DOI: 10.66069/ojspub.27450821

Risk Factors and Research Progress on Integrated Traditional Chinese and Western Medicine Treatment for Hypercoagulable State in Advanced Lung Cancer Patientss

Min Liu1, Jianfeng Quan[2,*]

[1]Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China
[2]Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang 712000, Shaanxi, China
**Correspondence Author*

Abstract: ***Patients with advanced lung cancer frequently exhibit varying degrees of coagulation abnormalities and a hypercoagulable state, which constitute an important pathological basis for cancer-associated thrombosis (CAT), particularly venous thromboembolism (VTE), and are closely associated with tumor progression, treatment interruption, impaired quality of life, and poor prognosis. The mechanisms underlying hypercoagulability in advanced lung cancer are complex and reflect the combined effects of tumor biology, host factors, and anticancer therapy. Modern medical research indicates that increased tumor tissue factor expression, inflammatory responses, platelet activation, vascular endothelial injury, formation of neutrophil extracellular traps, and specific tumor molecular characteristics can all promote activation of the coagulation system; advanced or metastatic disease, older age, prolonged immobilization, previous VTE, elevated platelet counts, chemotherapy, targeted therapy, immunotherapy, and central venous catheterization further increase thrombotic risk. Although traditional Chinese medicine (TCM) has no disease entity directly corresponding to "hypercoagulability," its pathogenesis and clinical manifestations can be understood within categories such as "blood stasis," "phlegm-stasis," and "mass accumulation (Zheng Ji)." Blood stasis runs throughout the development and progression of advanced lung cancer and interacts with qi deficiency, yin deficiency, phlegm turbidity, qi stagnation, and cancer toxin. Some clinical studies suggest that modern coagulation markers such as D-dimer are associated with blood stasis syndrome and its concurrent patterns in advanced lung cancer, providing a basis for the objectification of TCM syndrome differentiation. Current Western medical prevention and treatment mainly rely on dynamic risk assessment, basic preventive measures, and individualized anticoagulation strategies using low-molecular-weight heparin and direct oral anticoagulants. TCM approaches mainly include supplementing qi and activating blood, regulating qi and activating blood, nourishing yin and activating blood, and resolving phlegm and dispelling stasis. Existing studies suggest that some blood-activating and stasis-resolving formulas may improve coagulation parameters, hemorheological status, and related symptoms; however, high-quality evidence for reducing clinically important endpoints such as symptomatic VTE, recurrent VTE, and mortality remains insufficient. Future studies should establish dynamic risk-assessment systems integrating clinical characteristics, tumor molecular features, coagulation biomarkers, and TCM syndromes, and conduct high-quality integrative Chinese-Western medicine research on the basis of standard anticoagulant therapy to achieve precise prevention and treatment of hypercoagulability in advanced lung cancer.***

Keywords: Advanced lung cancer, Hypercoagulable state, Cancer-associated thrombosis, Risk factors, Integrated traditional Chinese and Western medicine**.**

1. Introduction

Lung cancer is one of the malignancies with the greatest global disease burden. GLOBOCAN 2022 data show that lung cancer remains among the leading cancers worldwide in both incidence and mortality [1]. A substantial proportion of patients are already at a locally advanced or metastatic stage at diagnosis and require systemic multimodal treatment, including chemotherapy, molecular targeted therapy, immunotherapy, and radiotherapy. Coagulation abnormalities are important pathological changes accompanying advanced malignancy. A hypercoagulable state refers to a pathological condition in which enhanced activation of the coagulation system, weakened endogenous anticoagulant mechanisms, or impaired fibrinolysis predisposes the body to thrombosis. It is not synonymous with clinically established VTE, but it provides an important basis for the development of CAT, including deep-vein thrombosis and pulmonary embolism. The risk of VTE is markedly higher in patients with cancer than in the general population, and lung cancer is among the solid tumors associated with relatively high thrombotic risk [2, 3]. CAT can lead not only to interruption of anticancer therapy, prolonged hospitalization, and impaired quality of life, but also to increased risks of recurrence, bleeding, and death.

Hypercoagulability in advanced lung cancer is distinctly multifactorial and dynamic. The traditional Virchow triad — hypercoagulability, blood-flow stasis, and vascular endothelial injury—remains the basic pathophysiological framework. In recent years, however, advances in tumor genomics, the tumor immune microenvironment, extracellular vesicles, and inflammation-coagulation interactions have further expanded understanding of the mechanisms underlying lung cancer-associated hypercoagulability [3-5]. Meanwhile, TCM interprets cancer-related hypercoagulability from perspectives such as blood stasis, phlegm-stasis, and qi-deficiency with blood stasis, and increasing attention has been paid to correlations between TCM syndromes and objective indicators such as D-dimer and fibrinogen.

Accordingly, this review summarizes the risk factors, pathological mechanisms, risk assessment, and advances in prevention and treatment of hypercoagulability in patients with advanced lung cancer from the perspectives of both modern medicine and TCM, with the aim of providing a reference for clinical risk identification and comprehensive

management.

2. The Modern Medical Mechanism of Hypercoagulability in Advanced Lung Cancer

2.1 Tumor Cells Directly Activate the Coagulation System

Lung cancer cells can express and release multiple procoagulant substances, among which tissue factor (TF) is considered a key molecular link between cancer and the coagulation system. Binding of TF to coagulation factor VIIa initiates the extrinsic coagulation pathway, promotes factor X activation and thrombin generation, and ultimately increases fibrin formation [3-5] In addition to soluble procoagulant molecules, tumor cells can release TF-bearing microparticles or small extracellular vesicles, allowing procoagulant signals to disseminate through the circulation to distant sites and thereby contribute to systemic hypercoagulability. Activation of cancer-associated oncogenes and loss of tumor-suppressor genes may also enhance coagulation and inhibit fibrinolysis by regulating TF, plasminogen activator inhibitor-1, and other molecules [4].

2.2 Inflammatory Response and vascular Endothelial Injury

Advanced lung cancer is often accompanied by chronic low-grade or even systemic inflammation. Tumor cells and immune cells can release inflammatory cytokines such as IL-6, IL-1β, and TNF-α, which promote endothelial activation, upregulate TF, factor VIII, and von Willebrand factor, and suppress anticoagulant molecules such as thrombomodulin, thereby shifting the vascular endothelium from an anticoagulant to a procoagulant phenotype [3-5]. In addition, chemotherapy, radiotherapy, surgery, and certain targeted agents can themselves cause vascular endothelial injury, amplifying coagulation activation together with malignancy-associated systemic inflammation.

2.3 Platelet Activation and Neutrophil Extracellular Trap Network

In addition to their conventional role in hemostasis, platelets are closely involved in tumor progression and CAT formation. Lung cancer cells can promote platelet adhesion and aggregation through mucins, TF-positive microparticles, and inflammatory mediators; activated platelets can in turn release procoagulant mediators such as P-selectin and promote survival and distant metastasis of circulating tumor cells. Neutrophil extracellular traps (NETs) have attracted increasing attention in recent years. NETs are composed of DNA, histones, and neutrophil proteases and can provide an adhesive scaffold for platelets and coagulation factors, thereby further promoting thrombin generation and thrombus stabilization. Tumor-associated inflammation and immunotherapy may promote NET formation through different pathways [5].

2.4 New Insights into the Microenvironment Promoting Thrombosis in the Lungs

Recent basic research has suggested that the lungs may not only be the primary site of lung cancer and a target organ for pulmonary embolism, but may also participate in systemic CAT formation. Tumor-derived chemokines can act through the circulation on pulmonary interstitial macrophages, inducing them to produce small extracellular vesicles with platelet-activating properties and thereby generating remote prothrombotic effects [5]. CXCL13 and integrin β2-associated small extracellular vesicles have therefore been proposed as potential novel CAT biomarkers. However, the current evidence is derived mainly from basic and translational studies; their assay methods, thresholds, clinical predictive performance, and value as therapeutic targets require further validation in prospective clinical studies and cannot yet replace established VTE risk-assessment methods.

3. Risk Factors for Hypercoagulable State in Patients with Advanced Lung Cancer

Hypercoagulability in patients with advanced lung cancer does not result from a single factor, but rather from the cumulative and interacting effects of tumor-related, host-related, and treatment-related factors.

3.1 Tumor-related Factors

Disease stage is an important modifier of CAT risk. A meta-analysis by Singh et al. [6] showed an overall increase in the burden of VTE with advancing cancer stage, with patients with stage III or IV disease having a markedly greater burden than those with earlier-stage disease. Patients with advanced lung cancer generally have a higher tumor burden, more intense inflammatory responses, greater release of procoagulant substances, and frequent distant metastases, venous compression, and reduced mobility, all of which facilitate hypercoagulability. Thrombotic risk also varies among histological subtypes of lung cancer. Previous studies suggest that patients with lung adenocarcinoma may have a higher risk of VTE than those with squamous cell carcinoma, potentially because of mucin release, stronger platelet-activating capacity, and TF expression [5, 7]. Therefore, dynamic thrombotic-risk assessment should be strengthened in patients with advanced lung adenocarcinoma, particularly those with persistent thrombocytosis. With the development of precision therapy for NSCLC, associations between oncogenic driver alterations and VTE have become an important research focus. Evidence linking ALK and ROS1 rearrangements with higher VTE risk is relatively strong, and some studies have reported VTE incidences exceeding 30% in patients with ROS1 rearrangements [7, 8]. BRAF mutations, RET fusions, and STK11 alterations have also been reported to be associated with thrombotic risk, but current evidence is derived largely from retrospective studies or small cohorts and remains inconsistent [4, 9, 10]. Associations of EGFR, KRAS, and MET alterations with thrombotic risk are likewise controversial. Tumor genomic features may therefore become important components of future risk-prediction models, but current evidence does not support determining prophylactic anticoagulation solely on the basis of a single molecular alteration.

3.2 Patient Individual Factors

Older age, obesity, restricted mobility, prolonged bed rest, infection, cardiopulmonary insufficiency, prior VTE, and

inherited thrombophilia can all increase VTE risk [10]. Because patients with advanced lung cancer frequently experience cachexia, bone metastases, pain, and declining performance status, their physical activity is often markedly reduced, further aggravating venous stasis in the lower extremities. A history of VTE is a strong risk factor for recurrence. In addition, inherited thrombophilic conditions such as Factor V Leiden and the prothrombin G20210A mutation may further increase baseline thrombotic risk, although their prevalence varies considerably among ethnic populations; whether routine screening is appropriate should therefore be determined according to the individual clinical context [10]. Elevated platelet counts are also an important factor in cancer-associated VTE risk assessment. The Khorana score includes a pretreatment platelet count of ≥350 × 10^9/L as a predictor of VTE. Thrombocytosis is not uncommon in lung cancer and is associated with inflammatory activity and tumor burden. It should be emphasized that genetic epidemiological studies linking elevated platelet count to "risk of developing lung cancer" cannot be directly interpreted as evidence of a causal relationship between platelet elevation and "VTE risk in patients with lung cancer"; these are distinct research questions and should be distinguished when interpreting and citing the literature.

3.3 Factors Related to Anti-tumor Treatment

Chemotherapy can promote hypercoagulability through vascular endothelial injury, release of inflammatory mediators, platelet activation, and increased tissue factor expression. Platinum-based chemotherapy, particularly cisplatin, has been associated with a higher thrombotic risk [11] [13]. Agents such as gemcitabine have also been reported to increase the risk of venous or arterial thrombotic events [12]. Immune checkpoint inhibitors (ICIs) have become an important treatment option for advanced NSCLC. While activating antitumor immunity, ICIs may also affect inflammation, endothelial function, platelets, and NET formation, thereby theoretically increasing the likelihood of thrombosis [13-15]. Current studies remain heterogeneous as to whether ICIs independently increase VTE risk in lung cancer. The actual risk may be influenced by tumor burden, previous treatment, combination regimens, baseline inflammatory status, and survival duration. Therefore, immunotherapy should not be simplistically regarded as a definite independent high-risk factor; ongoing dynamic assessment is more appropriate. Antiangiogenic agents can disrupt vascular endothelial homeostasis by inhibiting VEGF signaling and may thereby increase both thrombotic and bleeding risks; bevacizumab is among the most extensively studied agents in this regard [16]. Thrombotic events have also been reported with some tyrosine kinase inhibitors, but considerable differences exist among individual agents and molecular subtypes. At present, it is inappropriate to generalize that all EGFR-TKIs significantly increase VTE risk; clinical evaluation should integrate the specific drug, baseline patient risk, and tumor molecular characteristics. Central venous devices such as peripherally inserted central catheters (PICCs) and implantable venous ports can injure the vascular endothelium and cause local flow disturbances and are important risk factors for catheter-related thrombosis. Because patients with advanced lung cancer often require prolonged infusions and multiple treatment cycles, central venous access is common; catheter position, infection, and changes in limb symptoms should therefore be carefully monitored.

4. The Understanding of the Hypercoagulable State in Advanced Lung Cancer by Traditional Chinese Medicine

4.1 Blood Stasis is One of the Main Pathological Mechanisms

Although TCM has no disease name directly equivalent to "hypercoagulability," its etiology, pathogenesis, and clinical characteristics can be understood within categories such as "blood stasis," "phlegm-stasis," and "mass accumulation (Zheng Ji)." Lung cancer is located primarily in the lung but is closely associated with dysfunction of multiple zang-fu organs, including the spleen, kidney, and liver. With prolonged disease, cancer toxin consumes healthy qi, the lung loses its functions of diffusion and descending, qi movement becomes impaired, and the distribution of body fluids is disrupted. Phlegm-dampness, qi stagnation, and blood stasis then become mutually entangled, eventually producing a complex pathogenesis characterized by coexistence of deficiency and excess and the interaction of phlegm, stasis, and toxin [17, 18]. Blood stasis is not the only pathogenesis of advanced lung cancer, but it commonly runs throughout disease progression and comprehensive treatment. Common clinical patterns include qi-deficiency with blood stasis, yin-deficiency with blood stasis, qi-stagnation with blood stasis, and phlegm-stasis binding.

4.2 Deficient Qi Causing Retention and Stagnation" and Hypercoagulability in Lung Cancer

Based on the theory of "deficient qi causing retention and stagnation," hypercoagulability in advanced lung cancer can be further explained as "root deficiency with blood stasis as the manifestation" [19]. The lung governs qi and respiration, and pectoral qi contributes to the propulsion of blood. With a prolonged course of lung cancer or repeated radiotherapy and chemotherapy, deficiency of lung and spleen qi and insufficiency of pectoral qi weaken the driving force of blood circulation, leading to sluggish blood flow and obstruction of the collaterals. Prolonged qi deficiency may further involve deficiency of yin or yang. When both qi and yin are deficient, depletion of yin fluids and inadequate nourishment of the vessels lead to rough and sluggish blood flow; when qi and yang are deficient, weakened warming and propelling functions can also cause cold-induced blood stasis. Meanwhile, deficiency of lung and spleen qi can impair fluid distribution, causing retention of dampness and formation of phlegm. Phlegm obstructs qi movement, qi stagnation further impedes blood circulation, and blood stasis is aggravated, forming a mutually reinforcing pathological chain of "qi deficiency–phlegm obstruction–qi stagnation–blood stasis."

4.3 Association of Blood Stasis Syndrome with D-Dimer and Other Indicators

D-dimer is a degradation product generated after fibrin formation and breakdown and reflects activation of coagulation and secondary fibrinolysis. Zhou et al. [17] reported that D-dimer levels in patients with advanced

NSCLC were associated to some extent with the distribution of blood stasis syndrome and concurrent TCM patterns; accompanying patterns such as qi deficiency, yin deficiency, qi stagnation, phlegm turbidity, and blood heat changed dynamically with disease stage and treatment modality. Other studies have found that patients with lung cancer characterized by qi-deficiency and blood-stasis syndrome may exhibit abnormalities in D-dimer, fibrinogen, and other coagulation indicators, with associations with tumor stage and metastasis [20]. These findings provide a preliminary basis for the objectification of TCM syndrome differentiation. However, D-dimer is highly sensitive but insufficiently specific and may be elevated in malignancy, infection, surgery, and advanced age. Therefore, D-dimer cannot be equated with "blood stasis syndrome" and should not be used alone to determine a TCM pattern; it should instead be interpreted together with clinical syndrome differentiation and modern medical thrombotic-risk assessment. Some studies have also explored the biological basis of blood-stasis constitution or blood-stasis syndrome in lung cancer from the perspective of genetic polymorphisms, including CHRNB4- associated polymorphisms [21], but sample sizes and external replication remain limited, and their clinical significance requires further clarification.

5. Advances in Prevention and Treatment with TCM and Integrated Chinese-Western Medicine

5.1 Blood-Activating and Stasis-Resolving Therapy

Activating blood and resolving stasis is a basic therapeutic principle for blood-stasis syndrome in lung cancer. However, patients with advanced disease commonly present with deficiency of healthy qi together with pathogenic excess; treatment should therefore not focus solely on aggressively removing stasis, but should be flexibly combined according to concurrent patterns such as qi deficiency, yin deficiency, phlegm turbidity, and qi stagnation. Taohong Siwu Decoction is a classic formula used to nourish and activate blood. Yang et al. [22] reported that treatment with Taohong Siwu Decoction improved D-dimer, fibrinogen, platelet aggregation, and some hemorheological parameters in patients with lung cancer, suggesting a potential role in regulating hypercoagulability. Wan et al. [23] also investigated the effects of Taohong Siwu Decoction combined with Wuling San on coagulation and hemorheological indices in patients with NSCLC and reported favorable changes. However, existing studies generally have small sample sizes and vary in design, outcome measures, and background anticancer therapy. These findings therefore do not establish antithrombotic efficacy equivalent to LMWH, and these formulas cannot be considered substitutes for guideline-based anticoagulant therapy.

5.2 Qi-Supplementing and Blood-Activating Therapy

Qi-deficiency with blood stasis is a common pattern combination in advanced lung cancer. In TCM, "qi is the commander of blood," and supplementation of qi is considered to promote blood circulation; accordingly, supplementing qi and activating blood is a representative therapeutic approach for hypercoagulability in advanced lung cancer. Shengmai Yin combined with Xuefu Zhuyu Decoction is intended to supplement qi, nourish yin, activate blood, and resolve stasis. Studies suggest that it may improve D-dimer and other hypercoagulability-related indicators in patients with NSCLC while alleviating symptoms of qi deficiency and blood stasis [24] [35]. A clinical study of Xiaoyan Granules combined with LMWH in patients with advanced NSCLC characterized by qi-deficiency and blood- stasis syndrome suggested that adding TCM to standard anticoagulation may further improve D-dimer, the neutrophil- to-lymphocyte ratio (NLR), related symptoms, and quality of life [25]. This model is more consistent with the current role of integrated Chinese-Western medicine in CAT management than using TCM as a replacement for anticoagulants: the aim is to explore additive efficacy, toxicity reduction, and symptom improvement on the basis of standard modern medical therapy.

5.3 Qi-Regulating / Blood-Activating and Yin-Nourishing / Blood-Activating Therapies

Qi stagnation can impede blood circulation, and patients with advanced lung cancer may develop impaired qi movement because of disease-related stress, chest and hypochondriac discomfort, and emotional changes. Lin et al. [26] used a Shugan Huoxue Formula in patients with advanced NSCLC characterized by qi-stagnation and blood-stasis syndrome and reported improvements in TCM syndrome scores, some coagulation indicators, and emotional status. Treatment modality may also influence the evolution of TCM patterns. Some studies suggest that qi deficiency, yin deficiency, and qi stagnation are more common after chemotherapy, whereas yin deficiency and blood-heat manifestations may become more prominent after targeted therapy [17]. Therefore, depending on the treatment stage and changing pattern presentation, clinical approaches may include supplementing qi and activating blood, regulating qi and activating blood, nourishing yin and activating blood, or cooling blood and activating blood rather than mechanically applying a single blood-activating formula.

5.4 Studies of Other TCM Compound Formulas

Xuefu Zhuyu Decoction, Bufei Huayu Decoction, Yiqi Guben Xiaoai Formula, Yiqi Fuzheng Xiaoji Formula, and Yiqi Kang'ai Huoxue Formula have all been investigated as adjunctive treatments for NSCLC [27-32]. These studies report potential benefits in TCM syndrome scores, immune function, quality of life, and some coagulation indicators. However, evidence for "improving the overall condition of patients with lung cancer" must be distinguished from evidence for "direct prevention or treatment of VTE." In many formula studies, primary outcomes were quality of life, immune parameters, or antitumor efficacy rather than symptomatic VTE incidence, VTE recurrence, or major bleeding; such treatments therefore should not be directly classified as proven antithrombotic therapies. Studies of Siwei Poji Pill, for example, have mainly focused on symptoms, quality of life, or survival benefit during maintenance treatment for advanced NSCLC [33]. Because direct evidence linking this intervention to hypercoagulability is lacking, it is more appropriately regarded as part of comprehensive TCM management of advanced lung cancer rather than as core evidence for CAT prevention or treatment.

5.5 Safety of Integrated Chinese-Western Medicine

Patients with advanced lung cancer often receive anticancer drugs, anticoagulants, and multiple supportive therapies simultaneously. When TCM agents with blood-activating and stasis-resolving properties are combined with LMWH, DOACs, or antiplatelet drugs, there is a theoretical risk of additive bleeding. Clinical monitoring should therefore include mucocutaneous bleeding, gastrointestinal bleeding, hemoglobin and platelet changes, and hepatic and renal function. In particular, for patients with confirmed DVT or PE, TCM should currently be positioned as an adjunct to standard anticoagulant therapy. Anticoagulants should not be reduced or discontinued solely because D-dimer levels decrease or TCM syndrome scores improve. The focus of integrated Chinese-Western medicine research should shift from asking whether TCM can "replace anticoagulants" to determining whether it can further improve hypercoagulability markers, reduce recurrence, relieve symptoms, and improve quality of life when added to standard anticoagulation.

6. Current Problems and Future Perspectives

Important challenges remain in the prevention and treatment of hypercoagulability in advanced lung cancer.

First, disease-specific dynamic prediction models better suited to advanced lung cancer are needed. Current tools such as the Khorana score do not fully capture lung cancer stage, histological subtype, molecular features such as ALK/ROS1 alterations, or contemporary treatment factors such as immunotherapy and targeted therapy. Future models may incorporate D-dimer, thrombin-antithrombin complexes (TAT), prothrombin fragment 1+2 (F1+2), platelet counts, inflammatory markers, and tumor genomic features [34]. Second, the translational clinical value of novel biomarkers should be investigated. CXCL13 and integrin β2-associated extracellular vesicles may help elucidate new mechanisms of lung cancer-associated CAT, but assay standardization and validation in large clinical cohorts are still required. Third, the evidence base for TCM needs to be strengthened. Existing studies commonly have small samples, single-center designs, incompletely standardized syndrome criteria, heterogeneous herbal formulas, and short follow-up. Future research should use rigorous randomized controlled designs and include clinically meaningful endpoints such as symptomatic VTE, VTE recurrence, major bleeding, progression-free survival, overall survival, and quality of life, while establishing systematic evaluation of herb-anticoagulant interactions and safety. In addition, an integrated assessment model combining "modern medical risk stratification + TCM syndrome differentiation" could be explored. For example, after defining tumor stage, molecular features, and VTE risk category, patients could be stratified according to patterns such as qi-deficiency with blood stasis, qi-stagnation with blood stasis, yin-deficiency with blood stasis, or phlegm-stasis binding to improve the precision of TCM interventions. Finally, novel anticoagulant targets deserve attention. Factor XI inhibitors have emerged as an important direction for next-generation anticoagulants because of their potential to preserve antithrombotic efficacy while reducing bleeding risk [35]. Their efficacy and safety in patients with active cancer, particularly advanced lung cancer, require further clinical investigation.

References

[1] BRAY F, LAVERSANNE M, SUNG H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries [J]. CA Cancer J Clin, 2024, 74(3): 229–63.

[2] KHORANA A A, FRANCIS C W, CULAKOVA E, et al. Thromboembolism is a leading cause of death in cancer patients receiving outpatient chemotherapy [J]. J Thromb Haemost, 2007, 5(3): 632–4.

[3] KIM A S, KHORANA A A, MCCRAE K R. Mechanisms and biomarkers of cancer-associated thrombosis [J]. Transl Res, 2020, 225: 33–53.

[4] PELEGRíN-MATEO F J, ZAMBRANO C B, VáZQUEZ E B, et al. Cancer genetic profile and risk of thrombosis [J]. Eur J Intern Med, 2025, 136: 19–26.

[5] SUN H, ZHAI Q, XIN B, et al. Pulmonary origin and risk assessment of cancer-associated thrombosis [J]. Thromb J, 2026, 24(1): 22.

[6] SINGH V, TABASSUM H, KOHLI S, et al. Burden and distribution of venous thromboembolism across cancer types and stages: a meta-analysis of observational studies [J]. Front Oncol, 2025, 15: 1619554.

[7] ZUGAZAGOITIA J, BIOSCA M, OLIVEIRA J, et al. Incidence, predictors and prognostic significance of thromboembolic disease in patients with advanced ALK-rearranged non-small cell lung cancer [J]. Eur Respir J, 2018, 51(5).

[8] CHIARI R, RICCIUTI B, LANDI L, et al. ROS1-rearranged Non-small-cell Lung Cancer is Associated With a High Rate of Venous Thromboembolism: Analysis From a Phase II, Prospective, Multicenter, Two-arms Trial (METROS) [J]. Clin Lung Cancer, 2020, 21(1): 15–20.

[9] APARICIO I, IRANZO P, REYES R, et al. Brief report: High incidence of peridiagnosis thromboembolic events in patients with BRAF-mutant lung cancer [J]. Thromb Res, 2023, 232: 133–7.

[10] PASTORI D, CORMACI V M, MARUCCI S, et al. A Comprehensive Review of Risk Factors for Venous Thromboembolism: From Epidemiology to Pathophysiology [J]. Int J Mol Sci, 2023, 24(4).

[11] MOORE R A, ADEL N, RIEDEL E, et al. High incidence of thromboembolic events in patients treated with cisplatin-based chemotherapy: a large retrospective analysis [J]. J Clin Oncol, 2011, 29(25): 3466–73.

[12] QI W X, LIN F, SUN Y J, et al. Risk of venous and arterial thromboembolic events in cancer patients treated with gemcitabine: a systematic review and meta-analysis [J]. Br J Clin Pharmacol, 2013, 76(3): 338–47.

[13] CHARPIDOU A, GEROTZIAFAS G, POPAT S, et al. Lung Cancer Related Thrombosis (LCART): Focus on Immune Checkpoint Blockade [J]. Cancers (Basel), 2024, 16(2).

[14] MOIK F, CHAN W E, WIEDEMANN S, et al. Incidence, risk factors, and outcomes of venous and arterial thromboembolism in immune checkpoint inhibitor therapy [J]. Blood, 2021, 137(12): 1669–78.

[15] SUSSMAN T A, GIOBBIE-HURDER A, DRYG I D, et al. Immune checkpoint inhibitor-associated risk for

venous thromboembolism: a comprehensive analysis [J]. J Immunother Cancer, 2025, 13(5).
[16] NALLURI S R, CHU D, KERESZTES R, et al. Risk of venous thromboembolism with the angiogenesis inhibitor bevacizumab in cancer patients: a meta-analysis [J]. Jama, 2008, 300(19): 2277–85.
[17] Zhou Heran, Huang Ting, Yang Xuefei, et al. Correlation between D-dimer Level and Distribution Patterns of Blood Stasis Syndrome and Its Subtypes in Patients with Advanced Non-Small Cell Lung Cancer [J]. Chinese Journal of Traditional Medical Science and Technology, 2024, 31(2): 191–5+9.
[18] Liu Dianlong, Hou Wei. Discussion on mechanism of syndrome differentiation and treatment of lung cancer from phlegm and stasis [J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2020, 35(2): 783–5.
[19] He Jiawen, Han Bing, Lu Jiaxuan, et al. Discussion on the pathogenesis and treatment of the hypercoagulable state of lung cancer based on the theory of "deficient qi leading to stasis" [J]. Journal of Beijing University of Traditional Chinese Medicine, 2023, 46(12): 1767–71.
[20] Li Xiaojuan, Chen Binhai, Yang Xuejing, et al. Clinical study of lung cancer with qi deficiency and blood stasis syndrome: Toxin-stasis pathogenesis [J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2019, 34(2): 773–7.
[21] Han Zhiqiang, Deng Dehou, Feng Yunhui, et al. Study on Correlation between Polymorphism of CHRNB4 rs7178270 and Blood Stasis Patients with Lung Cancer [J]. Chinese Archives of Traditional Chinese Medicine, 2020, 38(6): 90–3+269.
[22] Yang Changqing, Xu Ya, Jiang Li, et al. Study on Effect of Taohong Siwu Decoction on Hypercoagulable State of Blood in Patients with Lung Cancer [J]. Acta Chinese Medicine, 2017, 32(7): 1154–6.
[23] Wan Xiaoyan, Qi Xiaoxia. The effect of Taohong Siwu Tang combined with Wuling San on coagulation status and hemorheology in non-small cell lung cancer [J]. Guiding Journal of Traditional Chinese Medicine and Pharmacy, 2018, 24(5): 81–3+7.
[24] Zhang Yile, Chen Qi, Zhang Wei. A prospective, parallel, random, placebo-controlled clinical study on effects of Fuzheng Kangyan Formula combined with gefitinib on non- small cell lung cancer (stage IV) of qi deficiency and blood stasis type [J]. Shanghai Journal of Traditional Chinese Medicine, 2019, 53(3): 37–41.
[25] Du Mengnan, Zhang Ying, Yi Dan, et al. Clinical observation of Xiaoyan Particle combined with low-molecular-weight heparin sodium on the hyper-coagulable state of qi deficiency and blood stasis type in advanced non-small-cell lung cancer patients [J]. Tianjin Journal of Traditional Chinese Medicine, 2021, 38(8): 1004–8.
[26] Lin Shaozhen, Hong Chaozhang, Qiu Yuanliang, et al. Soothing the Liver and Promoting Blood Circulation Prescription in the Treatment of Advanced NSCLC with Qi Stagnation and Blood Stasis Syndrome [J]. Chinese Medicine Modern Distance Education of China, 2025, 23(8): 131–4.
[27] Wang Ting, Lv Yubao, Wang Xuan, et al. Research progress on Xuefu Zhuyu Decoction in treatment of lung cancer: from clinical application to mechanism exploration [J]. Shanghai Journal of Traditional Chinese Medicine, 2026, 60(3): 19–27.
[28] Li Yan, Liu Huaimin, Jiang Lifeng, et al. Effect of Xuefu Zhuyu Decoction on quality of life in patients with hypercoagulable state with deficiency of blood and blood stasis type of non-small cell lung cancer [J]. Journal Of Community Medicine, 2018, 16(10): 47–8.
[29] Wang Fang, Yang Xingyuan, Sun Cong, et al. Clinical Characteristics of Stasis-Toxin Pathogenesis in Patients with NonsmallCell Lung Cancer of Blood Stasis and Qi Stagnation Syndrome and theInterventional Mechanism of Adjuvant Therapy with Bufei Huayu Decoction [J]. Journal of Guangzhou University of Traditional Chinese Medicine, 2024, 41(1): 68–77.
[30] Wang Dong, Li Jun, Yu Zhipeng, et al. Yiqi Guben Xiaoai Decoction combined with Chemotherapy in the Treatment of Elderly Patients with Non-small Cell Lung Cancer (Qi deficiency and blood stasis) Randomized Parallel Control Study [J]. Journal of Practical Traditional Chinese Internal Medicine, 2019, 33(1): 53–6.
[31] Guo Guanghui, Zheng Lan, Yang Junshu, et al. Influence of supplementing chemotherapy with Yiqi Fuzheng Xiaoji Formula on the quality of life and side effects in advanced lung cancer patients with syndrome of qi stagnation and blood stasis [J]. China Medical Herald, 2023, 20(10): 109–12+21.
[32] Liu Feng, Wang Kan, Zhou Wei. Clinical Efficacy of Yiqi Kangai Huoxue FormulaCombined with Concurrent Radiochemotherapyin Treatment of Non-Small Cell Lung Cancer Patients with Qi Deficiency and Blood Stasis [J]. World Journal of Integrated Traditional and Western Medicine, 2022, 17(6): 1242–6.
[33] Wang Jiafeng, Jiang Xiaofeng, Hao Jianjun, et al. Observation on the efficacy of Siwei Poji Pills third-line therapy in patients with stageIIII B/IV non-small cell lung cancer of qi stagnation and blood stasis type [J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2025, 40(10): 5094–7.
[34] MUñOZ A, AY C, GRILZ E, et al. A Clinical-Genetic Risk Score for Predicting Cancer-Associated Venous Thromboembolism: A Development and Validation Study Involving Two Independent Prospective Cohorts [J]. J Clin Oncol, 2023, 41(16): 2911–25.
[35] POENOU G, HEESTERMANS M, LAFAIE L, et al. Inhibition of Factor XI: A New Era in the Treatment of Venous Thromboembolism in Cancer Patients? [J]. Int J Mol Sci, 2023, 24(19).