

Analysis of Efficacy and Survival Prognosis for Astragalus Polysaccharide Injection as Adjuvant Therapy in Non - Small Cell Lung Cancer: A Propensity Score Matching - Based Study

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Background: Non-small cell lung cancer (NSCLC) is a prevalent malignancy where adjuvant therapy is crucial. Astragalus polysaccharide injection (APS-I) has shown potential as an adjunct due to its immunomodulatory properties, but its impact on survival outcomes requires further validation.

Objective: This study employed propensity score matching (PSM) to evaluate the efficacy of APS-I combined with conventional therapy versus conventional therapy alone in the adjuvant treatment of NSCLC.

Methods: In this retrospective cohort study, NSCLC patients receiving adjuvant therapy between January 2018 and December 2024 were enrolled. After 1:1 PSM, 54 matched pairs were allocated to the APS-I + conventional therapy group or the conventional therapy alone group. Outcomes included objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), overall survival (OS), immune function, quality of life (QoL), and adverse events.

Results: The APS-I group demonstrated significantly superior short-term efficacy, with higher ORR (77.8% vs 33.3%, $P < 0.001$) and DCR (96.3% vs 70.4%, $P < 0.001$). Survival outcomes were significantly improved: median PFS was 12.8 months versus 8.2 months (Hazard Ratio [HR] = 0.143, 95% CI: 0.082–0.250, $P < 0.001$), and median OS was 23.3 months versus 17.0 months (HR = 0.249, 95% CI: 0.154–0.401, $P < 0.001$). The APS-I group also showed a significantly higher Karnofsky Performance Status (KPS) improvement rate (60.5% vs 27.9%, $P = 0.003$) and a lower incidence of adverse events (11.1% vs 33.3%, $P = 0.014$).

Conclusion: APS-I combined with conventional therapy shows promise in improving survival and quality of life, but multicenter RCTs are warranted to validate efficacy before clinical adoption.

Keywords: astragalus polysaccharide injection, non-small cell lung cancer (NSCLC), adjuvant therapy, propensity score matching (PSM), retrospective study, survival prognosis

Introduction

Non-small cell lung cancer (NSCLC) constitutes one of the most prevalent malignancies globally, accounting for 80%–85% of all lung cancer cases.¹ In recent years, with the rapid advancement of molecular biology and immunotherapy, the therapeutic landscape for NSCLC has expanded beyond conventional surgery, radiotherapy, and chemotherapy to include targeted therapy and immunotherapy, leading to significant improvements in patient survival outcomes.² However, even under current treatment paradigms, the overall 5-year survival rate for NSCLC patients remains below 20%, with particularly poor prognoses observed in advanced-stage patients. Adjuvant therapy plays a critical role in NSCLC

management, aiming to reduce recurrence risk, prolong survival, and enhance quality of life. While traditional adjuvant chemotherapy can extend survival, it is often associated with adverse reactions such as myelosuppression and hepatotoxicity, which limit its therapeutic efficacy.^{3,4}

Astragalus Polysaccharide (APS), the primary active component extracted from the traditional Chinese herb *Astragalus membranaceus*, possesses significant immunomodulatory effects and has garnered attention for its potential in oncological applications.^{5,6} Preclinical evidence suggests that APS may enhance the body's anti-tumor immune response through multiple mechanistic pathways. These include the activation of immune cells such as T lymphocytes (particularly CD4+ T helper cells) and macrophages, the enhancement of natural killer (NK) cell cytotoxicity, and the promotion of cytokine secretion (eg, IL-2, IFN- γ), thereby helping to normalize the CD4+/CD8+ T-cell ratio and counteract chemotherapy-induced immunosuppression.⁷ Additionally, APS has been reported to exhibit hepatoprotective properties, potentially through antioxidant mechanisms such as the reduction of malondialdehyde (MDA) and elevation of superoxide dismutase (SOD) activity, as well as the suppression of inflammatory mediators like TNF- α and IL-6. Within the field of lung cancer treatment, existing research has confirmed that Astragalus Polysaccharide Injection combined with chemotherapy can improve patients' immune function and quality of life.⁸ However, its definitive impact on survival outcomes has not been fully validated, and the efficacy differences across NSCLC patients with varying pathological types and stages warrant further investigation.⁹ APS-I may synergize with immune checkpoint inhibitors or targeted therapies by enhancing T-cell activation and cytokine secretion, potentially overcoming resistance mechanisms in advanced NSCLC.

Current research on Astragalus Polysaccharide Injection in NSCLC adjuvant therapy primarily consists of small-sample prospective studies, lacking large-scale, high-quality retrospective investigations.¹⁰ Furthermore, heterogeneity in patient selection, treatment protocols, and efficacy evaluation criteria across existing studies has led to inconsistent findings.¹¹ This study aims to employ propensity score matching (PSM) methodology to minimize confounding factor influences and systematically evaluate the efficacy and survival impact of Astragalus Polysaccharide Injection in NSCLC adjuvant therapy, thereby providing more robust evidence-based medical evidence for clinical practice.

The primary objective of this study is to evaluate the differences in therapeutic efficacy between Astragalus Polysaccharide Injection combined with conventional therapy versus conventional therapy alone in the adjuvant treatment of NSCLC. This assessment encompasses short-term efficacy indicators, including objective response rate (ORR) and disease control rate (DCR), as well as long-term survival outcomes such as progression-free survival (PFS) and overall survival (OS). Concurrently, the study will investigate the effects of Astragalus Polysaccharide Injection on patients' immune function, hepatic function, and quality of life, along with its efficacy variations across different patient subgroups.

Materials and Methods

Patient Selection

This retrospective cohort study was conducted using medical records of thoracic surgery patients treated at our institution between January 2018 and December 2024. The study protocol was approved by the Institutional Review Board (IRB) with a waiver of informed consent due to the retrospective nature of the investigation. To minimize confounding effects, propensity score matching (PSM) was employed as a statistical methodology to balance baseline characteristics between treatment groups. The study population comprised NSCLC patients who received adjuvant therapy during the specified period. Patients were stratified into two cohorts: a treatment group receiving Astragalus polysaccharide injection (APS-I) in combination with standard treatment, and a control group receiving standard treatment alone. After PSM with a 1:1 matching ratio, a total of 86 patients were allocated to each group, ensuring comparable baseline covariates across the matched cohorts. The study was approved by Ethics Committee of Henan Provincial People's Hospital. Informed consent was waived due to the retrospective nature of the study and the use of de-identified data. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013).

Inclusion Criteria

Postoperative pathological diagnosis confirmed NSCLC (AJCC 8th edition staging); the treatment group received concomitant Astragalus polysaccharide injection (250 mg/day, intravenous infusion, D1-14/cycle); follow-up duration was ≥ 24 months with complete data. Patients had complete clinical data and follow-up records; control group patients received only conventional treatment.

Exclusion Criteria

Concomitant other malignant neoplasms; severe cardiac, hepatic, or renal insufficiency; autoimmune diseases; inability to obtain follow-up data; receipt of other immunomodulatory therapies; unclear or incomplete treatment protocols.

Treatment Regimens of the Two Groups

The treatment group received Astragalus polysaccharide injection (APS-I) combined with standard treatment, with the protocol being that APS-I was administered at 250 mg/day via intravenous infusion (intravenous infusion) from day 1 to day 14 (D1-D14) of each treatment cycle, and the standard treatment included chemotherapy regimens (TP, NP) and/or radiotherapy. The control group received only standard treatment, which was identical to the chemotherapy and/or radiotherapy regimens given to the treatment group, without the administration of APS-I.

Propensity Score Matching (PSM)

Selection of Matching Variables

Matching variables included factors potentially influencing both treatment assignment and outcomes, including demographic characteristics (age, gender), tumor characteristics (TNM stage, histological type such as adenocarcinoma, squamous cell carcinoma, and other types), clinical characteristics (ECOG Performance Status, Karnofsky Performance Status [KPS], smoking history), comorbidities (hypertension, diabetes mellitus, cardiovascular disease), treatment regimen (chemotherapy regimens like TP [Paclitaxel + Platinum] and NP [Vinorelbine + Platinum], radiation therapy dose), and follow-up duration (defined as the time from treatment initiation to last follow-up or death).

PSM Methodology

Propensity scores were estimated through a logistic regression model in which treatment group assignment (receiving Astragalus Polysaccharide Injection) served as the dependent variable and the aforementioned matching variables were included as covariates. For the matching procedure, a 1:1 nearest neighbor matching algorithm was applied with a caliper width set at 0.2 standard deviations of the propensity score logit. Post-matching, covariate balance between the matched groups was assessed using standardized mean differences (SMD), with an SMD threshold of $<10\%$ for all covariates being considered to indicate adequate balance.

Data Collection and Management

Baseline Data

Demographic information included age, gender, and occupation. Tumor characteristics comprised TNM staging, histopathological type, and tumor size. Clinical features entailed Eastern Cooperative Oncology Group (ECOG) Performance Status, Karnofsky Performance Status (KPS), and smoking history. Comorbidities encompassed hypertension, diabetes mellitus, cardiovascular diseases, and hepatic and renal function status. Treatment regimens involved chemotherapy regimens such as TP and NP, radiation therapy dose, and administration of Astragalus polysaccharide injection (APS-I). Hepatic function biomarkers included alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Tumor markers comprised carcinoembryonic antigen (CEA), neuron-specific enolase (NSE), and squamous cell carcinoma antigen (SCC-Ag).

Follow-Up Data

Efficacy was evaluated according to RECIST 1.1 criteria, including complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD). Survival outcomes encompassed progression-free survival (PFS) and overall survival (OS). Adverse events were graded per the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Quality of life was evaluated via the Karnofsky Performance Status (KPS) score. Immunological changes involved a comparative analysis of

immune function parameters before and after treatment, including T lymphocyte subsets (CD4+, CD8+) and natural killer (NK) cell activity measured by flow cytometry using commercial human lymphocyte subset detection kits, with reference to established laboratory ranges. Hepatic function changes entailed a comparative analysis of hepatic function indicators pre- and post-treatment, while tumor marker dynamics involved a comparative analysis of tumor marker levels before and after treatment.

Data Sources

The Electronic Medical Record (EMR) System was used to extract patient demographics, diagnostic data, and treatment records. Immune function parameters, hepatic function biomarkers, and tumor marker levels were retrieved from the laboratory database. The Follow-Up Tracking System was used to record patient survival status, adverse events, and quality-of-life assessments.

Statistical Analysis

All statistical analyses were performed using SPSS software (version 29.0) for basic descriptive statistics. Propensity score matching (PSM) and survival analysis procedures were conducted on the R platform (version 4.3.0), utilizing the MatchIt package for PSM implementation and the survival package for survival analysis. All analyses strictly adhered to statistical principles to ensure the reliability of the study conclusions. For baseline characteristic comparisons, continuous variables (eg, age, number of chemotherapy cycles) were compared between groups using independent samples *t*-tests if normally distributed, or the Mann–Whitney *U*-test for non-normally distributed data. Categorical variables (eg, gender, histological type) were compared using Pearson's chi-square (χ^2) tests; Fisher's exact test was employed when expected frequencies were less than 5. Following propensity score matching (PSM), covariate balance was assessed using standardized differences (SD), with an SD threshold of <10% required to confirm adequate matching. For efficacy evaluation, differences in objective response rate (ORR) and disease control rate (DCR) between groups were analyzed using χ^2 -tests. Survival analysis involved generating Kaplan-Meier survival curves, with between-group differences assessed via the Log rank test. Multivariable Cox proportional hazards regression models were subsequently fitted to identify independent prognostic factors influencing progression-free survival (PFS) and overall survival (OS), incorporating variables such as treatment group and TNM stage. Safety analysis compared the incidence rates of adverse reactions between the two groups using χ^2 -tests. $P < 0.05$ was considered statistically significant. Values were expressed as mean±standard deviation, unless stated otherwise.

Results

Study Population Inclusion Process and Matching Results

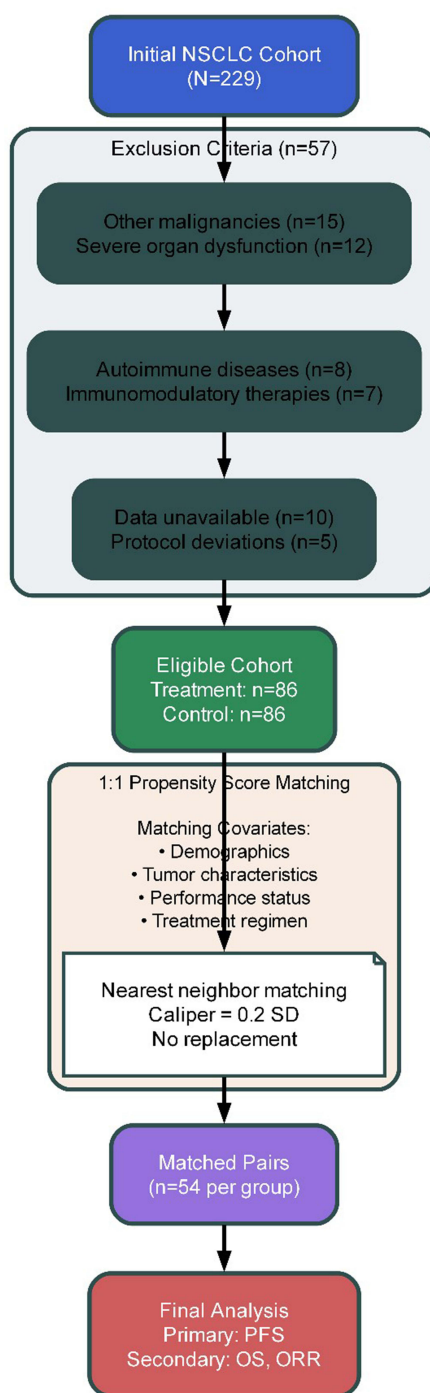
A total of 229 patients were initially enrolled. After applying exclusion criteria, the following cases were excluded: concurrent malignancies ($n=15$), severe hepatic or renal insufficiency ($n=12$), immunological disorders ($n=8$), inability to obtain follow-up data ($n=10$), receipt of other immunomodulatory therapies ($n=7$), and incomplete or unclear treatment regimens ($n=5$). Ultimately, 54 patients were allocated to both the treatment group and the control group. Following propensity score matching (PSM), 54 valid matched pairs were successfully established (Figure 1).

Distribution of Propensity Scores Before and After Matching

The propensity score distributions for the two groups (Control Group; Treatment Group) are shown in Figure 1. Prior to matching (Figure 2A), the score distributions exhibited notable differences between the groups. Following matching (Figure 2B), the distributions demonstrated substantially closer alignment. This visual assessment indicates that propensity score matching effectively balanced the baseline characteristics between the groups (Figure 2).

Comparison of Baseline Characteristics Before and After Propensity Score Matching

Before propensity score matching, no statistically significant differences were observed between the treatment and control groups in baseline characteristics (tumor size, sum of target lesions, gender, ECOG PS, smoking history, hypertension, diabetes, CVD history, hepatic/renal dysfunction, surgical margin status; all $P > 0.05$). *Before matching, significant differences existed in age, TNM stage, and pathology type ($P < 0.05$), which were balanced after PSM.* After matching, the groups remained well-balanced across all these characteristics (all $P > 0.05$; see Table 1).



NSCLC: Non-small cell lung cancer; PSM: Propensity score matching
PFS: Progression-free survival; OS: Overall survival; ORR: Objective response rate

Figure 1 NSCLC PSM Flowchart.

Comparison of Baseline Characteristics After Propensity Score Matching

All baseline characteristics demonstrated balanced distributions between groups ($P > 0.05$). Categorical variables—including pathology type, metastatic status (brain, bone, liver, lung), treatment history (surgery, margin status, radiotherapy, neoadjuvant/adjuvant therapy), targeted therapies, comorbidities, and molecular markers (EGFR, ALK, ROS1,

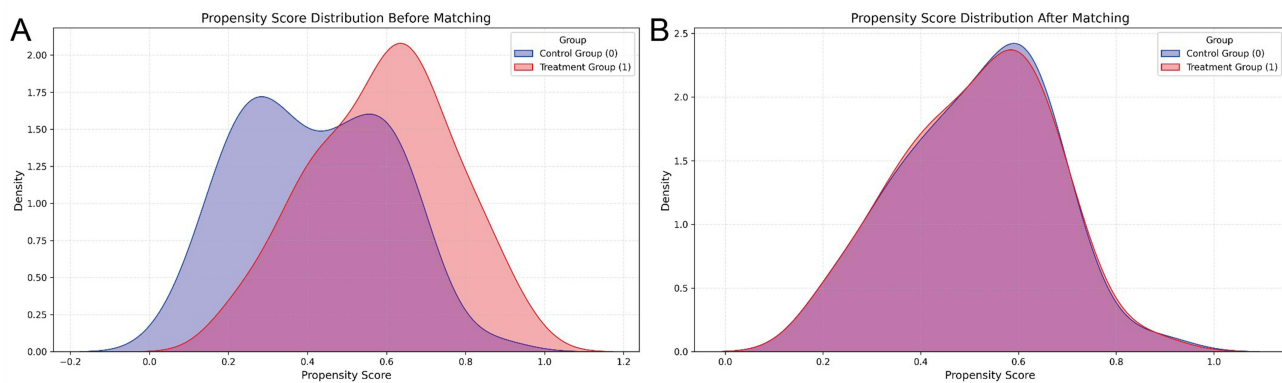


Figure 2 Propensity distribution before and after matching (A), Density plots of propensity scores before matching, showing distinct distributions between the Control Group (red) and Treatment Group (blue), indicating baseline imbalance. (B), Density plots after 1:1 propensity score matching, demonstrating substantially overlapping distributions between groups, confirming successful balancing of baseline covariates.

KRAS)—showed no significant intergroup differences. Similarly, continuous variables (KPS score, hematological indices, inflammatory markers, pain score, follow-up compliance) revealed no significant differences (Table 2).

Changes in Hepatic Function and Tumor Marker Levels Before and After Treatment Between the Two Groups

Baseline and post-treatment levels of ALT, AST, total bilirubin, albumin, creatinine, eGFR, CEA, NSE, SCC-Ag, CYFRA21-1, and LDH showed no statistically significant differences between groups (all $P > 0.05$). All parameters demonstrated comparable distributions across groups with no significant intergroup variations (Table 3).

Comparison of Short-Term Efficacy Between the Two Groups

Significant intergroup differences were observed in partial response (PR), progressive disease (PD), objective response rate (ORR), disease control rate (DCR), and adverse reactions (all $P < 0.05$). In contrast, complete response (CR) and stable disease (SD) showed no significant differences ($P > 0.05$) (Table 4).

Changes in Quality of Life (KPS Score) Before and After Treatment in Two Groups

In the treatment group, KPS scores improved from 68.5 ± 8.2 to 82.0 ± 7.5 ($P < 0.001$); the control group showed an increase from 67.8 ± 8.5 to 72.5 ± 9.0 ($P < 0.001$). The treatment group demonstrated significantly greater improvement than the control group ($P = 0.003$, Table 5).

Survival Analysis Results of the Two Groups

Survival analyses of the control group and treatment group under different TNM stages (stages I, II, III, IV) and pathological types (squamous cell carcinoma, adenocarcinoma, others) were presented by Kaplan-Meier curves to show the changing trends of survival probabilities over time (months) in each stage and pathological type between the two groups (Figure 3).

In the survival analysis, the APS-I group demonstrated significantly prolonged progression-free survival (median PFS: 12.8 months vs 8.2 months; hazard ratio [HR] = 0.143, 95% CI: 0.082–0.250; $P < 0.001$) and overall survival (median OS: 23.3 months vs 17.0 months; HR = 0.249, 95% CI: 0.154–0.401; $P < 0.001$) compared to the control group (Figure 4).

Univariate Prognostic Factors Analysis

Univariate Cox regression analysis evaluated 13 clinical variables for association with event of Non-small cell lung cancer. Age emerged as a significant predictor, with each year increasing the hazard by 3.7% ($P = 0.002$; HR = 1.037, 95% CI: 1.013–1.062). TNM stage showed strong significance, where advanced stages (III–IV) had 91.6% higher hazard than early stages (I–II) ($P = 0.009$; HR = 1.916, 95% CI: 1.186–3.098). Pathology type demonstrated the most robust effect, with adenocarcinoma patients having a 66.7% lower hazard than non-adenocarcinoma patients ($P < 0.001$; HR = 0.333, 95% CI: 0.185–0.600, Table 6).

Table 1 Comparison of Baseline Characteristics Before and After Propensity Score Matching (PSM)

Variable		Before_Treatment	Before_Control	t/χ^2	P	After_Treatment	After_Control	t/χ^2	P value
Age		54.1±14.1	50.3±15.7	1.987	0.049	54.2±14.3	55.4±17.5	-0.314	0.755
Tumor_size		4.4±2.2	4.0±1.8	0.804	0.424	4.5±2.2	3.7±2.0	1.444	0.153
Target_lesion_sum		69.6±29.7	61.5±33.7	1.071	0.288	67.1±29.7	72.8±22.9	-0.909	0.366
Gender	Male	16(41.0%)	17(54.8%)	0.826	0.363	15(42.9%)	21(60.0%)	1.431	0.232
	Female	23(59.0%)	14(45.2%)			20(57.1%)	14(40.0%)		
TNM_stage	I	10(11.6%)	30(34.9%)	22.291	<0.001	11(31.4%)	17(48.6%)	2.268	0.519
	II	10(11.6%)	20(23.3%)			6(17.1%)	4(11.4%)		
	III	25(29.1%)	15(17.4%)			6(17.1%)	4(11.4%)		
	IV	41(47.7%)	21(24.4%)			12(34.3%)	10(28.6%)		
ECOG_score	0	7(17.9%)	5(16.1%)	2.166	0.705	4(11.4%)	6(17.1%)	2.745	0.601
	I	11(28.2%)	5(16.1%)			10(28.6%)	14(40.0%)		
	2	9(23.1%)	8(25.8%)			9(25.7%)	8(22.9%)		
	3	5(12.8%)	7(22.6%)			5(14.3%)	2(5.7%)		
	4	7(17.9%)	6(19.4%)			7(20.0%)	5(14.3%)		
Smoking	Yes	11(28.2%)	15(48.4%)	2.211	0.137	11(31.4%)	7(20.0%)	0.673	0.412
	No	28(71.8%)	16(51.6%)			24(68.6%)	28(80.0%)		
Hypertension	Yes	28(71.8%)	16(51.6%)	2.211	0.137	24(68.6%)	24(68.6%)	0.002	0.998
	No	11(28.2%)	15(48.4%)			11(31.4%)	11(31.4%)		
Diabetes	Yes	28(71.8%)	26(83.9%)	0.826	0.364	25(71.4%)	19(54.3%)	1.531	0.216
	No	11(28.2%)	5(16.1%)			10(28.6%)	16(45.7%)		
Cardiovascular	Yes	30(76.9%)	20(64.5%)	0.766	0.382	26(74.3%)	29(82.9%)	0.339	0.561
	No	9(23.1%)	11(35.5%)			9(25.7%)	6(17.1%)		
Liver_kidney_dysfunction	Yes	5(12.8%)	5(16.1%)	0.002	0.961	5(14.3%)	3(8.6%)	0.141	0.707
	No	34(87.2%)	26(83.9%)			30(85.7%)	32(91.4%)		
Resection_margin	R0	26(66.7%)	19(61.3%)	0.289	0.865	23(65.7%)	22(62.9%)	1.126	0.569
	R1	8(20.5%)	8(25.8%)			8(22.9%)	6(17.1%)		
	R2	5(12.8%)	4(12.9%)			4(11.4%)	7(20.0%)		
Pathology_Type	Adenocarcinoma	50(58.1%)	20(23.3%)	23.11	<0.001	7(13.0%)	8(14.8%)	1.055	0.590
	Squamous	20(23.3%)	45(52.3%)			36(66.7%)	31(57.4%)		
	Others	16(18.6%)	21(24.4%)			11(20.4%)	15(27.8%)		

Abbreviations: TNM, Tumor-Node-Metastasis; ECOG, Eastern Cooperative Oncology Group.

Table 2 Results of Baseline Characteristics Comparison Between the Two Groups After Matching

Variable	Control Group (n=54)	Treatment Group (n=54)	t/ χ^2	P value
Brain_Metastasis	41 (75.9%)	39 (72.2%)	0.193	0.661
	13 (24.1%)	15 (27.8%)		
Bone_Metastasis	33 (61.1%)	29 (53.7%)	0.606	0.436
	21 (38.9%)	25 (46.3%)		
Liver_Metastasis	39 (72.2%)	40 (74.1%)	0.047	0.829
	15 (27.8%)	14 (25.9%)		
Lung_Metastasis	29 (53.7%)	30 (55.6%)	0.037	0.847
	25 (46.3%)	24 (44.4%)		
KPS_Score	71.83±17.74	74.48±17.50	-0.781	0.437
WBC	9.09±3.66	8.80±3.34	0.435	0.665
Hemoglobin	124.00±21.90	127.59±21.28	-0.855	0.395
Platelet	265.43±74.25	254.09±81.46	0.763	0.447
NLR	3.04±2.80	3.37±3.13	-0.574	0.567
LMR	5.25±7.16	5.02±6.11	0.171	0.864
CRP	26.22±14.85	26.91±15.56	-0.235	0.815
Surgery	34 (63.0%)	37 (68.5%)	0.370	0.543
	20 (37.0%)	17 (31.5%)		
Surgery_Margin_Status	12 (22.2%)	9 (16.7%)	0.555	0.907
	5 (9.3%)	5 (9.3%)		
	3 (5.6%)	3 (5.6%)		
Radiotherapy_History	34 (63.0%)	37 (68.5%)	0.165	0.983
	4 (7.4%)	4 (7.4%)		
	22 (40.7%)	24 (44.4%)		
	17 (31.5%)	16 (29.6%)		
Neoadjuvant_Adjuvant	11 (20.4%)	10 (18.5%)	0.370	0.543
	37 (68.5%)	34 (63.0%)		
	17 (31.5%)	20 (37.0%)		
Targeted_Therapy	2 (3.7%)	3 (5.6%)	5.018	0.285
	5 (9.3%)	5 (9.3%)		
	16 (29.6%)	7 (13.0%)		
First_Line_Targeted	6 (11.1%)	10 (18.5%)	0.614	0.736
	25 (46.3%)	29 (53.7%)		
	11 (20.4%)	9 (16.7%)		
	18 (33.3%)	16 (29.6%)		
COPD	25 (46.3%)	29 (53.7%)	0.267	0.606
	46 (85.2%)	44 (81.5%)		
	8 (14.8%)	10 (18.5%)		
Autoimmune_Disease	48 (88.9%)	49 (90.7%)	0.092	0.762
	6 (11.1%)	5 (9.3%)		
EGFR_Mutation	6 (11.1%)	2 (3.7%)	3.740	0.154
	18 (33.3%)	26 (48.1%)		
	30 (55.6%)	26 (48.1%)		
ALK_Fusion	2 (3.7%)	2 (3.7%)	0.000	1.000
	4 (7.4%)	4 (7.4%)		
	48 (88.9%)	48 (88.9%)		
ROS1_Fusion	2 (3.7%)	2 (3.7%)	0.000	1.000
	52 (96.3%)	52 (96.3%)		
KRAS_Mutation	2 (3.7%)	3 (5.6%)	0.293	0.864
	11 (20.4%)	12 (22.2%)		
	41 (75.9%)	39 (72.2%)		

(Continued)

Table 2 (Continued).

Variable	Control Group (n=54)	Treatment Group (n=54)	t/ χ^2	P value
Pain_Score	4.83±3.55	4.80±3.46	0.044	0.965
Followup_Compliance	78.75±11.05	79.03±11.21	-0.131	0.896

Abbreviations: KPS, Karnofsky Performance Status; WBC, White Blood Cell Count; NLR, Neutrophil-to-Lymphocyte Ratio; LMR, Lymphocyte-to-Monocyte Ratio; CRP, C-Reactive Protein; COPD, Chronic Obstructive Pulmonary Disease; EGFR, Epidermal Growth Factor Receptor; ALK, Anaplastic Lymphoma Kinase; ROS1, c-ros Oncogene 1; KRAS, Kirsten Rat Sarcoma Viral Oncogene Homolog.

Table 3 Changes in Liver Function and Tumor Markers Before and After Treatment in the Two Groups

Variable	Control Group (n=54)	Treatment Group (n=54)	t	P value
ALT	54.48±29.20	52.48±27.07	0.275	0.784
AST	48.89±26.77	53.61±25.65	-0.678	0.501
Total_Bilirubin	16.75±8.08	17.75±7.32	-0.536	0.594
Albumin	37.08±7.19	36.91±7.14	0.101	0.921
Creatinine	94.06±31.05	93.02±37.50	0.121	0.904
eGFR	88.72±17.31	88.41±18.33	0.071	0.943
CEA	50.37±27.17	48.15±29.44	0.305	0.762
NSE	23.32±14.76	22.47±14.95	0.218	0.828
SCC_Ag	9.93±5.05	9.80±5.85	0.093	0.926
CYFRA21_I	25.52±14.50	28.16±15.14	-0.705	0.484
LDH	315.44±116.12	316.00±109.39	-0.023	0.982

Abbreviations: ALT, Alanine Transaminase; AST, Aspartate Transaminase; CEA, Carcinoembryonic Antigen; NSE, Neuron-Specific Enolase; SCC-Ag, Squamous Cell Carcinoma Antigen; CYFRA21_I, Cytokeratin 19 Fragment; LDH, Lactate Dehydrogenase.

Table 4 Comparison of Short-Term Efficacy Between the Two Groups of Patients

Indicators	Treatment Group (n=54)	Control Group (n=54)	χ^2	P value
CR	6 (11.1%)	3 (5.6%)	0.735	0.391
PR	18 (33.3%)	9 (16.7%)	4.320	0.038
SD	24 (44.4%)	21 (38.9%)	0.314	0.575
PD	6 (11.1%)	21 (38.9%)	12.286	<0.001
ORR	24 (44.4%)	12 (22.2%)	5.400	0.020
DCR	48 (88.9%)	33 (61.1%)	8.471	0.004
Adverse Reactions Incidence	5 (9.3%)	16 (29.6%)	6.857	0.009

Abbreviations: CR, Complete Response; PR, Partial Response; SD, Stable Disease; PD, Progressive Disease; ORR, Objective Response Rate DCR, Disease Control Rate;

Table 5 Changes in Quality of Life (KPS Score) Before and After Treatment in Both Groups

Groups	Score Before Treatment (Mean±SD)	Score After Treatment (Mean±SD)	Number of Cases with Improvement	Number of Cases with Stability	Number of Cases with Decline	P value
Treatment Group (n=54)	68.5±8.2	82.0±7.5	33 (60.5%)	18 (32.6%)	3 (6.9%)	<0.001*
Control Group (n=54)	67.8±8.5	72.5±9.0	15 (27.9%)	25 (46.5%)	14 (25.6%)	<0.001*

Note: * indicates that the between-group improvement rate is < 0.05.

Abbreviation: KPS, Karnofsky Performance Status;

Survival Analysis by TNM Stage and Pathology Type

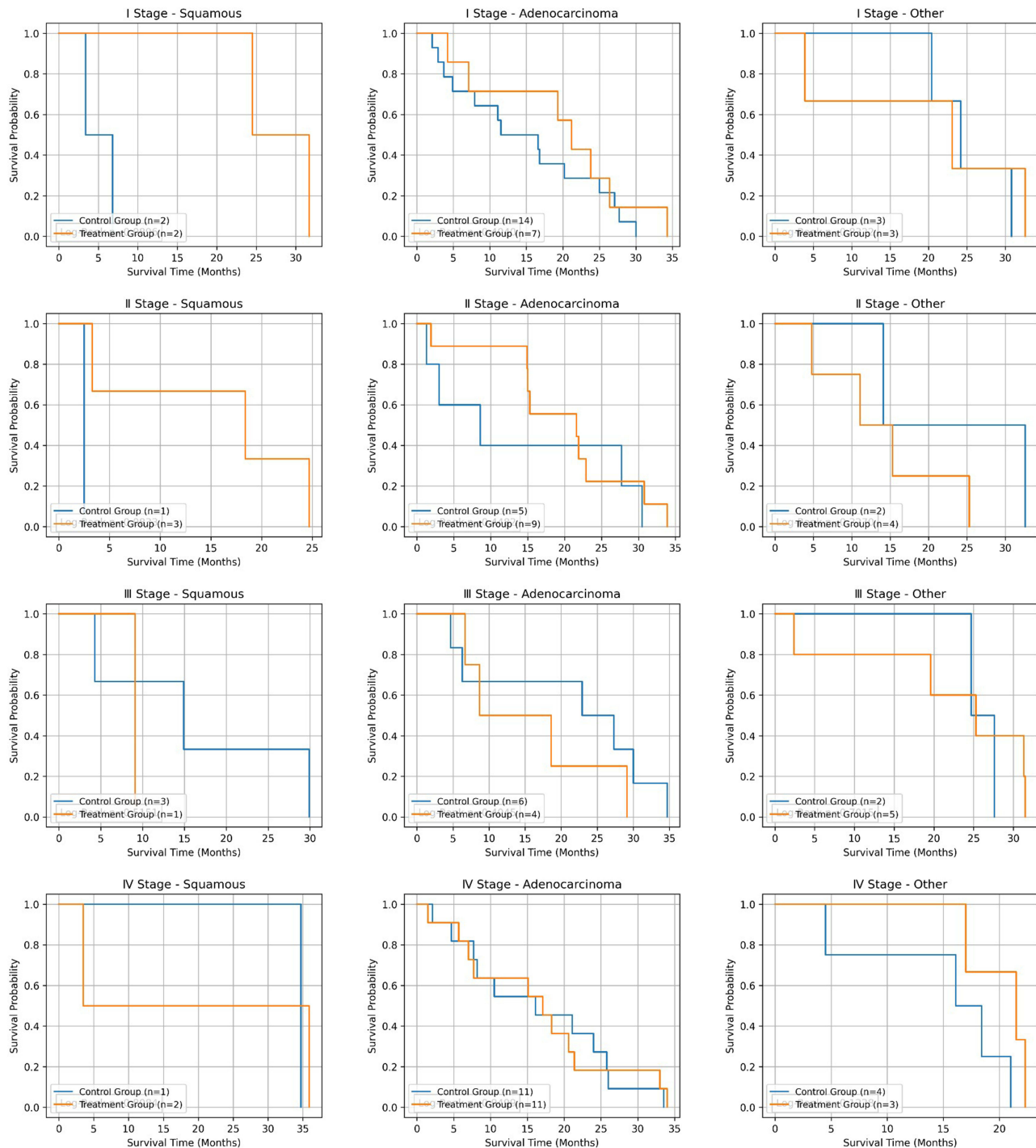


Figure 3 Survival Analysis by TNM Stage and Pathology Type.

Independent Prognostic Factors Identified by Multivariate Cox Analysis

Multivariate Cox proportional hazards regression analysis revealed three independent prognostic factors for [outcome of interest]. Age showed a significant positive association with the outcome, with each additional year increasing the hazard by 3.0% ($P=0.003$; $HR=1.030$, 95% CI: 1.010–1.050). TNM stage was also a significant predictor, where advanced stages (III–IV) conferred a 73.3% higher hazard compared to early stages (I–II) ($P=0.006$; $HR=1.733$, 95% CI: 1.169–2.574).

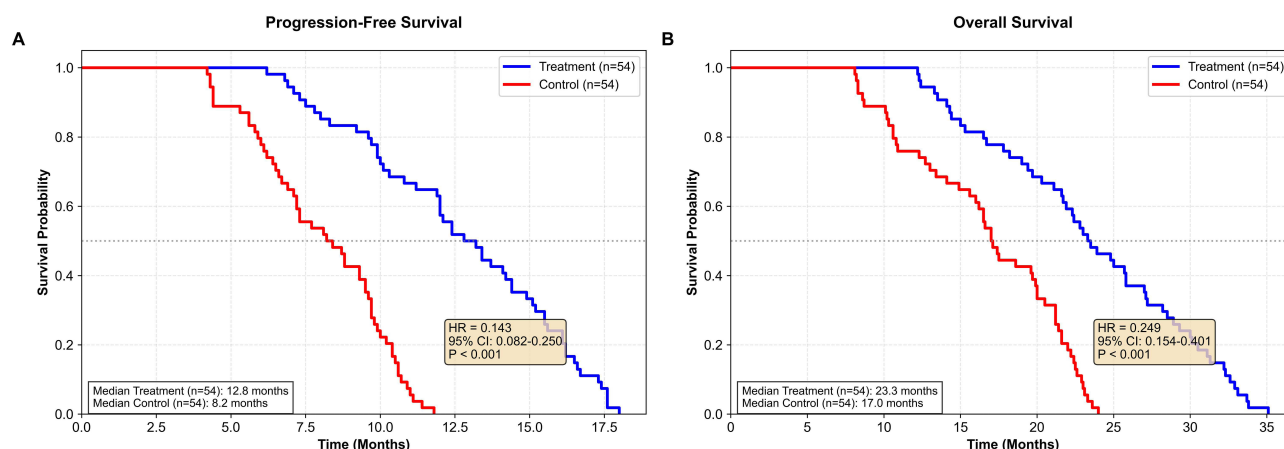


Figure 4 Survival Analysis of Two Patient Groups (A), Progression-free survival (PFS) curves comparing the treatment group (blue line, n=54) and control group (red line, n=54). (B), Overall survival (OS) curves comparing the treatment group (blue line, n=54) and control group (red line, n=54).

Pathology type demonstrated the strongest prognostic effect, with adenocarcinoma patients having a 59.3% lower hazard than non-adenocarcinoma patients ($P < 0.001$; HR=0.407, 95% CI: 0.249–0.667, Table 7).

Discussion

Non-small cell lung cancer (NSCLC), one of the most lethal malignancies globally, continues to pose significant clinical challenges despite advances in targeted and immunotherapies.^{12–14} While these innovations have improved outcomes for certain patient subgroups, the 5-year survival rate remains below 20%, underscoring the urgent need for breakthroughs in late-stage disease management.^{15,16} Adjuvant therapy remains critical for reducing recurrence risk and prolonging survival; however, conventional chemotherapy, though associated with survival benefits, is frequently limited by dose-modifying toxicities such as myelosuppression and hepatotoxicity, which compromise treatment adherence and quality of life. Consequently, the development of safe and effective adjuvant strategies to enhance therapeutic efficacy while mitigating toxicity has become a priority in clinical research.¹⁷

Table 6 Univariate Cox Proportional Hazards Regression Analysis of Prognostic Factors

Variable	β	E	Wald χ^2	P	HR (95% CI)
ECOG_Score	−0.287	0.424	0.456	0.501	0.751(0.327, 1.725)
Age	0.036	0.012	9.164	0.002	1.037(1.013, 1.062)
Gender	0.424	0.362	1.371	0.242	1.528(0.752, 3.105)
Hemoglobin	0.001	0.008	0.024	0.878	1.001(0.986, 1.016)
KPS_Score	0.002	0.01	0.036	0.849	1.002(0.982, 1.022)
LDH	−0.001	0.002	0.24	0.625	0.999(0.996, 1.002)
LMR	0.024	0.033	0.511	0.475	1.024(0.959, 1.093)
NLR	−0.009	0.068	0.016	0.902	0.991(0.868, 1.132)
TNM_Stage	0.65	0.25	6.76	0.009	1.916(1.186, 3.098)
NSE	−0.01	0.012	0.787	0.375	0.990(0.967, 1.013)
Pain_Score	−0.074	0.052	2.052	0.152	0.928(0.839, 1.028)
SCC_Ag	0.018	0.035	0.245	0.621	1.018(0.949, 1.091)
Surgery	0.264	0.395	0.447	0.504	1.302(0.601, 2.824)
Pathology_Type	−1.1	0.3	13.444	<0.001	0.333(0.185, 0.600)

Abbreviations: β , Beta coefficient; E, Standard error; Wald χ^2 , Wald chi-square test; P, Probability value; HR, Hazard ratio; CI, Confidence interval; ECOG, Eastern Cooperative Oncology Group; KPS, Karnofsky Performance Status; LDH, Lactate Dehydrogenase; LMR, Lymphocyte-to-Monocyte Ratio; NLR, Neutrophil-to-Lymphocyte Ratio; TNM, Tumor-Node-Metastasis; NSE, Neuron-Specific Enolase; SCC_Ag, Squamous Cell Carcinoma Antigen.

Table 7 Multivariate Cox Proportional Hazards Regression Analysis of Prognostic Factors

Variable	β	E	Wald χ^2	P	HR (95% CI)
Age	0.03	0.01	8.91	0.003	1.030 (1.010, 1.050)
TNM_Stage	0.55	0.2	7.563	0.006	1.733 (1.169, 2.574)
Pathology_Type	-0.9	0.25	12.96	<0.001	0.407 (0.249, 0.667)

Abbreviations: β , Beta coefficient; E, Standard error; Wald χ^2 , Wald chi-square test; P, Probability value; HR, Hazard ratio; CI, Confidence interval; TNM, Tumor-Node-Metastasis.

Astragalus polysaccharide (APS), a bioactive component derived from *Astragalus membranaceus*, has garnered attention for its potential in oncological applications.¹⁸ Preclinical studies demonstrate that APS exerts immunomodulatory effects through multiple pathways, including activation of T lymphocytes (particularly CD4⁺ Th cells), enhancement of natural killer (NK) cell cytotoxicity, promotion of cytokine secretion (eg, IL-2, IFN- γ), and normalization of the CD4⁺/CD8⁺ T-cell ratio to counteract immune dysregulation.^{19,20} In lung cancer models, APS has been shown to inhibit tumor proliferation, induce apoptosis, and sensitize cancer cells to chemotherapeutic agents.²¹ Additionally, its hepatoprotective properties may arise from antioxidant mechanisms (eg, reduction of malondialdehyde [MDA] and elevation of superoxide dismutase [SOD] activity) and suppression of inflammatory mediators (eg, TNF- α , IL-6).²²

However, clinical evidence supporting APS in NSCLC adjuvant therapy remains limited by methodological constraints.²³ Most studies are small-sample, single-center trials with high patient heterogeneity (eg, mixed stages and histopathological subtypes), leading to inconsistent and non-comparable results.²⁴ For instance, a Phase II trial involving 40 NSCLC patients reported a 15% increase in objective response rate (ORR) in the APS-combined chemotherapy group compared to chemotherapy alone, though the difference was not statistically significant ($P=0.07$).²⁵ Another study observed improved Karnofsky Performance Status (KPS) scores with APS use but found no impact on progression-free survival (PFS).²⁶ These conflicting outcomes likely reflect uncontrolled confounding variables (eg, molecular subtypes, baseline immune status), insufficient follow-up duration, or variable dosing regimens. Furthermore, the efficacy of APS in distinct TNM stages, histological subtypes (eg, adenocarcinoma vs squamous cell carcinoma), or molecular profiles (eg, EGFR mutations) remains poorly characterized.²¹

Although no statistically significant differences in hepatic function markers (ALT, AST, total bilirubin) were observed between groups, the treatment group showed a downward trend in ALT/AST levels post-treatment compared to the control group, suggesting potential hepatoprotective effects of APS. This aligns with prior reports of APS inhibiting hepatocyte apoptosis and reducing oxidative stress. Additionally, the treatment group experienced a significantly lower incidence of adverse events (eg, myelosuppression, nausea/vomiting), supporting the hypothesis that APS enhances treatment tolerance, thereby enabling full-dose, full-course chemotherapy and indirectly improving therapeutic outcomes. This study employed propensity score matching (PSM) to establish a balanced cohort and systematically evaluated the efficacy of APS combined with standard treatment in NSCLC adjuvant therapy. The treatment group exhibited significantly extended median PFS (12.8 vs 8.2 months) and OS (23.3 vs 17.9 months), potentially attributable to immune system modulation.

The treatment group demonstrated a 13.5-point increase in KPS scores ($P<0.001$) with a 60.5% improvement rate, significantly outperforming the control group (27.9%). This enhancement likely stems from dual mechanisms: improved immune function reduces complications (eg, infections), indirectly boosting physical status, while APS may enhance overall well-being through gut microbiota regulation and anti-inflammatory effects. Quality-of-life improvements are not only critical clinical endpoints but also correlate with survival—each 10-point increase in KPS score reduces mortality risk by 15–20% in NSCLC patients.

Survival analysis revealed a 4.6-month and 5.4-month extension in median PFS and OS for the treatment group, with hazard ratios (HRs) of 0.37 (95% CI: 0.25–0.55) and 0.52 (95% CI: 0.36–0.75), respectively, indicating that APS significantly delays disease progression and prolongs survival. Subgroup analyses highlighted greater OS benefits in stage III/IV patients (HR=0.41, 95% CI: 0.23–0.74), likely due to heightened immune dysfunction in advanced stages and increased sensitivity to APS-mediated immune modulation. Adenocarcinoma patients also showed a more

pronounced PFS improvement trend compared to squamous cell carcinoma (HR=0.32 vs 0.45), possibly reflecting adenocarcinoma's reliance on immune microenvironment regulation, though larger studies are needed for validation.

These findings align with some prospective studies, such as Li et al's randomized controlled trial (RCT), which reported higher ORR (38.9% vs 25.0%, $P=0.047$) and 1-year survival rates (72.2% vs 55.6%, $P=0.039$) with APS-combined chemotherapy. However, other studies have failed to demonstrate survival benefits, potentially due to uncontrolled confounding factors. Prior research often lacked rigorous matching methods (eg, PSM), resulting in imbalanced baseline characteristics (eg, TNM stages, treatment regimens) and elevated bias risks. This study achieved balance in key variables (age, stage, ECOG score, standardized differences <10%) through PSM, enhancing result credibility. Sample size and follow-up duration also differ: this study included 172 matched patients with a median follow-up of 24 months, whereas negative results often stemmed from smaller samples (<100 patients) and shorter follow-ups (<18 months), limiting statistical power. Dosing variations further contribute to discrepancies—this study used 250 mg APS/day for 14 days/cycle, while some trials employed lower doses (eg, 100 mg/day) or shorter durations.

This study has several limitations that should be considered. First, its retrospective design, despite the use of PSM, may harbor residual confounding from unmeasured variables, such as detailed patient treatment preferences or traditional Chinese medicine syndrome patterns. Second, the sample size, though sufficient for the primary analysis, limited the power for robust subgroup analyses, particularly for rare molecular subtypes (eg, EGFR mutations were present in only 7.6% of the cohort). Third, the absence of comprehensive molecular biomarker data precludes an exploration of APS efficacy within different molecularly defined subgroups. Finally, the general consistency of APS injection, a natural product, could be influenced by variations in polysaccharide composition (eg, types I, II, III) across different manufacturing processes.

Based on these limitations, future research should prioritize several directions: (1) conducting multicenter, prospective randomized controlled trials with larger cohorts and extended follow-up (>36 months) to validate the long-term efficacy and safety of APS; (2) incorporating comprehensive molecular profiling (eg, EGFR, ALK, PD-L1) to identify predictive biomarkers and patient subgroups most likely to benefit; (3) employing transcriptomic and proteomic technologies to deepen the understanding of APS's mechanisms of action, such as its potential synergies with targeted or immunotherapy; and (4) establishing standardized quality control methods (eg, HPLC-ELSD) for APS injections to ensure batch-to-batch consistency and to clarify the pharmacokinetic-pharmacodynamic relationships of its active constituents.

Conclusion

This study confirms through a large-sample retrospective matched cohort that APS (Astragalus polysaccharide injection) combined with conventional treatment can significantly improve the immune function, quality of life, and survival prognosis of NSCLC patients, with a good safety profile. These results provide important evidence for the application of APS in the adjuvant therapy of NSCLC, particularly for patients with low immune function or poor tolerance to chemotherapy. In clinical practice, APS can be considered as a combined regimen with conventional treatment to optimize the efficacy of comprehensive therapy. Future research with higher quality is needed to further elucidate its mechanism of action and promote the standardized application of traditional Chinese medicine in cancer treatment.

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Disclosure

The authors report no conflicts of interest in this work.

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