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Original Article

PD-1 inhibitor therapy combined with argon-helium cryoablation is effective against non-small cell lung cancer

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Abstract: Objective: To evaluate the clinical efficacy of programmed death-1 (PD-1) inhibitor therapy combined with argon-helium cryoablation in patients with non-small cell lung cancer (NSCLC). Methods: A total of 108 NSCLC patients were enrolled. The control group included 52 patients who received PD-1 inhibitor monotherapy, while 56 patients received combination therapy with PD-1 inhibitors and argon-helium cryoablation (research group). Treatment efficacy, incidence of adverse events, serum tumor marker levels (carcinoembryonic antigen, cytokeratin fragment 19), and humoral immune function (immunoglobulin (Ig) G, IgM, and IgA), and quality of life (as measured by the Karnofsky Performance Status [KPS]) were compared between the two groups. Independent predictors of treatment response were identified through univariate analysis followed by binary logistic regression. A nomogram was subsequently developed to visualize the risk of treatment failure. Results: Although the incidence of adverse events was comparable between groups (P>0.05), the research group demonstrated a significantly higher overall response rate (P<0.05). Post-treatment analyses revealed significant reductions in serum tumor markers and increases in immunoglobulin levels and KPS scores in the research group (all P<0.05). Logistic regression identified age ≥55 years (odds ratio [OR]: 2.427) and tumor diameter ≥6.00 cm (OR: 3.394) as independent predictors of poor treatment response (all P<0.05). The nomogram model exhibited moderate discriminative ability, though calibration suggested a tendency to overestimate response rates in the low-risk subgroup. Conclusion: PD-1 inhibitor therapy combined with argon-helium cryoablation offers a promising and effective treatment strategy for patients with NSCLC.

Keywords: Non-small cell lung cancer, PD-1 inhibitor therapy, argon-helium cryoablation, clinical efficacy

Introduction

Lung cancer (LC) remains the leading cause of cancer-related mortality, with an estimated 2,206,771 new cases and 1,796,144 deaths reported in 2020, making it the most lethal cancer globally [1]. Among LC subtypes, non-small cell LC (NSCLC) is the most prevalent and imposes a significant health burden. Despite advances in early diagnosis and treatment, outcomes for NSCLC - especially in advanced stages (TNM stage IIIB-IV) - remain poor, often due to unresectable tumors and limited therapeutic options [2]. The five-year survival rate for such patients is approximately 20%, highlighting the urgent need for novel therapeutic strategies [3].

Argon-helium cryoablation, a minimally invasive technology, has emerged as a possible treatment for advanced NSCLC. By using both thermal and cryogenic mechanisms - where high-pressure argon rapidly freezes tumor tissue to ultra-low temperatures, followed by helium-induced thawing - this method induces protein denaturation, cell lysis, and tissue necrosis, resulting in local tumor destruction [4, 5]. However, its ability to achieve curative outcomes remains limited, particularly due to suboptimal systemic effects such as insufficient enhancement of immune function [6].

Programmed death-1 (PD-1) inhibitors, a key component of immune checkpoint blockade therapy, have shown favorable tolerance pro-

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files and promising major pathological response rates in NSCLC. Notably, stromal PD-1 expression has been associated with tumor regression [7, 8]. Moreover, PD-1 inhibitors have demonstrated the ability to downstage locally advanced NSCLC, making surgical resection feasible in previously inoperable patients [9]. Recent evidence suggests that combining PD-1 blockade with cryoablation enhances treatment efficacy, with studies confirming the safety and efficacy of this integrated approach [10].

This study investigates the therapeutic efficacy of combining PD-1 inhibitor therapy with argon-helium cryoablation in NSCLC patients, aiming to establish a novel integrative treatment paradigm. The innovation of this study lies in three key aspects. First, it quantitatively assesses the enhanced antitumor effect achieved through combining PD-1 inhibitors with cryoablation, addressing the limitations of monotherapy and proposing a new local-systemic treatment strategy. Second, by employing a multidimensional evaluation framework - including clinical efficacy, safety, serum tumor markers, humoral immune function, and quality of life - this study demonstrates a statistically significant superiority of the combined approach. Third, the identification of independent predictors of treatment response through multivariate regression enables precise risk stratification, offering quantitative support for individualized treatment planning.

Materials and methods

Patients and study design

This retrospective study included 108 patients with NSCLCtreated at Lijiang Hankang Tumor Hospital between June 2021 and January 2023. Patients were divided into a control group (n=52) receiving PD-1 inhibitor monotherapy and a research group (n=56) receiving PD-1 inhibitor therapy combined with argon-helium cryoablation. This study was approved by the Ethics Committee of Lijiang Hankang Tumor Hospital.

Inclusion criteria were as follows: histologically confirmed NSCLC (including large cell carcinoma, squamous cell carcinoma, and adenocarcinoma) in accordance with the Chinese Primary Lung Cancer Diagnosis and Treatment Specification (2015); TNM stage IIIB-IV; ineligibility for surgical resection; age ≥18 years; absence of contraindications to PD-1 inhibitors; adequate functional status (Eastern Cooperative Oncology Group [ECOG] performance status score 0-2); and complete clinical data.

Exclusion criteria included: severe dysfunction of vital organs; coexisting malignancies or other pulmonary diseases; major surgery within the preceding three months; abnormal coagulation; immunodeficiency; contraindications to cryoablation; diffuse LC or bilateral metastatic disease; expected survival <3 months; significant cardiovascular disease (e.g., unstable angina, recent myocardial infarction within 3 months, severe arrhythmias, congestive heart failure); hematologic disorders associated with bleeding risk (e.g., leukemia, myelodysplastic syndrome, platelet count $<50\times10^9$/L); and history of seizure, stroke (within 6 months), or cognitive impairment.

Intervention methods

Patients in the research group received a combined regimen of PD-1 inhibitor and argon-helium cryoablation. Sintilimab (200 mg per dose; intravenous infusion every 3 weeks; Amyjet Scientific Inc., PSI-10-919-0.1 mg) was administered for 1-2 cycles as induction therapy. Argon-helium cryoablation was performed 7-14 days after completion of induction. Maintenance sintilimab therapy resumed within 7 days post-ablation, following the same dosage and cycle. The combined protocol was continued until disease progression (based on RECIST 1.1 criteria) or for a maximum of 24 months, whichever occurred first.

Cryoablation procedure: Under imaging guidance, patients were positioned to optimally expose the tumor site. Computed tomography (CT) was used to identify the puncture point and to determine the ideal insertion level, angle, and depth (**Figure 1A**, **1B**). Following local anesthesia and a small skin incision, the argon-helium probe was inserted. Two cryoablation cycles were conducted, each consisting of a 15-minute freeze phase at -170°C, followed by passive rewarming to 40°C and active helium-assisted rewarming to 20°C. The ablation zone was extended at least 10 mm beyond the tumor margin to ensure complete coverage (**Figure 1C**). Post-operatively, patients received intravenous Camrelizumab (200 mg/day, Jiangsu Henrui Pharmaceutical Co., LTD.,

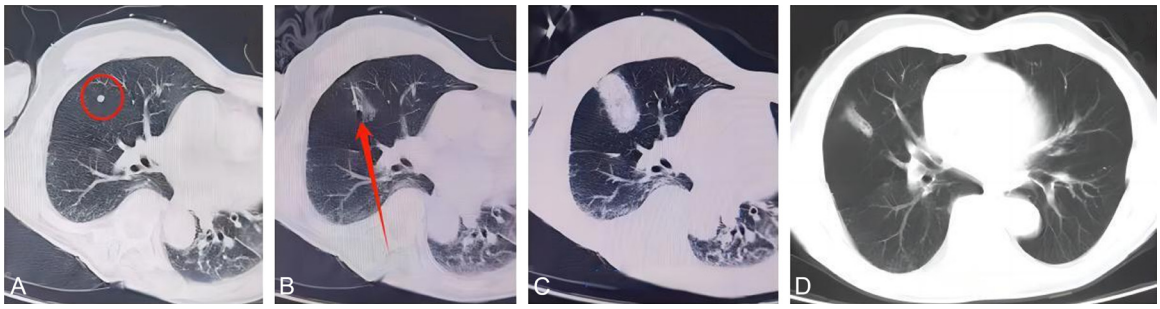

Figure 1. Illustration of procedure of percutaneous cryosurgery. A. Identification of Pulmonary Lesion Nodule; the circle marks the location of pulmonary nodular lesions. B. Puncture Site for Argon-Helium Knife Application. C. Cryoablation with ice balls; the arrow indicates the puncture site for argon-helium cryoablation. D. Follow-up examination 1 month after Percutaneous Cryosurgery.

China) on day 2, with a follow-up CT scan conducted one month later (**Figure 1D**).

Patients in the control group (PD-1 inhibitors) received sintilimab monotherapy using the same schedule and maximum treatment duration as the research group.

Outcome measures

Treatment efficacy: Responses were classified as: Complete Response (CR): complete disappearance of all target lesions, confirmed by repeat imaging for ≥4 weeks.

Partial response (PR): ≥50% reduction in total tumor burden, sustained ≥4 weeks.

No change (NC): <25% increase or <50% decrease in tumor size, stable for ≥4 weeks.

Progressive disease (PD): new lesions or ≥25% increase in tumor diameter. Response rate (RR) = (CR + PR)/total number of patients.

Adverse events: Incidence rates of treatment-related adverse events - including thyroid dysfunction, pneumonitis, colitis, rash, and pneumothorax - were recorded and compared between groups.

Serum tumor markers: Serum levels of carcinoembryonic antigen (CEA), cytokeratin fragment 19 (CYFRA21-1), and carbohydrate antigen 125 (CA125) were measured pre- and post-treatment using enzyme-linked immunosorbent assay (ELISA; Amyjet Scientific Inc., NDC-KBB-A7F95S-5×96, GBS-IT1781, NDC-KBB-URDN-7M-96).

Humoral immune function: Serum levels of immunoglobulin (Ig) G, IgM, and IgA were assessed using immunoturbidimetric analysis (Shanghai Wellan Biotechnology Co., Ltd.; WS5421W, WS6421W, WS4421W).

Quality of life [11]: Assessed by the Karnofsky Performance Status (KPS) scale (0-100), with higher scores reflecting better functional capacity and well-being.

Primary endpoints included treatment efficacy, adverse events, tumor markers, and humoral immune function. KPS scores were considered secondary outcomes.

Statistical methods

All data were analyzed using SPSS 26.0. Quantitative variables with normal distribution were expressed as mean ± standard deviation ($\bar{x}\pm s$) and analyzed using independent-sample t-tests (between groups) or paired t-tests (within groups). Categorical variables were expressed as frequencies and percentages [n (%)] and compared using the χ^2 test. Univariate and multivariate analyses (binary logistic regression) were performed to identify independent predictors of treatment efficacy. Internal validation was conducted using 1,000 bootstrap resamples, and calibration curves were plotted to evaluate model accuracy. A two-sided *P*-value <0.05 was considered significant.

Results

Comparison of patient baseline characteristics

There were no significant differences between the two groups in terms of age, sex, body mass index, tumor diameter, TNM stage, or pathologic subtype (all P>0.05, **Table 1**).

Table 1. Comparison of clinical characteristics

Data	n	Control group (n=52)	Research group (n=56)	χ^2/t	P
Age (years, $\bar{x}\pm s$)	108	54.42±10.09	52.71±10.15	0.877	0.382
Sex [n (%)]				0.812	0.368
Male	68	35 (67.31)	33 (58.93)		
Femsle	40	17 (32.69)	23 (41.07)		
Body mass index (kg/m^2, $\bar{x}\pm s$)	108	23.04±1.81	23.21±1.93	0.471	0.638
Tumor diameter (cm, $\bar{x}\pm s$)	108	5.46±2.34	5.84±2.45	0.823	0.412
TNM [n (%)]				0.496	0.781
IIIB	46	21 (40.38)	25 (44.64)		
IIIC	20	9 (17.31)	11 (19.64)		
IV	42	22 (42.31)	20 (35.71)		
Pathologic type [n (%)]				1.027	0.795
Adenocarcinoma	63	29 (55.77)	34 (60.71)		
Squamous carcinoma	37	20 (38.46)	17 (30.36)		
Large cell carcinoma	5	2 (3.85)	3 (5.36)		
Others	3	1 (1.92)	2 (3.57)		

Note: TNM: Tumor, Node, Metastasis.

Table 2. Comparison of curative effects

Data	Control group (n=52)	Research group (n=56)	χ^2	P
CR	2 (3.85)	12 (21.43)		
PR	26 (50.00)	30 (53.57)		
NC	15 (28.85)	14 (25.00)		
PD	9 (17.31)	0 (0.00)		
RR	28 (53.85)	42 (75.00)	5.291	0.021

Note: CR, complete response; PR, partial response; NC, no change; PD, progressive disease; RR, response rate.

Comparison of therapeutic outcomes

The RR was significantly higher in the research group compared to the control group (P<0.05, **Table 2**).

Factors affecting treatment efficacy

Univariate analysis identified age, BMI, tumor diameter, and treatment regimen as factors significantly associated with treatment response (all P<0.05).

Subsequent binary logistic regression confirmed age ≥55 years (odds ratio [OR]: 2.427) and tumor diameter ≥6.00 cm (OR: 3.394) as independent predictors of treatment efficacy (both P<0.05).

Based on these findings, a nomogram was constructed to visualize the estimated risk of treatment failure, spanning a range from 15.0% to 55.0% (**Tables 3**, **4**; **Figure 2**).

Model performance was evaluated using 1,000 bootstrap resamples. The concordance index (C-index) of the predictive model was 0.693 (95% confidence interval [CI]: 0.594-0.788), indicating moderate discriminatory power for patient stratification.

The calibration curve showed a tendency to overestimate response probabilities below 25%, while predictions between 25% and 75% were well-calibrated (**Figure 2**).

Comparison of adverse events

There was no significant difference in the overall incidence of treatment-related adverse events between the two groups (P>0.05, **Table 5**).

Comparison of serum tumor marker levels

Serum levels of CEA, CYFRA21-1, and CA125 were measured. Baseline levels were similar between the two groups (all P>0.05).

Table 3. Univariate analysis of factors affecting treatment efficacy

Data	n	Non-response group (n=38)	Response group (n=70)	χ^2	P
Age (years)				5.291	0.021
<55	56	14 (36.84)	42 (60.00)		
≥55	52	24 (63.16)	28 (40.00)		
Sex				0.149	0.699
Male	68	23 (60.53)	45 (64.29)		
Female	40	15 (39.47)	25 (35.71)		
Body mass index (kg/m^2)				3.900	0.048
<23	42	10 (26.32)	32 (45.71)		
≥23	66	28 (73.68)	38 (54.29)		
Tumor diameter (cm)				5.757	0.016
<6.00	51	12 (31.58)	39 (55.71)		
≥6.00	57	26 (68.42)	31 (44.29)		
TNM				2.897	0.235
IIIB	46	13 (34.21)	33 (47.14)		
IIIC	20	10 (26.32)	10 (14.29)		
IV	42	15 (39.47)	27 (38.57)		
Pathologic type				1.479	0.687
Adenocarcinoma	63	22 (57.89)	41 (58.57)		
Squamous carcinoma	37	12 (31.58)	25 (35.71)		
Large cell carcinoma	5	2 (5.26)	3 (4.29)		
Others	3	2 (5.26)	1 (1.43)		
Treatment modality				5.291	0.021
Argon-helium cryoablation	52	24 (63.16)	28 (40.00)		
PD-1 inhibitor therapy + argon-helium cryoablation	56	14 (36.84)	42 (60.00)		

Note: TNM: Tumor, Node, Metastasis; PD-1, programmed death receptor 1.

After treatment, both groups exhibited significant reductions in all three markers (all P< 0.05), with the research group showing lower post-treatment levels than the control group (all P<0.05, **Figure 3**).

Comparison of humoral immune function

Serum immunoglobulin levels (IgG, IgM, and IgA) were used to assess humoral immune function. No significant differences were observed at baseline (all P>0.05).

Following treatment, both groups showed significant increases in IgG, IgM, and IgA levels (all P<0.05), with greater improvements in the research group compared to the control group (all P<0.05, **Figure 4**).

Comparison of quality of life

KPS scores were used to evaluate patient-reported quality of life. Baseline scores did not differ significantly between groups (P>0.05).

KPS scores were similar at baseline, and improved after treatment (P<0.05), with the research group achieving greater gains than the control group (P<0.05, **Figure 5**).

Discussion

Non-small cell lung cancer (NSCLC), a malignancy arising from the bronchial glands, mucosa, and alveolar epithelium, represents a major global health challenge due to its high morbidity and mortality rates [12, 13]. Although early surgical intervention can be curative, most NSCLC cases are diagnosed at advanced stages, precluding radical resection and necessitating alternative treatment approaches [14].

Argon-helium cryoablation is a minimally invasive technique that uses rapid freezing and controlled rewarming to ablate tumor tissue. The extreme cold induces protein denaturation, cell lysis, and ischemic necrosis, thereby achieving tumor destruction while preserving surrounding tissue integrity [15-17]. However,

Table 4. Multivariate analysis of factors influencing therapeutic outcome

Factor	B	SE	Wald	P	Exp (B)	95% CI	
						Lower bound	Upper bound
Age (years)	0.887	0.449	3.896	0.048	2.427	1.006	5.856
Body mass index (kg/m^2)	0.831	0.487	2.920	0.087	2.297	0.885	5.960
Tumor diameter (cm)	1.222	0.465	6.919	0.009	3.394	1.365	8.437
Treatment modality	0.860	0.448	3.688	0.055	2.362	0.982	5.681

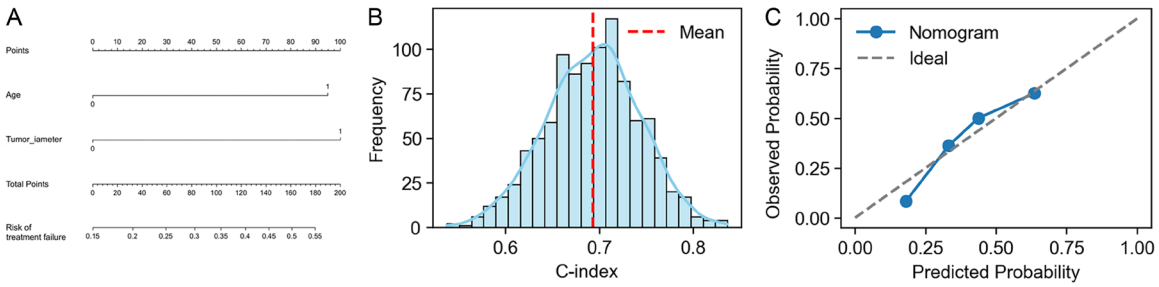

Figure 2. Nomogram for predicting the risk of treatment failure in patients and relevant validation. A. Nomogram for predicting the risk of treatment failure in patients. B. C-index distribution. C. Calibration curve.

Table 5. Comparison of adverse events

Data	Control group (n=52)	Research group (n=56)	χ^2	P
Thyroid dysfunction	5 (9.62)	8 (14.29)		
Pneumonia	3 (5.77)	5 (8.93)		
Colitis	3 (5.77)	4 (7.14)		
Rash	4 (7.69)	5 (8.93)		
Pneumothorax	2 (3.85)	5 (8.93)		
Total	17 (32.69)	27 (48.21)	2.691	0.101

its limitations include suboptimal systemic effects and limited capacity to prevent recurrence and metastasis [18]. PD-1 inhibitors, a class of immune checkpoint inhibitors, block the PD-1/PD-L1 axis and restore T-cell-mediated antitumor immunity [19]. While they have demonstrated significant clinical efficacy in NSCLC, challenges such as treatment resistance and immune-related adverse events persist [20, 21].

Our results demonstrate that combining PD-1 inhibitors with argon-helium cryoablation significantly enhances treatment efficacy in NSCLC without increasing the overall incidence of adverse events. These findings are consistent with prior studies. Gao et al. [22] reported that the combination therapy significantly reduced tumor burden and improved immune function in a cohort of 20 patients with advanced NSCLC. Similarly, Feng et al. [23] observed improved outcomes with nivolumab plus cryoablation without a notable rise in toxicity.

Preclinical studies provide mechanistic insights into this synergy. In murine breast cancer models, PD-1 monoclonal antibodies enhanced cryoablation-induced antitumor immune responses [24]. Additionally, in Lewis lung adenocarcinoma models, this combination therapy was shown to activate the PI3K/AKT/mTOR signaling pathway, further augmenting antitumor immunity [25]. In our study, thyroid dysfunction, pneumonitis, and colitis were the most common immune-related adverse events. Given the established correlation between such adverse events and improved treatment responses [21], our findings underscore the delicate balance between therapeutic benefit and immune toxicity.

Multivariate analysis identified older age (≥55 years) and larger tumor size (≥6.00 cm) as inde-

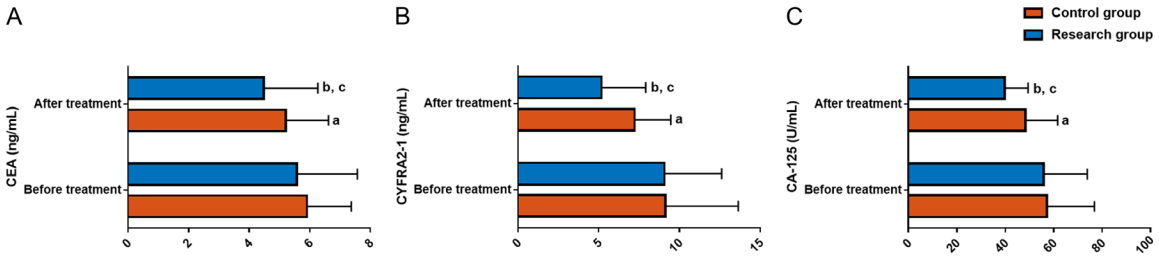

Figure 3. Comparison of Serum tumor marker levels in the two groups. A. CEA levels pre- and post-treatment in control and research groups. B. CYFRA21-1 levels pre- and post-treatment control and research groups. C. CA-125 levels pre- and post-treatment control and research groups. Note: CEA, carcinoembryonic antigen; CYFRA21-1, cytokeratin fragment 19; CA125, carbohydrate antigen 125. aP<0.05, bP<0.01 vs. pre-treatment; cP<0.05 vs. control group.

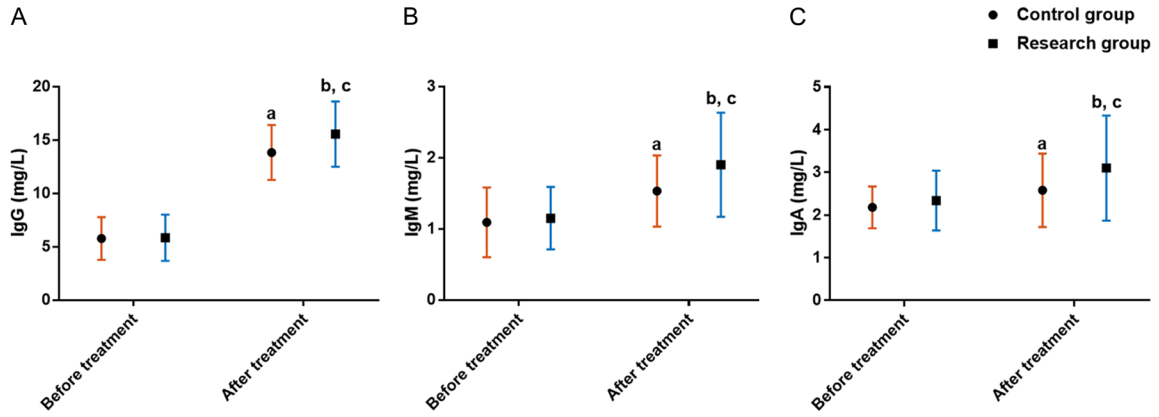

Figure 4. Comparison of humoral immune function in both groups. A. IgG changes pre- and post-treatment in control and research groups. B. IgM changes pre- and post-treatment in control and research groups. C. IgA changes pre- and post-treatment in control and research groups. Note: IgG/M/A, immunoglobulin G/M/A. aP<0.05, bP<0.01 vs. pre-treatment; cP<0.05 vs. control group.

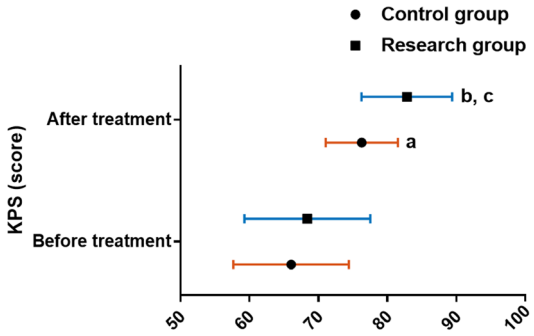

Figure 5. Comparison of quality of life in both groups. Note: KPS, Karnofsky Performance Status. aP<0.05, bP<0.01 vs. pre-treatment; cP<0.05 vs. control group.

pendent predictors of poor treatment response. Possible mechanisms include: (1) immunosenescence-associated impairments in innate and adaptive immunity in elderly patients, reducing treatment responsiveness; and (2) the elevated tumor burden associated with larger lesions may promote immunosuppressive signaling and immune escape [26, 27]. These observations align with findings by Bai et al. [28], who reported that patients with EGFR-mutant advanced NSCLC and favorable prognostic features - such as prolonged PFS-TKI, prior extracranial radiotherapy, and higher BMI - benefited more from immunotherapy.

In addition to higher response rates, our study showed that combination therapy was superior in suppressing serum tumor markers (CEA, CYFRA21-1, CA125), enhancing humoral immune function (IgG, IgM, IgA), and improving quality-of-life scores. We also developed a nomogram incorporating significant multivariate predictors to facilitate individualized risk stratification. Internal validation using 1,000 bootstrap iterations revealed moderate discriminative performance. The model tended to overestimate response probabilities below

25%, but provided reliable estimates within the 25-75% range.

Despite its strengths, our study had several limitations. The single-center retrospective design, relatively small sample size, and limited survival follow-up may introduce bias. Future research should include larger, multicenter prospective trials with long-term follow-up to validate and extend these findings. Furthermore, while our nomogram shows promise as a clinical decision-making tool, it has not undergone external validation and should be used cautiously in practice until further confirmation is obtained.

In conclusions, this study highlighted the therapeutic potential of combining argon-helium cryoablation with PD-1 inhibitor therapy in patients with advanced NSCLC. The combination appears to improve clinical efficacy, immune function, and quality of life without substantially increasing adverse events. Further studies are needed to confirm long-term benefits and optimize clinical application of this combined treatment.

Disclosure of conflict of interest

None.

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References

[1] 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.

[2] Neupane S, Nevalainen J, Raitanen J, Talala K, Kujala P, Taari K, Tammela TLJ, Steyerberg EW and Auvinen A. Prognostic index for predicting prostate cancer survival in a randomized screening trial: development and validation. Cancers (Basel) 2021; 13: 435.

[3] Alzubaidi SJ, Liou H, Saini G, Segaran N, Scott Kriegshauser J, Naidu SG, Patel IJ and Oklu R. Percutaneous image-guided ablation of lung tumors. J Clin Med 2021; 10: 5783.

[4] Shen MY, Di YX, Wang X, Tian FX, Zhang MF, Qian FY, Jiang BP, Zhou XP and Zhou LL. Panax notoginseng saponins (PNS) attenuate Th17 cell differentiation in CIA mice via inhibition of nuclear PKM2-mediated STAT3 phosphorylation. Pharm Biol 2023; 61: 459-472.

[5] Mueller LE, Issa PP, Hussein MH, Elshazli RM, Haidari M, Errami Y, Shama M, Fawzy MS, Kandil E and Toraih E. Clinical outcomes and tumor microenvironment response to radiofrequency ablation therapy: a systematic review and meta-analysis. Gland Surg 2024; 13: 4-18.

[6] Hung WT, Tsai SC, Wu TC, Tu HT, Lin HC, Su CL, Wu YC, Lin LC and Lin FC. Enhancing precision in lung tumor ablation through innovations in CT-guided technique and angle control. Thorac Cancer 2024; 15: 867-877.

[7] Gao S, Li N, Gao S, Xue Q, Ying J, Wang S, Tao X, Zhao J, Mao Y, Wang B, Shao K, Lei W, Wang D, Lv F, Zhao L, Zhang F, Zhao Z, Su K, Tan F, Gao Y, Sun N, Wu D, Yu Y, Ling Y, Wang Z, Duan C, Tang W, Zhang L, He S, Wu N, Wang J and He J. Neoadjuvant PD-1 inhibitor (Sintilimab) in NSCLC. J Thorac Oncol 2020; 15: 816-826.

[8] Upadhaya S, Neftelinov ST, Hodge J and Campbell J. Challenges and opportunities in the PD1/PDL1 inhibitor clinical trial landscape. Nat Rev Drug Discov 2022; 21: 482-483.

[9] Chen T, Ning J, Campisi A, Dell'Amore A, Ciarrocchi AP, Li Z, Song L, Huang J, Yang Y, Stella F and Luo Q. Neoadjuvant PD-1 inhibitors and chemotherapy for locally advanced NSCLC: a retrospective study. Ann Thorac Surg 2022; 113: 993-999.

[10] Liu Q, Zhang C, Chen X and Han Z. Modern cancer therapy: cryoablation meets immune checkpoint blockade. Front Oncol 2024; 14: 1323070.

[11] Sasagasako T, Ueda A, Mineharu Y, Mochizuki Y, Doi S, Park S, Terada Y, Sano N, Tanji M, Arakawa Y and Okuno Y. Postoperative karnofsky performance status prediction in patients with IDH wild-type glioblastoma: a multimodal approach integrating clinical and deep imaging features. PLoS One 2024; 19: e0303002.

[12] Dora D, Szocs E, Soos A, Halasy V, Somodi C, Mihucz A, Rostas M, Mogor F, Lohinai Z and Nagy N. From bench to bedside: an interdisciplinary journey through the gut-lung axis with insights into lung cancer and immunotherapy. Front Immunol 2024; 15: 1434804.

[13] Zhan S, Wang L, Wang W and Li R. Insulin resistance in NSCLC: unraveling the link between development, diagnosis, and treatment. Front Endocrinol (Lausanne) 2024; 15: 1328960.

[14] Kratzer TB, Bandi P, Freedman ND, Smith RA, Travis WD, Jemal A and Siegel RL. Lung cancer statistics, 2023. Cancer 2024; 130: 1330-1348.

[15] Chen Y, Fang X, Wang D, Li Q, Zhang K, Li Y, Li J, Pang H, Cheng Z, Zhang C, Zhang C, Yang W, Zhu B, Fan H, Han C, An Y, Zhang L, Luo B,

Zhang S, Lu T, Meng Y, Jiao Q, Tang H, Zhou T and Hu K. Is cryoablation still suitable for advanced non-small cell lung cancer after failure of first-line chemotherapy? A multicenter, prospective, randomized-controlled trial of eighty-seven patients. Cryobiology 2024; 115: 104864.

[16] Ye X, Fan W, Wang Z, Wang J, Wang H, Niu L, Fang Y, Gu S, Liu L, Liu B, Zhuang Y, Wei Z, Li X, Li X, Li Y, Li C, Yang X, Yang W, Yang P, Lin Z, Meng Z, Hu K, Liu C, Huang Y, Huang G, Huang K, Peng Z, Han Y, Jin Y, Lei G, Zhai B, Li H, Pan J, Filippiadis D, Kelekis A, Pua U, Futacsi B, Yumchinserchin N, Iezzi R, Tang A and Roy SH. Clinical practice guidelines on image-guided thermal ablation of primary and metastatic lung tumors (2022 edition). J Cancer Res Ther 2022; 18: 1213-1230.

[17] Zheng Z, Zhao Y, An Y, Li N, Bo C, Ma W, Guo Y, Zou C, Tian B and Zhang S. Efficacy of argon-helium cryoablation and its effects on immune function of patients with neck malignant tumours. Clin Otolaryngol 2021; 46: 206-212.

[18] Zhang X and Sun Y. Argon-helium cryoablation treatment of undifferentiated pleomorphic sarcoma of the thyroid: A case report and literature review. J Interv Med 2023; 6: 194-198.

[19] Yi M, Jiao D, Xu H, Liu Q, Zhao W, Han X and Wu K. Biomarkers for predicting efficacy of PD-1/PD-L1 inhibitors. Mol Cancer 2018; 17: 129.

[20] Bie F, Tian H, Sun N, Zang R, Zhang M, Song P, Liu L, Peng Y, Bai G, Zhou B and Gao S. Research progress of Anti-PD-1/PD-L1 immunotherapy related mechanisms and predictive biomarkers in NSCLC. Front Oncol 2022; 12: 769124.

[21] Zhao Z, Wang X, Qu J, Zuo W, Tang Y, Zhu H and Chen X. Immune-related adverse events associated with outcomes in patients with NSCLC treated with Anti-PD-1 inhibitors: a systematic review and meta-analysis. Front Oncol 2021; 11: 708195.

[22] Gao Z, Teng J, Qiao R, Qian J, Pan F, Ma M, Lu J, Zhang B, Chu T and Zhong H. Efficacy and safety of a therapy combining sintilimab and chemotherapy with cryoablation in the first-line treatment of advanced nonsquamous non-small cell lung cancer: protocol for a phase II, pilot, single-arm, single-center study. JMIR Res Protoc 2024; 13: e64950.

[23] Feng J, Guiyu D and Xiongwen W. The clinical efficacy of argon-helium knife cryoablation combined with nivolumab in the treatment of advanced non-small cell lung cancer. Cryobiology 2021; 102: 92-96.

[24] Yu ZP, Sun XW, He YP, Gu J and Jin Y. PD-1 monoclonal antibodies enhance the cryoablation-induced antitumor immune response: a breast cancer murine model research. Int J Hyperthermia 2023; 40: 2164625.

[25] Liu Q, Chen X, Qi M, Li Y, Chen W, Zhang C, Wang J, Han Z and Zhang C. Combined cryoablation and PD-1 inhibitor synergistically enhance antitumor immune responses in Lewis lung adenocarcinoma mice via the PI3K/AKT/mTOR pathway. Biochim Biophys Acta Mol Basis Dis 2024; 1870: 167262.

[26] Alexa-Stratulat T, Pavel-Tanasa M, Cianga VA and Antoniu S. Immune senescence in non-small cell lung cancer management: therapeutic relevance, biomarkers, and mitigating approaches. Expert Rev Anticancer Ther 2022; 22: 1197-1210.

[27] Dall'Olio FG, Marabelle A, Caramella C, Garcia C, Aldea M, Chaput N, Robert C and Besse B. Tumour burden and efficacy of immune-checkpoint inhibitors. Nat Rev Clin Oncol 2022; 19: 75-90.

[28] Bai M, Wang W, Gao X, Wu L, Jin P, Wu H, Yu J and Meng X. Efficacy of immune checkpoint inhibitors in patients with EGFR mutated NSCLC and potential risk factors associated with prognosis: a single institution experience. Front Immunol 2022; 13: 832419.