal Medicine Disease Diagnosis and Treatment Routine: National Standard Application" [9], and "Evidence-based Clinical Practice Guidelines in TCM - Internal Medicine Volume" [10]. For example, lung qi deficiency syndrome was diagnosed by low and weak coughing, shortness of breath, wheezing, thin clear white sputum, poor appetite, chest tightness, fatigue, spontaneous sweating, aversion to cold, pale tender tongue with white coating, and weak pulse.

Data Collection **General data collection:** Included age, gender, ethnicity, Tumor Node Metastasis (TNM) staging, pathological type, treatment modality, smoking history (defined as current or former smokers), family history of cancer, comorbid chronic respiratory diseases (including chronic bronchitis, COPD, asthma, idiopathic pulmonary fibrosis, tuberculosis, pneumoconiosis, chronic pharyngitis, allergic rhinitis, etc.), and living environment.

TCM syndrome collection: Included lung qi deficiency, blood stasis, lung yin deficiency, spleen qi deficiency, phlegm-dampness, phlegm-heat, qi stagnation, kidney qi deficiency, kidney yin deficiency, stomach qi deficiency, blood deficiency, lung heat, and kidney yang deficiency syndromes.

Patient self-assessment: (1) Pain: assessed using the Visual Analogue Scale (VAS) [11], scored 0-10 (0 = no pain, 10 = worst pain); (2) Physical condition: assessed using the Eastern Cooperative Oncology Group (ECOG) Performance Status scale [12], scored 0-5 (0 = normal activity, 5 = death); (3) Functional status: assessed using the Karnofsky Performance Status (KPS) scale [13], scored 0-100 (higher scores indicate better function); (4) Quality of life: assessed using the Quality of Life Questionnaire Core 30 (QLQ-C30) [14], including physical, role, social, and emotional function, scored 0-100 (higher scores indicate better quality); (5) Anxiety: assessed using the Self-Rating Anxiety Scale (SAS) [15], comprising 20 items scored 1-4 based on severity, with higher total scores indicating greater anxiety; (6) Depression: assessed using the Self-Rating Depression Scale (SDS) [16], comprising 20 items scored 1-4 based on severity, with higher total scores indicating greater depression.

Quality control: A quality control team was established to develop unified

clinical research protocols. Investigators at each center received on-site or online training before the survey, and consistency among trained investigators was verified using Kappa tests. The quality control team conducted regular sampling and verification of study cases.

Statistical Analysis Data were analyzed using IBM SPSS 26.0. Categorical data were expressed as frequencies and percentages, with inter-group comparisons using chi-square tests or Fisher' s exact test. Continuous data were non-normally distributed and described using median (P25, P75), with inter-group comparisons using Kruskal-Wallis tests. Categorical missing data were imputed using mode, and quantitative missing data using median. $P<0.05$ was considered statistically significant.

Results

Comparison of General Characteristics Across Regions A total of 2,340 lung cancer patients were included: Northeast (Liaoning) 194 cases (8.29%), North China (Beijing) 81 cases (3.46%), East China (Shandong, Shanghai) 470 cases (20.09%), South China (Guangxi) 200 cases (8.55%), Central China (Henan) 994 cases (42.48%), Northwest (Shaanxi) 200 cases (8.55%), and Southwest (Chengdu, Yunnan) 201 cases (8.59%). Significant regional differences were observed in age, gender, ethnicity, TNM stage, pathological type, treatment modality, smoking history, chronic respiratory disease comorbidities, family history of cancer, and living environment ($P<0.05$). The median age across all seven regions exceeded 60 years, with male and Han ethnicity predominating. North China had the highest proportion of male patients [59 cases (72.84%)], while Northeast had the highest proportion of female patients [95 cases (48.97%)]. For TNM staging, Stage IV patients accounted for the highest proportion in all regions (27.36%-74.07%). For pathological types, adenocarcinoma was most common across all regions (32.84%-73.00%), while squamous cell carcinoma was relatively more prevalent in North China and Northwest (25.92%, 26.50%), and small cell lung cancer was relatively more common in Northeast, Central China, and Northwest (15.98%, 15.09%, 14.50%). Regarding treatment modalities, Northeast commonly used chemotherapy (42.78%), surgery (35.05%), and targeted therapy (26.29%); North China primarily used chemotherapy (93.83%); East China frequently used chemotherapy (57.87%), surgery (47.87%), and targeted therapy (26.60%); Central China often used chemotherapy (72.43%), targeted therapy (41.35%), and surgery (17.30%); Northwest frequently used chemotherapy (71.50%), targeted therapy (38.00%), and radiotherapy (21.00%); Southwest commonly used chemotherapy (39.30%), immunotherapy (22.89%), and surgery (19.90%). Over 50% of patients in Northwest, Southwest, East China, and North China had a smoking history. East China and Southwest had relatively higher proportions of patients with chronic respiratory diseases (25.74%, 22.89%), with chronic bronchitis being the most common across all regions. East China had the highest proportion of patients with a family history of cancer (15.96%).

Except for Central China, urban residents outnumbered rural residents in all regions, consistent with national cancer statistics showing slightly higher urban prevalence .

Comparison of Multi-dimensional Self-assessment Across Regions Significant regional differences were observed in VAS, KPS, ECOG, QLQ-C30, SAS, and SDS scores ($P<0.05$). South China and Central China patients had higher VAS scores [3 (1.25, 4) and 2 (0, 4), respectively]. Northeast and Central China patients had lower KPS scores [80 (60, 90) and 80 (70, 90), respectively]. Northeast and Central China patients had higher ECOG scores [2 (1, 3) and 2 (1, 2), respectively]. North China patients had the highest QLQ scores [71.43 (57.14, 71.43)], while South China and Central China had relatively lower scores. South China patients had the highest SAS [43.00 (37.00, 48.75)] and SDS scores [50.00 (45.00, 52.00)], while North China had the lowest SAS [27.00 (26.00, 29.00)] and SDS scores [31.00 (30.00, 34.00)] .

Comparison of Basic Syndrome Distribution Across Regions The most common basic syndromes across the seven regions were, in descending order: lung qi deficiency, blood stasis, lung yin deficiency, spleen qi deficiency, phlegm-dampness, phlegm-heat, qi stagnation, kidney qi deficiency, kidney yin deficiency, stomach qi deficiency, lung heat syndrome, with significant regional variations ($P<0.001$). Specifically, the predominant syndromes were: lung qi deficiency (37.11%), lung yin deficiency (33.51%), and phlegm-dampness (20.10%) in Northeast; lung qi deficiency (85.19%), blood stasis (72.84%), and lung yin deficiency (44.44%) in North China; lung qi deficiency (69.15%), lung yin deficiency (44.47%), spleen qi deficiency (19.15%), and blood stasis (19.15%) in East China; lung qi deficiency (58.50%), lung yin deficiency (37.00%), and phlegm-dampness (21.00%) in South China; lung qi deficiency (51.51%), blood stasis (35.92%), and spleen qi deficiency (35.92%) in Central China; lung qi deficiency (74.00%), spleen qi deficiency (58.00%), and blood stasis (51.00%) in Northwest; and blood stasis (31.34%), lung qi deficiency (28.26%), and lung yin deficiency (18.41%) in Southwest. Significant regional differences were found in lung qi deficiency, blood stasis, lung yin deficiency, spleen qi deficiency, phlegm-dampness, phlegm-heat, qi stagnation, kidney qi deficiency, kidney yin deficiency, and lung heat syndromes ($P<0.05$), but not in blood deficiency or kidney yang deficiency ($P>0.05$) .

Discussion

TCM theory posits that due to regional differences in climate and lifestyle habits, diseases often exhibit distinct clinical characteristics and syndrome distribution patterns, as noted in *Suwen· Yifa Fangyi Lun*: "One disease treated differently, all cured···determined by geographical conditions" [17]. However, supporting clinical research remains limited. This study included 2,340 lung cancer patients from seven regions—Northeast (Liaoning), North China (Beijing), East China (Shandong, Shanghai), South China (Guangxi), Central China (Henan),

Northwest (Shaanxi), and Southwest (Chengdu, Yunnan)—to explore regional differences in clinical characteristics and syndrome distribution, providing evidence for region-specific clinical management.

The results revealed both common patterns and regional variations in age, gender, pathological type, and treatment modality. Median age exceeded 60 years across all regions, with male and Han ethnicity predominance, and advanced-stage patients being most common. Adenocarcinoma was the most prevalent pathological type, consistent with previous research [2,18]. Chemotherapy was the most common treatment across regions, but surgery rates were higher in Northeast and East China where early-stage patients were more prevalent. North China, dominated by advanced-stage disease, primarily used chemotherapy. Targeted therapy rates were relatively higher in South China, Central China, and Northwest, possibly related to regional differences in early screening accessibility [19-20], driver gene mutation patterns in non-small cell lung cancer [21-22], and targeted drug accessibility [23-24]. Smoking history rates were high across all regions, consistent with previous findings [25], though Northeast, South China, and Central China had more non-smoking patients, likely related to higher female patient proportions. The proportion of non-smoking female lung cancer patients in China far exceeds that in other countries [26], making exploration of clinical characteristics in non-smoking patients crucial for early screening in regions with high non-smoking populations [27-28].

Regarding chronic respiratory disease comorbidities, proportions ranged from 4.64% to 25.74% across regions, with chronic bronchitis being most common. Chronic pulmonary inflammation is a risk factor for lung cancer, promoting carcinogenesis through oxidative stress, immunosuppressive microenvironments, and abnormal signaling pathways [29], a hypothesis supported by this study. Current research on TCM prevention and treatment of lung cancer based on the "inflammation-cancer" transformation mechanism is ongoing [30-31]. Except for Central China, urban residents outnumbered rural residents, consistent with national cancer statistics [32]. Multi-dimensional self-assessment revealed regional differences in pain, functional status, physical condition, overall quality of life, anxiety, and depression. South China and Central China patients had relatively higher pain scores, poorer overall quality of life, and higher anxiety and depression scores, while North China patients showed better self-assessment across all domains, possibly related to regional economic levels and emphasis on quality of life, psychological status, and symptom management.

Regarding regional syndrome distribution, lung qi deficiency was the most common deficiency syndrome across all regions, while blood stasis was the most common excess syndrome in North China, East China, Central China, Northwest, and Southwest, and phlegm-dampness predominated in Northeast and South China. Northeast' s cold climate (average winter temperature -20°C) [33] causes qi constriction, leading to frequent qi stagnation, while the local preference for rich, fatty foods [34] generates dampness and phlegm, resulting

in higher phlegm-dampness prevalence. North China' s cold, dry climate [35] causes blood congelation and yin damage, leading to high rates of lung qi deficiency, blood stasis, and lung yin deficiency. East China' s warm, humid climate, combined with rapid urbanization and severe air pollution [36], contributes to frequent respiratory diseases; this study found the highest proportion of chronic respiratory disease history in East China, along with high smoking rates, explaining the prevalence of lung qi and yin deficiency. South China' s warm, rainy climate [37] makes dampness a common pathogenic factor [38], resulting in higher phlegm-dampness prevalence. Central China, described in classical texts as "flat and damp···with mixed diets," shows high spleen qi deficiency due to dampness obstructing spleen function. Northwest residents' consumption of raw, cold foods leads to spleen and stomach qi deficiency [39]; impaired spleen transformation fails to generate qi and blood, causing lung qi deficiency and blood stasis. Southwest' s warm, humid climate produces phlegm-heat, while dampness obstructs qi movement, causing qi stagnation.

In summary, this study explored clinical characteristics and basic syndrome distribution patterns among 2,340 lung cancer patients across seven Chinese regions, revealing regional differences in age, gender, pathological type, quality of life, and syndrome distribution influenced by climate, dietary habits, and local customs. These findings provide references for region-specific TCM management of lung cancer. However, limitations include uneven sample sizes across regions, possibly related to population size or disease prevalence, potentially introducing selection bias, and the use of cluster sampling, which may involve sampling error. Future research will expand sample size, ensure regional balance, and employ combined cluster and stratified sampling to provide high-quality clinical evidence for individualized TCM management of lung cancer.

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