Am J Transl Res 2025;17(10):7847-7857
www.ajtr.org /ISSN:1943-8141/AJTR0166575

Original Article

Efficacy and quality of life benefits of dexamethasone in advanced non-small cell lung cancer

Guanchu Liu[1], Hao Ding[1], Tao Pu[2], Lie Wang[1]

[1]Department of Thoracic Surgery, Affiliated Hospital of North Sichuan Medical College, Nanchong 637000, Sichuan, China; [2]Reproductive Medicine Center, Affiliated Hospital of North Sichuan Medical College, Nanchong 637000, Sichuan, China

Received June 4, 2025; Accepted September 20, 2025; Epub October 15, 2025; Published October 30, 2025

Abstract: Objective: To evaluate the impact of dexamethasone (Dex) on treatment outcomes in chemotherapy-treated advanced non-small cell lung cancer (NSCLC) patients. Methods: A total of 123 advanced NSCLC patients undergoing chemotherapy were enrolled. The control group received chemotherapy alone, while the research group was administered Dex in combination with chemotherapy. Short-term treatment efficacy, adverse reaction rates, humoral immunity, vascular endothelial growth factor (VEGF), hypoxia-inducible factor-1α (HIF-1α), quality of life, and treatment adherence were compared between the two groups. Univariate and multivariate analyses were performed to identify variables influencing short-term treatment efficacy. Results: The two groups were equivalent in the objective response rate, disease control rate, and overall side effects rate (all $P > 0.05$), though the incidences of nausea/vomiting were reduced ($P < 0.05$). Post-treatment evaluations revealed elevated humoral immunity markers, improved quality of life scores, and better treatment adherence in the research group (all $P < 0.05$). Furthermore, VEGF and HIF-1α expression were suppressed in the research group (both $P < 0.05$). Regression analysis identified Eastern Cooperative Oncology Group Performance Status (ECOG PS; OR=2.277), VEGF (OR=5.241), and HIF-1α (OR=2.687) as independent factors influencing short-term treatment efficacy (all $P < 0.05$). Conclusion: Dex administration in chemotherapy-treated advanced NSCLC patients improves clinical outcomes and enhances quality of life.

Keywords: Dexamethasone, advanced non-small cell lung cancer, chemotherapy, treatment outcomes, quality of life assessment

Introduction

Worldwide, non-small cell lung cancer (NSCLC) is a leading cause of cancer-related mortality, driven by genetic abnormalities that promote tumor growth [1]. In 2020, 11.4% of all cancer cases were newly diagnosed, with men bearing a higher burden of both disease onset and mortality [2, 3]. The disease is strongly linked to tobacco use, genetic predisposition, radiation exposure, and chronic lung conditions, with immune escape mechanisms playing a role as well [4]. Available treatments include chemotherapy, nanocarrier-based combination therapies, and immune checkpoint inhibitors [5, 6]. However, prognosis remains poor, particularly for advanced stages [7]. Despite the emergence of therapies like immune checkpoint blockade and nanoparticle-drug conjugates, chemotherapy continues to be the cornerstone of treatment for advanced NSCLC. Vinorelbine, a vinca alkaloid, disrupts microtubule formation to induce cell cycle arrest and is commonly used in combination with cisplatin, providing survival benefits. However, side effects such as nausea and vomiting (N/V) remain significant [8-10]. Thus, there is a pressing need for continuous optimization of chemotherapy to enhance both survival and quality of life (QoL).

Dexamethasone (Dex), primarily known for its antiemetic properties, has also been shown to inhibit lung tumor growth by modulating proliferating cell nuclear antigen-binding protein and hyperphosphorylation of cortical actin [11]. When co-administered with chemotherapeutics, Dex can enhance tumor cell chemosensitivity, improving treatment efficacy [11]. Dex's anti-tumor effects are also linked to immune evasion inhibition through downregula-

https://doi.org/10.62347/MLIY3475

tion of the PD-L1 and IDO1 pathways [12]. Li et al. [13] suggested that Dex-adjuvant immunotherapy may be a promising strategy for advanced NSCLC, offering comparable tumor response rates and toxicity profiles.

However, research on how Dex affects treatment outcomes and QoL in chemotherapy-treated advanced NSCLC patients is still lacking. This study aims to explore better treatment strategies for these patients. Key contributions include: (1) providing a multidimensional evaluation of Dex's effects beyond its antiemetic role, examining short-term efficacy, adverse reactions, immune changes, tumor microenvironment markers (VEGF/HIF-1α), QoL, and treatment adherence; (2) identifying key predictors of clinical response, establishing a framework for predicting chemotherapy failure in advanced NSCLC; and (3) revealing VEGF/HIF-1α as potential predictors of chemotherapy outcomes in late-stage NSCLC. Future studies could use these findings to identify populations that are responsive to Dex-based treatments.

Materials and methods

General information

This retrospective study was approved by the Ethics Review Board of the Affiliated Hospital of North Sichuan Medical College. We enrolled 123 advanced NSCLC patients undergoing chemotherapy from January 2022 to January 2025. Participants were allocated into two groups based on their treatment protocol: a control group (n=56) receiving standard chemotherapy and a research group (n=67) receiving Dex-assisted chemotherapy. Power analysis, based on a rate comparison between groups, determined that 48 subjects per arm would provide 80% power. After accounting for a 10% dropout rate (n=54 per group), our final enrollment meets these predetermined sample size targets.

Eligibility criteria

Inclusion criteria: (1) Histopathologically confirmed advanced NSCLC; (2) Stage III or IV disease, according to the International Association for the Study of Lung Cancer (IASLC) Tumor, Node, Metastasis (TNM) staging system [14]; (3) Eastern Cooperative Oncology Group Performance Status (ECOG PS) score [15]; (4) Expected survival > 3 months; (5) Normal baseline hematological, cardiac, hepatic, and renal parameters; (6) No contraindications to chemotherapy and presence of radiologically evaluable lesions; (7) Complete medical records.

Exclusion criteria: (1) Active severe infections or comorbid respiratory disorders; (2) Recent platinum-based therapy (within 4 weeks); (3) History of other malignancies; (4) Hematologic insufficiency (neutrophils $\leq 1.5\times10^9$/L or platelets $\leq 100\times10^9$/L); (5) Pregnancy, lactation, or elevated intracranial pressure; (6) Pre-existing gastrointestinal conditions, active nausea/vomiting, or psychiatric/communication impairments; (7) Uncontrolled diabetes mellitus.

Treatment protocols

In the control group, standard chemotherapy was administered. Prior to chemotherapy, ondansetron was given via intravenous (IV) push, or granisetron via IV drip. Additionally, metoclopramide and diphenhydramine were injected intramuscularly. Chemotherapy consisted of vinorelbine (25 mg/m^2, IV push) and cisplatin (30 mg/m^2, IV push for 3 consecutive days, starting from day 1 of chemotherapy), accompanied by hydration therapy. Each treatment cycle lasted 3 weeks, with a minimum of 3 courses (9 weeks in total).

In the research group, Dex was added to the standard chemotherapy regimen. Dex administration was based on prior study protocols [16]: 12 mg IV bolus (in 100 mL normal saline) on day 1, followed by 8 mg daily IV infusion on days 2-4, administered 30 minutes before chemotherapy for 8 consecutive days (with the treatment duration matching the control group).

Outcome measures

(1) Treatment efficacy: Treatment efficacy was assessed four weeks after completing the therapy regimen using the Response Evaluation Criteria in Solid Tumors (RECIST) guidelines [17]. Response categories included: Complete Response (CR): Complete disappearance of all target lesions lasting ≥ 4 weeks; Partial Response (PR): > 50% reduction in lesion size persisting ≥ 4 weeks; Stable Disease (SD): 25-50% reduction in lesion size; Progressive Disease (PD): < 25% reduction in lesion size or new lesion emergence. The objective response

rate (ORR) was calculated as the percentage of CR + PR cases relative to the total population. The disease control rate (DCR) represented the proportion of CR + PR + SD cases in the total cohort.

(2) Adverse events: Treatment-related toxicities, such as myelosuppression, neutropenia, hepatic/renal dysfunction, and N/V were documented.

(3) Humoral immunity assessment: Fasting venous blood (5 mL) was collected at baseline and after the 9-week treatment course. Immunoglobulin (Ig) A, IgM, and IgG concentrations were quantified using immunoturbidimetry.

(4) Serum biomarker analysis: Serum samples, obtained by centrifugation, were analyzed using enzyme-linked immunosorbent assay to measure pre- and post-treatment levels of VEGF and HIF-1α.

(5) QoL evaluation: QoL was assessed using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) [18]. The tool evaluates physical, role, and cognitive functioning, along with global health status. Scores range from 0 to 100, where higher scores indicate better QoL. Measurements were taken before treatment and after the 9-week course.

(6) Treatment compliance: Patients were classified as fully compliant if they strictly adhered to the chemotherapy protocol (dose and schedule) prescribed by their physician. Partial compliance indicated acceptance of the chemotherapy plan and dosage but inconsistent adherence to the schedule. Non-compliance was defined as occasional or symptom-driven participation with poor cooperation. The total compliance rate was calculated as the percentage of cases with full and partial compliance [19].

Statistical methods

Statistical analysis was performed using SPSS 24.0, with *P* values < 0.05 considered significant. Descriptive statistics included counts and percentages [n (%)] for categorical data, and mean ± standard deviation (SD) for continuous variables. Differences between groups for categorical data were analyzed using χ^2 tests (Fisher's exact test for cells with counts < 5). Continuous data, meeting Bartlett's (variance equality) and Kolmogorov-Smirnov (normality) assumptions, were analyzed using independent t-tests (between groups) and paired t-tests (within subjects). Univariate analysis followed by multivariate logistic regression was used to identify predictors of treatment outcomes.

Results

Comparison of baseline patient characteristics

The control and research groups showed similar baseline characteristics, including gender distribution, age, disease duration, ECOG PS, pathological subtype, tumor location, and TNM stage (all P > 0.05, **Table 1**).

Comparison of short-term treatment outcomes

The objective response rate (ORR) and disease control rate (DCR) in the control group were 53.57% and 78.57%, respectively. In contrast, the research group showed ORR and DCR of 55.22% and 88.06%, respectively. Statistical comparisons revealed no significant differences in either ORR or DCR between the two groups (both P > 0.05, **Table 2**).

Comparison of adverse event profiles

Evaluation of treatment-related adverse events, such as myelosuppression, neutropenia, and hepatic/renal dysfunction, indicated similar overall adverse reaction rates between the two groups (all P > 0.05). However, the research group had a significantly lower incidence of N/V compared to the control group (P < 0.05, **Table 3**).

Comparison of humoral immune function

Baseline humoral immune markers (IgA, IgM, IgG) were comparable between the groups (all P > 0.05). Post-treatment, all Ig levels increased significantly (all P < 0.05), with the research group showing higher IgA, IgM, and IgG levels than the control group (all P < 0.05, **Figure 1**).

Comparison of serum biomarkers

There were no significant intergroup differences in baseline VEGF or HIF-1α levels (both P > 0.05). Post-treatment, both groups showed substantial reductions in these biomarkers (both P < 0.05), with the research group achieving sig-

Table 1. Comparison of baseline patient characteristics

Data	Control group (n=56)	Research group (n=67)	χ^2/t	P
Gender			1.845	0.174
Male	40 (71.43)	40 (59.70)		
Female	16 (28.57)	27 (40.30)		
Age (years)	63.52±7.10	62.66±9.26	0.569	0.570
Disease duration (years)	5.18±2.22	5.76±2.19	1.454	0.149
ECOG PS (points)			0.858	0.651
0	26 (46.43)	33 (49.25)		
1	20 (35.71)	26 (38.81)		
2	10 (17.86)	8 (11.94)		
Pathological subtype			1.485	0.223
Adenocarcinoma	29 (51.79)	42 (62.69)		
Squamous-cell carcinoma	27 (48.21)	25 (37.31)		
Tumor location			0.061	0.805
Upper lobe	33 (58.93)	38 (56.72)		
Middle and lower lobes	23 (41.07)	29 (43.28)		
TNM stage			0.079	0.778
III	34 (60.71)	39 (58.21)		
IV	22 (39.29)	28 (41.79)		

Notes: ECOG PS, Eastern Cooperative Oncology Group Performance Status; TNM, Tumor, Node, Metastasis.

Table 2. Comparison of short-term treatment outcomes

Indicator	Control group (n=56)	Research group (n=67)	χ^2	P
Complete response	6 (10.71)	7 (10.45)		
Partial response	24 (42.86)	30 (44.78)		
Stable disease	14 (25.00)	22 (32.84)		
Progressive disease	12 (21.43)	8 (11.94)		
Objective response rate	30 (53.57)	37 (55.22)	0.034	0.855
Disease control rate	44 (78.57)	59 (88.06)	2.017	0.156

Table 3. Comparison of adverse reaction rates

Indicator	Control group (n=56)	Research group (n=67)	Fish/χ^2	P
Myelosuppression	2 (3.57)	2 (2.99)		> 0.999
Neutropenia	1 (1.79)	2 (2.99)		> 0.999
Hepatic/renal dysfunction	1 (1.79)	1 (1.49)		> 0.999
Nausea and vomiting	9 (16.07)	3 (4.48)		0.037
Total	13 (23.21)	8 (11.94)	2.738	0.098

nificantly lower levels than the control group (both P < 0.05, **Figure 2**).

Comparison of QoL

Statistical analysis confirmed no significant baseline differences in QoL scores (all P > 0.05). After treatment, both groups showed improvements across all domains, with the research group outperforming the control group in physical, role, cognitive, and global health status scores (all P < 0.05; **Figure 3**).

Comparison of treatment compliance

In the control group, 42 patients (75.00%) were compliant, compared to 61 patients (91.04%) in the research group. The research group ex-

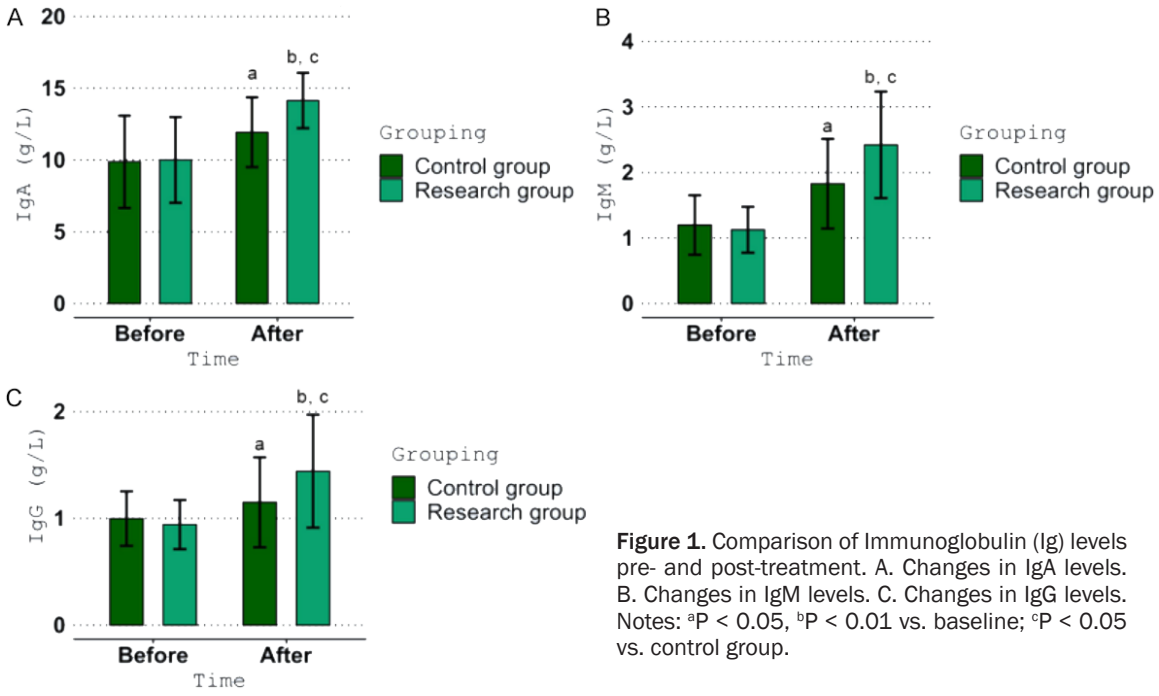

Figure 1. Comparison of Immunoglobulin (Ig) levels pre- and post-treatment. A. Changes in IgA levels. B. Changes in IgM levels. C. Changes in IgG levels. Notes: [a]P < 0.05, [b]P < 0.01 vs. baseline; [c]P < 0.05 vs. control group.

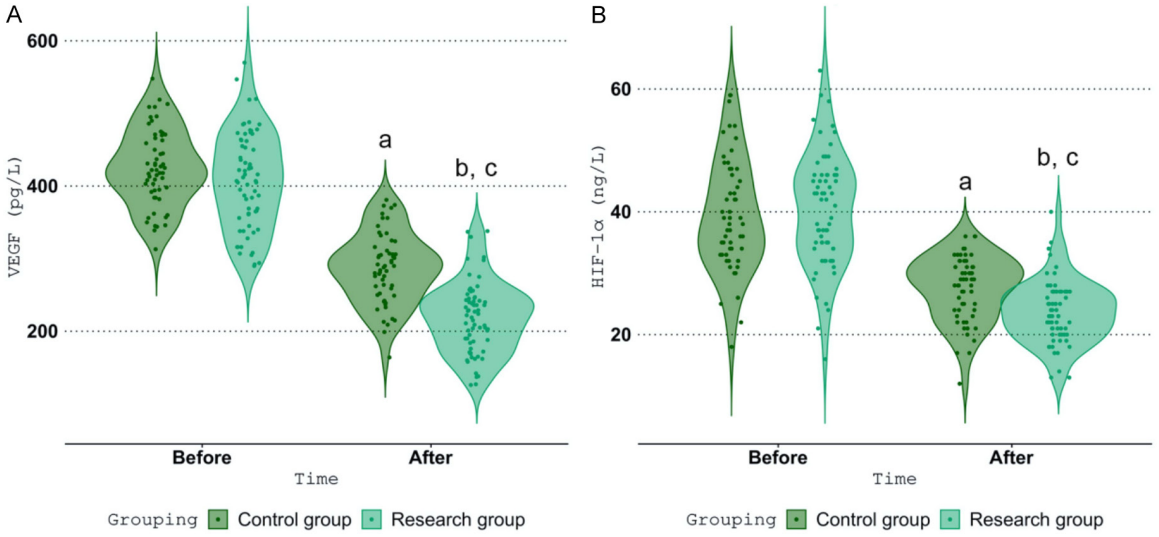

Figure 2. Comparison of VEGF and HIF-1α expression. A. VEGF levels pre- and post-treatment. B. HIF-1α levels pre- and post-treatment. Notes: VEGF, vascular endothelial growth factor; HIF-1α, hypoxia-inducible factor-1α; [a]P < 0.05, [b]P < 0.01 vs. baseline; [c]P < 0.05 vs. control group.

hibited significantly better compliance (P < 0.05; **Table 4**).

Identification of prognostic factors: univariate and multivariate analysis

Univariate analysis revealed significant associations between age, disease duration, ECOG PS, TNM stage, VEGF, and HIF-1α levels with short-term treatment responses (all P < 0.05). Multivariate analysis identified ECOG PS=1 or 2 (OR=2.277), VEGF ≥ 425 pg/L (OR=5.241), and HIF-1α ≥ 40 ng/L (OR=2.687) as independent predictors of inadequate short-term treatment efficacy (P < 0.05). Detailed results are presented in **Tables 5**, **6**. The cutoff values for IgA, IgM, IgG, VEGF, and HIF-1α were based on median or interquartile adjustments.

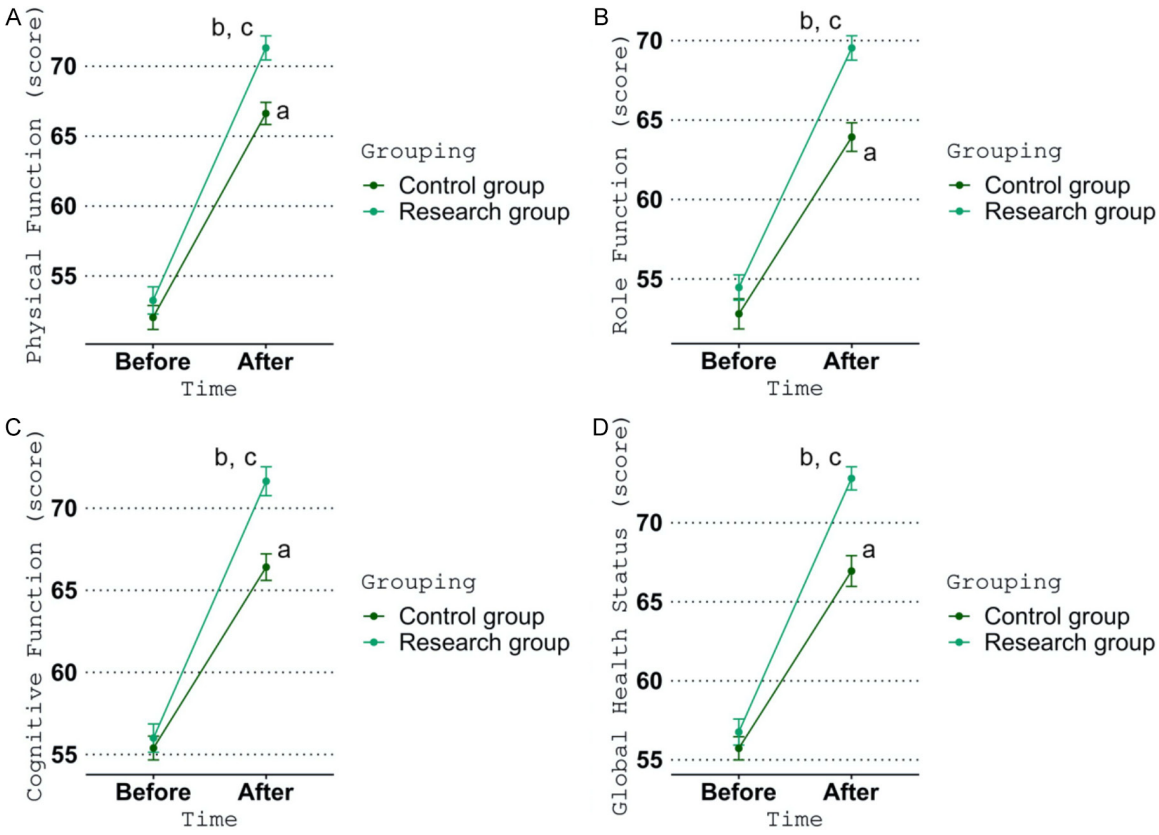

Figure 3. Comparison of EORTC QLQ-C30 domain scores pre- and post-treatment. A. Physical Function changes. B. Role Function changes. C. Cognitive Function changes. D. Global Health Status changes. Notes: EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; [a]P < 0.05, [b]P < 0.01 vs. baseline; [c]P < 0.05 vs. control group.

Table 4. Comparison treatment compliance

Indicator	Control group (n=56)	Research group (n=67)	χ^2	P
Good compliance	22 (39.29)	37 (55.22)		
Partial compliance	20 (35.71)	24 (35.82)		
Non-compliance	14 (25.00)	6 (8.96)		
Total compliance	42 (75.00)	61 (91.04)	5.767	0.016

Discussion

The therapeutic effects and QoL improvements conferred by Dex in advanced NSCLC patients receiving standard chemotherapy (vinorelbine + cisplatin) were examined. Further analysis explored adverse reaction rates, humoral immunity, serum biomarkers, and efficacy determinants. The results highlight Dex's role in enhancing therapeutic effects, regulating immune function, inhibiting vascularization, and improving QoL. Approximately one-third of lung cancers are classified as advanced NSCLC, a highly heterogeneous condition. Since standard therapies yield only modest results, incorporating new strategies like adjuvant treatments is essential for optimizing disease management and refining clinical outcomes [20, 21]. This study aimed to refine standard chemotherapy (vinorelbine plus cisplatin) to achieve better clinical outcomes and enhanced QoL for these patients.

Our initial finding revealed no significant difference between the Dex-combined approach and standard chemotherapy in controlling advanced NSCLC, as evidenced by comparable ORR and DCR. This suggests that although Dex combination therapy reshapes the tumor microenvironment and modulates immune responses, it has only a marginal effect on tumor shrinkage. Yu H et al. [22] also reported no significant impact of Dex on ORR or DCR in immunotherapy-treated advanced non-squamous NSCLC patients,

Table 5. Univariate predictors of short-term treatment response

Data	Non-response group (n=56)	Response group (n=67)	χ^2	P
Gender			1.689	0.194
Male (n=80)	33 (58.93)	47 (70.15)		
Female (n=43)	23 (41.07)	20 (29.85)		
Age (years)			6.851	0.009
< 65 (n=62)	21 (37.50)	41 (61.19)		
≥ 65 (n=61)	35 (62.50)	26 (38.81)		
Disease duration (years)			4.237	0.040
< 6 (n=63)	23 (41.07)	40 (59.70)		
≥ 6 (n=60)	33 (58.93)	27 (40.30)		
ECOG PS (score)			8.910	0.012
0 (n=59)	19 (33.93)	40 (59.70)		
1 (n=46)	25 (44.64)	21 (31.34)		
2 (n=18)	12 (21.43)	6 (8.96)		
Pathological subtype			0.236	0.627
Adenocarcinoma (n=71)	31 (55.36)	40 (59.70)		
Squamous-cell carcinoma (n=52)	25 (44.64)	27 (40.30)		
Tumor location			0.726	0.394
Upper lobe (n=71)	30 (53.57)	41 (61.19)		
Middle and lower lobes (n=52)	26 (46.43)	26 (38.81)		
TNM stage			5.284	0.022
III (n=73)	27 (48.21)	46 (68.66)		
IV (n=50)	29 (51.79)	21 (31.34)		
IgA (g/L)			2.554	0.110
< 10 (n=58)	22 (39.29)	36 (53.73)		
≥ 10 (n=65)	34 (60.71)	31 (46.27)		
IgM (g/L)			0.601	0.438
< 1.2 (n=64)	27 (48.21)	37 (55.22)		
≥ 1.2 (n=59)	29 (51.79)	30 (44.78)		
IgG (g/L)			0.144	0.705
< 1 (n=68)	32 (57.14)	36 (53.73)		
≥ 1 (n=55)	24 (42.86)	31 (46.27)		
VEGF (pg/L)			9.425	0.002
< 425 (n=69)	23 (41.07)	46 (68.66)		
≥ 425 (n=54)	33 (58.93)	21 (31.34)		
HIF-1α (ng/L)			4.949	0.026
< 40 (n=64)	23 (41.07)	41 (61.19)		
≥ 40 (n=59)	33 (58.93)	26 (38.81)		
Treatment compliance			2.017	0.156
Compliance (n=103)	44 (78.57)	59 (88.06)		
Non-compliance (n=20)	12 (21.43)	8 (11.94)		
Treatment modality			0.034	0.855
Chemotherapy + dexamethasone (n=67)	30 (53.57)	37 (55.22)		
Standard chemotherapy (n=56)	26 (46.43)	30 (44.78)		

Notes: ECOG PS, Eastern Cooperative Oncology Group Performance Status; TNM, Tumor, Node, Metastasis; Ig, immunoglobulin; VEGF, vascular endothelial growth factor; HIF-1α, hypoxia-inducible factor-1α. ECOG PS 0: The patient is fully active with no symptoms. ECOG PS 1: The patient can walk freely but struggles with demanding physical tasks (e.g., running, manual labor), though light or desk-based work remains possible. ECOG PS 2: The patient can perform self-care but cannot work, with less than 50% of daytime spent resting in bed.

Table 6. Multivariate logistic regression of significant prognostic factors

Factor	B	SE	Wald	P	OR	95% CI
Age (years)	0.778	0.433	3.221	0.073	2.177	0.931-5.090
Disease duration (years)	0.641	0.434	2.181	0.140	1.899	0.811-4.449
ECOG PS (score)	0.823	0.322	6.534	0.011	2.277	1.212-4.281
TNM stage	0.822	0.450	3.332	0.068	2.274	0.941-5.495
VEGF (pg/L)	1.656	0.472	12.298	< 0.001	5.241	2.076-13.227
HIF-1α (ng/L)	0.988	0.460	4.609	0.032	2.687	1.090-6.624

Notes: ECOG PS, Eastern Cooperative Oncology Group Performance Status; TNM, Tumor, Node, Metastasis; VEGF, vascular endothelial growth factor; HIF-1α, hypoxia-inducible factor-1α.

which aligns with our findings, despite differences in participant demographics. Subsequent safety assessments showed no significant inter-group differences, although Dex was associated with reduced nausea/vomiting episodes, suggesting its role in maintaining treatment safety and enhancing antiemetic protection. This observation is consistent with Wei et al. [23], who documented Dex's protection against cisplatin-induced emesis in chemotherapy patients. Dex's antiemetic effects are attributed to prostaglandin synthesis inhibition, noncompetitive modulation of 5-HT3 receptors, and its compensatory role in acute adrenal deficiency following platinum-agent therapy [24].

Further investigation demonstrated that Dex administration significantly enhanced humoral immune regulation, likely by suppressing VEGF and HIF-1α expression. Moreover, Dex may strengthen antitumor immunity by regulating B-cell function and counteracting chemotherapy-induced immunosuppression [25]. By stimulating THP-1 macrophages and inhibiting proangiogenic signaling (e.g., HIF-1α/VEGF axis) in the tumor microenvironment, Dex could slow malignant growth [26, 27]. Cook and colleagues [28] also reported enhanced immune regulation when Dex was administered alongside pemetrexed-platinum chemotherapy in oncology patients, which is consistent with our data. Furthermore, Kim et al. [29] confirmed Dex's immunoregulatory capacity, demonstrating synergistic activity with thalidomide in modulating T-cell responses in murine systems.

A notable improvement in QoL was observed in late-stage NSCLC patients when Dex was added as an adjunct therapy. Liu et al. [30] reported that Dex, when used in NSCLC patients receiving platinum-based chemotherapy, was well-tolerated and improved QoL by reducing symptom burden. Additionally, Dex-adjuvant therapy significantly increased treatment compliance, likely due to the marked reduction in post-treatment nausea/vomiting episodes. Treatment-related emesis and nausea accelerate functional decline in advanced NSCLC patients, substantially impairing their QoL [31], and further undermining adherence to therapy. Dex-mediated symptom control and QoL improvement likely contributed to the enhanced treatment adherence observed in the research group.

Univariate analysis showed significant associations between short-term treatment efficacy and age, disease duration, ECOG PS, TNM stage, VEGF, and HIF-1α. Multivariate modeling further confirmed that ECOG PS, VEGF, and HIF-1α were independent predictors of short-term efficacy. Tomasik et al. [32] suggested that NSCLC patients with poor performance status (ECOG PS ≥ 2) often respond less effectively to immunotherapy, possibly due to their compromised physical condition. This finding helps explain why ECOG PS influences short-term chemotherapy outcomes in advanced NSCLC. As a key mediator of tumor vascularization, VEGF modulates immune responses in the tumor microenvironment, particularly influencing immune cell behavior (e.g., myeloid cells) [33]. By suppressing immune cell function, VEGF contributes to tumor immunosuppression, both locally and systemically, making it a target for immunotherapy [34]. HIF-1α, a crucial transcription factor involved in regulating tumor cell proliferation and metastasis, has prognostic value in NSCLC, particularly for squamous cell carcinoma survival rates. Targeting HIF-1α opens new avenues for precision medicine strategies [35]. Targeting HIF-1α, which modulates canagliflozin's impact on NSCLC, has also been shown to suppress tumor growth [36]. In lung

adenocarcinoma, VEGF/HIF-1α signaling contributes to gefitinib resistance, and targeting these pathways may help overcome such resistance, explaining why VEGF/HIF-1α influences chemotherapy responses in advanced NSCLC [37]. Previous research has also shown that mutations in STK11/KEAP1 predict reduced immunotherapy response in advanced SMARCA4-deficient NSCLC [38]. Additionally, Hu et al. [39] identified smoking status, chemotherapy, and PD-L1 expression as protective factors for immune checkpoint inhibitor efficacy, while EGFR mutations, liver metastases, and antibiotic use were associated with worse outcomes.

Several limitations of this study warrant future attention. First, due to variations in the antiemetic protocols, future studies should better differentiate between Dex's direct tumor-suppressing effects and its indirect benefits from improved treatment tolerability. Second, the absence of extended follow-up data highlights the need for long-term monitoring to assess chronic concerns, such as immunosuppression and infection risks associated with prolonged Dex exposure. Third, current QoL assessments did not include lung cancer-specific measures, which is a limitation of retrospective studies. The Quality of Life Questionnaire-Lung Cancer 13 would provide a clearer understanding of how Dex impacts key QoL symptoms like coughing and breathing difficulties. Fourth, additional analysis of specific subcategories (e.g., IgG subtypes) and functional metrics (e.g., antibody affinity) could offer deeper insights into humoral immune regulation mechanisms. Fifth, Dex's influence on metabolic markers (e.g., glucose, blood pressure) was not explored, and addressing this would clarify its safety in patients with preexisting conditions. Finally, our study does not address whether Dex's antitumor effect is dose-dependent, an issue that should be explored in dedicated prospective randomized controlled trials with varying doses.

It is also important to note that in advanced NSCLC patients with diabetes, Dex should be avoided if they present with uncontrolled diabetes (HbA1c > 9%) or have a history of steroid-induced hyperglycemic crisis. Its use should also be avoided in patients already on high-dose steroid regimens [40]. In cases of significant glycemic variability, reducing the day 2-4 Dex dose to 6 mg combined with a basal-bolus insulin regimen can help mitigate hyperglycemia risk [41].

In conclusion, Dex improves QoL, treatment adherence, and humoral immunity without compromising short-term efficacy (ORR/DCR) in chemotherapy-treated advanced NSCLC patients, possibly by suppressing VEGF and HIF-1α.

Disclosure of conflict of interest

None.

Address correspondence to: Lie Wang, Department of Thoracic Surgery, Affiliated Hospital of North Sichuan Medical College, Nanchong 637000, Sichuan, China. Tel: +86-0817-2262160; E-mail: Liugc2019@163.com

References

[1] Jung HA, Lee DH, Lim SM, Yu H, Yoon S, Kim D, Kim KP, Jeong H, Doh H, Lim S, Kim J, Zhao X, Horsburgh D, Patel D, Kim JA and Toh KC. Epidemiology and outcomes of non-small cell lung cancer in South Korea. JAMA Netw Open 2024; 7: e2355331.

[2] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A and Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021; 71: 209-249.

[3] Gao S, Li N, Wang S, Zhang F, Wei W, Li N, Bi N, Wang Z and He J. Lung cancer in People's Republic of China. J Thorac Oncol 2020; 15: 1567-1576.

[4] Chen P, Liu Y, Wen Y and Zhou C. Non-small cell lung cancer in China. Cancer Commun (Lond) 2022; 42: 937-970.

[5] Zhong Y, Mao Y, Fu X and Huang H. Sintilimab combined with nanoparticle albumin-bound paclitaxel-based chemotherapy in severe locally advanced or metastatic squamous NSCLC showed good efficacy and safety: a pilot retrospective analysis. Int J Nanomedicine 2024; 19: 11433-11444.

[6] Li Y, Gong B, Guo Y, Liu W, Chen C, Jiang S, Pan F, Song J, Yang L and Zhou G. Non-small cell lung cancer and immune checkpoint inhibitor therapy: does non-alcoholic fatty liver disease have an effect? BMC Cancer 2024; 24: 535.

[7] Jachowski A, Marcinkowski M, Szydlowski J, Grabarczyk O, Nogaj Z, Marcin L, Plawski A, Jagodzinski PP and Slowikowski BK. Modern therapies of nonsmall cell lung cancer. J Appl Genet 2023; 64: 695-711.

[8] Chouaid C, Grossi F, Ta Thanh Minh C, Raymond R and Bosch-Barrera J. Pooled analysis of oral vinorelbine as single agents in patients

with advanced NSCLC. Lung Cancer Manag 2025; 14: 2477418.
[9] Al-Omar A, Asadi M, Mert U, Muftuoglu C, Karakus HS, Goksel T and Caner A. Effects of vinorelbine on M2 macrophages in non-small cell lung cancer. Int J Mol Sci 2025; 26: 2252.
[10] Shen G, Bian G, Yu H, Gao M, Kang D, Shen G and Hu S. Comparison between cisplatin plus vinorelbine and cisplatin plus docetaxel in the treatment of advanced non-small-cell lung cancer: a meta-analysis of randomized controlled trials. Mol Clin Oncol 2014; 2: 146-150.
[11] Srivastava S, Siddiqui S, Singh S, Chowdhury S, Upadhyay V, Sethi A and Kumar Trivedi A. Dexamethasone induces cancer mitigation and irreversible senescence in lung cancer cells via damaging cortical actin and sustained hyperphosphorylation of pRb. Steroids 2023; 198: 109269.
[12] Xiang Z, Zhou Z, Song S, Li J, Ji J, Yan R, Wang J, Cai W, Hu W, Zang L, Zhu Z, Zhang Z, Li M and Yu Y. Dexamethasone suppresses immune evasion by inducing GR/STAT3 mediated downregulation of PD-L1 and IDO1 pathways. Oncogene 2021; 40: 5002-5012.
[13] Li Y, He F, Liu S, Zhang Y, Li L, Wang B, Lan L and Pan Z. Effect of pretreatment with dexamethasone on the efficacy and immune-related adverse events of immunotherapy in first-line treatment for advanced non-small cell lung cancer: a network meta-analysis of randomized control trials. Am J Clin Exp Immunol 2021; 10: 93-102.
[14] Rami-Porta R, Nishimura KK, Giroux DJ, Detterbeck F, Cardillo G, Edwards JG, Fong KM, Giuliani M, Huang J, Kernstine KH Sr, Marom EM, Nicholson AG, Van Schil PE, Travis WD, Tsao MS, Watanabe SI, Rusch VW and Asamura H; Members of the IASLC Staging and Prognostic Factors Committee and of the Advisory Boards, and Participating Institutions. The International Association for the Study of Lung Cancer lung cancer staging project: proposals for revision of the TNM stage groups in the forthcoming (Ninth) edition of the TNM classification for lung cancer. J Thorac Oncol 2024; 19: 1007-1027.
[15] Mollica V, Rizzo A, Marchetti A, Tateo V, Tassinari E, Rosellini M, Massafra R, Santoni M and Massari F. The impact of ECOG performance status on efficacy of immunotherapy and immune-based combinations in cancer patients: the MOUSEION-06 study. Clin Exp Med 2023; 23: 5039-5049.
[16] Radhakrishnan V, Venkatakrishnan K, Perumal Kalaiyarasi J, Selvarajan G, Mahaboobasha N, Victor PV, Anbazhagan M, Sivanandam DM and Rajaraman S. Dexamethasone-free antiemetic prophylaxis for highly emetogenic chemotherapy: a double-blind, phase III randomized controlled trial (CINV POD study). JCO Glob Oncol 2024; 10: e2300301.
[17] Feng X, Liu X, Guan H, Chen C, Gao F, Gao X, Chen M, Zhao J, Xu Y and Wang M. Safety and efficacy of radiotherapy combined with sintilimab in advanced NSCLC patients who progressed on first or second line therapy: a prospective, multiple center, and single-arm study. Thorac Cancer 2025; 16: e70043.
[18] Heinzerling JH, Mileham KF, Robinson MM, Symanowski JT, Induru RR, Brouse GM, Corso CD, Prabhu RS, Haggstrom DE, Moeller BJ, Bobo WE, Fasola CE, Thakkar VV, Pal SE, Gregory JM, Norek SL, Begic XJ, Kesarwala AH, Burri SH and Simone CB 2nd. Primary lung tumour stereotactic body radiotherapy followed by concurrent mediastinal chemoradiotherapy and adjuvant immunotherapy for locally advanced non-small-cell lung cancer: a multicentre, single-arm, phase 2 trial. Lancet Oncol 2025; 26: 85-97.
[19] Chen YL, Xie YQ, Wei MY and Xu DM. Clinical effects of detailed nursing management interventions on medication adherence and disease perception in patients with drug-resistant tuberculosis. World J Clin Cases 2024; 12: 4191-4198.
[20] Miao D, Zhao J, Han Y, Zhou J, Li X, Zhang T, Li W and Xia Y. Management of locally advanced non-small cell lung cancer: state of the art and future directions. Cancer Commun (Lond) 2024; 44: 23-46.
[21] Laird BJA, Skipworth R, Bonomi PD, Fallon M, Kaasa S, Giorgino R, McMillan DC and Currow DC. Anamorelin efficacy in non-small-cell lung cancer patients with cachexia: insights from ROMANA 1 and ROMANA 2. J Cachexia Sarcopenia Muscle 2025; 16: e13732.
[22] Yu H, Chen J, Zhou Y, Sheng J, Zhang X, He L, Chen L, Chu Q, Zhang L and Hong S. Impact of prophylactic dexamethasone on the efficacy of immune checkpoint inhibitors plus platinum-based chemotherapy in patients with advanced non-squamous non-small-cell lung cancer. Int Immunopharmacol 2023; 125: 111138.
[23] Wei H, Sun Y, Xie L, Jia Y, He J, Deng X, Huang W, Hu Y and Zhu J. Huo Xiang Zheng Qi oral liquid combined with 5-HT3 receptor antagonists and dexamethasone can prevent chemotherapy-induced nausea and vomiting for patients receiving multiday cisplatin-based regimen: a multicenter trial. J Integr Complement Med 2023; 29: 501-509.
[24] Janowitz T, Kleeman S and Vonderheide RH. Reconsidering dexamethasone for antiemesis when combining chemotherapy and immunotherapy. Oncologist 2021; 26: 269-273.

[25] Park HW, Dahlin A, Qiu W and Tantisira KG. Gene expression changes in lymphoblastoid cell lines and primary B cells by dexamethasone. Pharmacogenet Genomics 2019; 29: 58-64.
[26] Chen N, Xie QM, Song SM, Guo SN, Fang Y, Fei GH and Wu HM. Dexamethasone protects against asthma via regulating Hif-1alpha-glycolysis-lactate axis and protein lactylation. Int Immunopharmacol 2024; 131: 111791.
[27] Devraj G, Guerit S, Seele J, Spitzer D, Macas J, Khel MI, Heidemann R, Braczynski AK, Ballhorn W, Gunther S, Ogunshola OO, Mittelbronn M, Kodel U, Monoranu CM, Plate KH, Hammerschmidt S, Nau R, Devraj K and Kempf VAJ. HIF-1alpha is involved in blood-brain barrier dysfunction and paracellular migration of bacteria in pneumococcal meningitis. Acta Neuropathol 2020; 140: 183-208.
[28] Cook AM, McDonnell AM, Lake RA and Nowak AK. Dexamethasone co-medication in cancer patients undergoing chemotherapy causes substantial immunomodulatory effects with implications for chemo-immunotherapy strategies. Oncoimmunology 2015; 5: e1066062.
[29] Kim EJ, Kim JY, Choi HY, Lee H, Lee J, Kim MS, Kim YS, Huh KH and Kim BS. Systemic immunomodulatory effects of combinatorial treatment of thalidomide and dexamethasone on T cells and other immune cells. Yonsei Med J 2021; 62: 137-148.
[30] Liu J, Liu X, Dong M, Zhao H, Li M, Zhang H, Ji H, Shi Y, Cui Y, Wu D, Chen G and Chen J. Symptom trajectories during chemotherapy in patients with non-small cell lung cancer (NSCLC) and the function of prolonging low dose dexamethasone in promoting enhanced recovery after chemotherapy. Thorac Cancer 2021; 12: 783-795.
[31] Wei H, Yue Z, Han J, Chen P, Xie K, Sun Y and Zhu J. Oral compound probiotic supplements can improve the quality of life for patients with lung cancer during chemotherapy: A randomized placebo-controlled study. Thorac Cancer 2024; 15: 182-191.
[32] Tomasik B, Bienkowski M, Braun M, Popat S and Dziadziuszko R. Effectiveness and safety of immunotherapy in NSCLC patients with ECOG PS score ≥2 - Systematic review and meta-analysis. Lung Cancer 2021; 158: 97-106.
[33] Zhao Y, Chen G, Chen J, Zhuang L, Du Y, Yu Q, Zhuang W, Zhao Y, Zhou M, Zhang W, Zhang Y, Wan Y, Li W, Song W, Wang ZM, Li B, Xia M, Yang Y, Fang W, Huang Y and Zhang L. AK112, a novel PD-1/VEGF bispecific antibody, in combination with chemotherapy in patients with advanced non-small cell lung cancer (NSCLC): an open-label, multicenter, phase II trial. EClinicalMedicine 2023; 62: 102106.
[34] Zhao Y, Guo S, Deng J, Shen J, Du F, Wu X, Chen Y, Li M, Chen M, Li X, Li W, Gu L, Sun Y, Wen Q, Li J and Xiao Z. VEGF/VEGFR-targeted therapy and immunotherapy in non-small cell lung cancer: targeting the tumor microenvironment. Int J Biol Sci 2022; 18: 3845-3858.
[35] Zheng H, Ning Y, Zhan Y, Liu S, Yang Y, Wen Q and Fan S. Co-expression of PD-L1 and HIF-1alpha predicts poor prognosis in patients with non-small cell lung cancer after surgery. J Cancer 2021; 12: 2065-2072.
[36] Biziotis OD, Tsakiridis EE, Ali A, Ahmadi E, Wu J, Wang S, Mekhaeil B, Singh K, Menjolian G, Farrell T, Abdulkarim B, Sur RK, Mesci A, Ellis P, Berg T, Bramson JL, Muti P, Steinberg GR and Tsakiridis T. Canagliflozin mediates tumor suppression alone and in combination with radiotherapy in non-small cell lung cancer (NSCLC) through inhibition of HIF-1alpha. Mol Oncol 2023; 17: 2235-2256.
[37] Zhang D, Tian X, Wang Y, Liu F, Zhang J, Wang H, Zhang N, Yan T, Lin C, Shi Z, Liu R and Jiang S. Polyphyllin I ameliorates gefitinib resistance and inhibits the VEGF/VEGFR2/p38 pathway by targeting HIF-1a in lung adenocarcinoma. Phytomedicine 2024; 129: 155690.
[38] Liu H, Hong Q, Zheng S, Zhang M and Cai L. Effective treatment strategies and key factors influencing therapeutic efficacy in advanced SMARCA4-deficient non-small cell lung cancer. Lung Cancer 2024; 198: 108022.
[39] Hu D, Pang X, Luo J, Zhou J, Wang N, Tang H, Wang L and Zhao X. The correlation between the influencing factors and efficacy of immune checkpoint inhibitor therapy: an umbrella meta-analysis of randomized controlled trials. Ann Med 2023; 55: 2215543.
[40] Wright J, Nielsen T, Burns S, Weekes N, Pradhan A, Teus JK and McErlean G. Management of glucocorticoid-induced hyperglycemia in cancer patients: a feasibility study. Clin Nurs Res 2025; 34: 3-11.
[41] Natalicchio A, Marrano N, Montagnani M, Gallo M, Faggiano A, Zatelli MC, Argentiero A, Del Re M, D'Oronzo S, Fogli S, Franchina T, Giuffrida D, Gori S, Ragni A, Marino G, Mazzilli R, Monami M, Morviducci L, Renzelli V, Russo A, Sciacca L, Tuveri E, Cortellini A, Di Maio M, Candido R, Perrone F, Aimaretti G, Avogaro A, Silvestris N and Giorgino F. Glycemic control and cancer outcomes in oncologic patients with diabetes: an Italian Association of Medical Oncology (AIOM), Italian Association of Medical Diabetologists (AMD), Italian Society of Diabetology (SID), Italian Society of Endocrinology (SIE), Italian Society of Pharmacology (SIF) multidisciplinary critical view. J Endocrinol Invest 2024; 47: 2915-2928.