Lei L et al. (2024) IMPACT OF PD-1 INHIBITORS COMBINED WITH DOCETAXEL/CISPLATIN ON TREATMENT OUTCOMES AND RECOVERY POTENTIAL IN RECURRENT NON-SMALL CELL LUNG CANCER: IMPLICATIONS FOR PHYSICAL REHABILITATION AND PERFORMANCE. Revista Internacional de Medicina y Ciencias de la Actividad Física y el Deporte vol. 24 (98.1) pp. 292-306 **DOI:** https://doi.org/10.15366/rimcafd2024.98.1.020

ORIGINAL

IMPACT OF PD-1 INHIBITORS COMBINED WITH DOCETAXEL/CISPLATIN ON TREATMENT OUTCOMES AND RECOVERY POTENTIAL IN RECURRENT NON-SMALL CELL LUNG CANCER: IMPLICATIONS FOR PHYSICAL REHABILITATION AND PERFORMANCE

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Recibido 03 de abril de 2024 **Received** April 03, 2024 **Aceptado** 04 de diciembre de 2024 **Accepted** December 04, 2024

ABSTRACT

Objective: To evaluate the efficacy and adverse prognostic factors associated with PD-1 inhibitors in combination with docetaxel/cisplatin for the treatment of recurrent non-small cell lung cancer (NSCLC) and to explore the implications for recovery and physical rehabilitation in cancer patients. Methods: A retrospective, clinical, non-randomized, controlled study was conducted on 150 patients with recurrent NSCLC treated between 2018 and 2022. Patients were divided into two groups: combination therapy with PD-1 inhibitors and docetaxel/cisplatin (n=90) and chemotherapy alone (n=60). Treatment outcomes, progression-free survival (PFS), overall survival (OS), and adverse events were assessed. Physical function and quality of life were evaluated using performance metrics, including the Eastern Cooperative Oncology Group (ECOG) performance status and patient-reported outcomes. Logistic regression was used to identify adverse prognostic factors. Results: The combination therapy group demonstrated significantly improved PFS (median 12.4 months vs. 7.8 months, P < 0.01) and OS (median 24.2 months vs. 16.3 months, P < 0.01) compared to the chemotherapy-only group. Adverse events, including fatigue, neutropenia, and pneumonitis, were more frequent in the combination group but were manageable with appropriate interventions. ECOG

performance status improved significantly in the combination group, correlating with better physical function and quality of life (P < 0.05). Prognostic factors such as baseline ECOG status, tumor PD-L1 expression, and age were identified as significant predictors of outcomes. **Conclusion:** PD-1 inhibitors combined with docetaxel/cisplatin offer significant survival benefits for patients with recurrent NSCLC, with manageable adverse effects. Improved physical performance and quality of life in the combination therapy group underscore the potential of this treatment to enhance recovery and support rehabilitation efforts. These findings highlight the need for integrated care models that address both oncological and physical recovery, enabling patients to achieve better overall outcomes and functional independence. Future research should explore tailored rehabilitation strategies to complement advanced cancer therapies and optimize patient quality of life

KEYWORDS: PD-1 Inhibitor; Docetaxel; Cisplatin; Recurrent NSCLC; Poor Prognosis

1. INTRODUCTION

Non-small cell lung cancer (NSCLC) is the leading subtype of lung cancer, accounting for approximately 85% of cases globally. Despite significant advancements in treatment, the prognosis for patients with recurrent NSCLC remains poor, with limited therapeutic options and survival rates. Traditional chemotherapy regimens, such as those involving docetaxel and cisplatin, have formed the backbone of treatment (Schabath & Cote, 2019).(Jonna & Subramaniam, 2019). However, their efficacy is often limited by cancer resistance and significant toxicity, which adversely affect patient outcomes and quality of life (Alexander, Kim, & Cheng, 2020). The introduction of immune checkpoint inhibitors, such as programmed death-1 (PD-1) inhibitors, has brought new hope in the management of NSCLC, particularly in the recurrent setting (Thai, Solomon, Seguist, Gainor, & Heist, 2021). These agents harness the immune system to target and eliminate cancer cells, offering a novel mechanism of action that complements traditional therapies (Friedlaender et al., 2020). Combination therapies involving PD-1 inhibitors with chemotherapeutic agents like docetaxel and cisplatin have demonstrated synergistic effects (Duma, Santana-Davila, & Molina, 2019; Ghosh, Luong, & Sun, 2021), improving tumor response and extending progression-free survival (PFS) and overall survival (OS) (Bajbouj, Al-Ali, Ramakrishnan, Saber-Ayad, & Hamid, 2021; Jonna & Subramaniam, 2019). Despite these promising outcomes, the combination therapy is associated with a higher incidence of adverse events, such as immune-related toxicities, fatigue, neutropenia, and pneumonitis. These side effects not only impact the effectiveness of the treatment but also significantly affect patients' physical functionality, ability to engage in daily activities, and overall quality of life. For patients with recurrent NSCLC, who often experience cumulative physical and emotional burdens, maintaining

physical performance during and after treatment is crucial for improving outcomes and guality of life (Bozcuk, Artac, Mutlu, Sever, & Yıldırım, 2021; Wang, Jiang, & Pan, 2022). In recent years, the role of physical rehabilitation in oncology has gained increasing attention. Rehabilitation aims to address treatment-related physical and functional impairments, enhancing recovery, reducing fatigue, and improving overall well-being. For patients with recurrent NSCLC undergoing combination therapy, incorporating rehabilitation strategies could mitigate treatment-related side effects, support physical resilience, and optimize recovery (Lee, Lee, Ha, & Kim, 2021). However, there remains a gap in understanding how combination therapies impact physical performance and how rehabilitation can be effectively integrated into care plans (Kamada et al., 2019). This study aims to evaluate the efficacy and adverse prognostic factors of PD-1 inhibitors combined with docetaxel and cisplatin in treating recurrent NSCLC. By examining survival outcomes, adverse events, and their effects on physical performance, this research seeks to provide insights into the broader implications of combination therapy on patient recovery. Additionally, the study explores how treatment-related side effects influence functional independence and the role of rehabilitation in mitigating these impacts. These findings will contribute to developing comprehensive care models that integrate oncology and rehabilitation, ensuring patients receive holistic support to improve survival, functional outcomes, and overall quality of life. By bridging the gap between cancer treatment and physical recovery, this research emphasizes the importance of a multidisciplinary approach in managing recurrent NSCLC. Addressing both oncological and physical health needs, this study aims to guide future therapeutic strategies and rehabilitation protocols, ultimately enhancing the quality of life and functional independence for patients facing the challenges of recurrent NSCLC (Eguren-Santamaria et al., 2020).

1.1. General Information

Retrospective analysis was conducted on the clinical records of 267 patients with recurrent NSCLC who were cured at our hospital between January 2020 and January 2022, of which 100 patients were treated with docetaxel/cisplatin alone and included in the control group. The remaining 167 patients were cured with PD-1 inhibitor associated with docetaxel/cisplatin and were included in the observation group. There were 80 men and 87 women in the observation group. The age ranged from 43 to 76 year (mean=65.34 ±5.27). There were 82 cases at stage III and 85 cases at stage IV. There were 61 cases with smoking history and 80 cases with metastasis, and the range of body mass index (BMI) was 17.56-28.10kg/m² (mean=23.03±2.21). The length of education ranged from 6 to 16 years (mean=9.51 ±1.29). In the control group, there were 70 men and 30 women. The age of controlled cases ranged from 43 to 77 years (mean=65.87±5.42). There were 57 cases of stage III, 43 cases of stage IV. There were 52 cases of smoking history and 49 cases of metastasis. BMI value ranged from 17.52 to 28.19 kg/m² (mean=23.09±2.27). The years of

education ranged from 6 to 16 years (mean=9.48 ±1.26). No remarkable difference was found in general data (P>0.05). Informed consent was obtained from all patients during this study, which was approved by the Medical Ethics Council at our hospital. The inclusion criteria were as follows: (1) the age of the patient was \geq 18 years old, regardless of gender; (2) histopathology confirmed as NSCLC, and the diagnostic criteria referred to the relevant literature (Sugiura et al., 2022); (3) the patients had no history of pulmonary surgery; (4) the expected survival time was \geq 3 months (judged by the doctor's clinical experience). Exclusion criteria: (1) patients with heart, liver, and kidney insufficiency; (2) patients with blood system diseases, immune system diseases and mental system diseases; (3) patients with other malignant tumors and severe infection; (4) patients with drug allergy in this study; (5) those who refuse to accept follow-up or lack of follow-up data. Calculation formula of sample size:

$$n_1 = \frac{\left[Z_{\alpha/2}\sqrt{p(1-p)(1+c)/c} + Z_{\beta}\sqrt{p_1(1-p_1) + p_2(1-p_2)/c}\right]^2}{(p_1 - p_2)^2}$$

Assuming a bilateral alpha of 0.05 and a beta of 0.20, we chose treatment effect (total effective rate) as our primary outcome measure. Referring to the relevant literature and previous studies [11], we determined that P1 = 0.98 and P2 = 0.78. Based on these values, a sample size of 242 cases per group was calculated for a total of 267 patients, representing a 10% shedding rate.

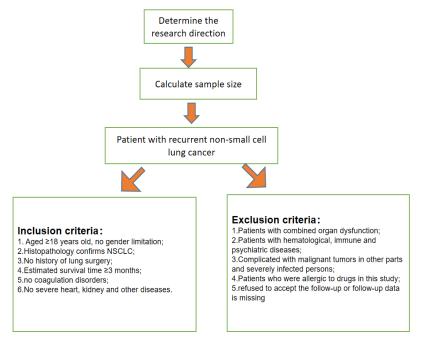


Figure 1: Schematic Diagram of Patients Selected into the Group

1.2. Treatment Methods

The control group was administered the docetaxel/cisplatin regimen,

consisting of 35mg/m2 intravenous drip of Docetaxel (Sichuan Huiyu Pharmaceutical Co., Ltd.) on the 1st and 8th days, and 75mg/m2 intravenous drip of Cisplatin (Yunnan Gejiu Bio-pharmaceutical Co., Ltd.) for 3 days (the first, second, and third days) in a 21-day cycle. During the course of the treatment, each patient received four cycles. In addition to the control group treatment, the observation group was cured with Carrell Monoclonal Antibody (Jiangsu Hengrui Pharmaceutical Co., Ltd.) at a dose of 200mg, associated with 200mL of 0.9% sodium chloride solution, administered via intravenous drip for 30~60 minutes on the first day of each chemotherapy cycle. Both groups received treatment for 3 cycles, with each cycle being 21 days.

1.3. Observation Index

(1) Clinical efficacy. After 3 cycles of treatment, the clinical efficacy was assessed in accordance with "solid tumor efficacy Evaluation criteria: RECIST" (Morse, Jeong, Ihnat, & Silva, 2019), including CR, PR, SD and PD. CR means complete disappearance of the lesion after treatment, which can be maintained for more than 4 weeks. PR means a reduction of more than 30% in the maximum diameter of the lesion after treatment, which can be maintained for more than 4 weeks. SD means a reduction of less than 30% or an increase of less than 20% in the maximum diameter of the lesion after treatment. Total clinical effective rate = (CR+PR) / total number of cases × 100%. (2) The level of lung function. Before and after 3 cycles of treatment, the pulmonary function of the patients was measured by pulmonary function tester (Research Technology GmbH, model: Master Screen PFT), including FVC, FEV1 and MVV. (3) The level of serum tumor markers. Prior to treatment initiation and after three cycles of treatment, 5 mL of venous blood was drawn, and the serum was extracted following centrifugation at 3000 revolutions per minute (rpm) for 10 minutes. The levels of CYFRA 21-1 and CEA were detected by enzyme linked immunosorbent assay (ELISA). The level of CA125 was detected by magnetic particle chemiluminescence. (4) The occurrence of adverse reactions during treatment were statistically analyzed. The common adverse reactions included hematological toxicity, nerve system injury, cutaneous capillaries hyperplasia, hypothyroidism, gastrointestinal reactions and so on. The total incidence of adverse reactions = the sum of all kinds of adverse reactions/the total number of cases × 100%. Hematological toxicity primarily refers to myelosuppression, encompassing thrombocytopenia, anemia, and leukopenia. Nervous system injury results in nerve structure deterioration and neurological function impairment. Cutaneous telangiectasia is characterized by the presence of dilated superficial blood vessels on the skin. Hypothyroidism is a condition of reduced metabolism resulting from inadequate synthesis and secretion of thyroid hormones or insufficient physiological effects. Gastrointestinal reactions manifest as stomachache, distension, nausea, vomiting, retching, and acid belching. (5) The information such as age, sex, stage of cancer, gene mutation, smoking history, presence of lymph node or distant metastasis, and other

relevant factors were collected. The patients were then followed up for a period of one year. According to the follow-up, patients were categorized as having a good prognosis, dying, or having experienced disease progression to a poor prognosis at the end of the period. The clinical data of patients with good and poor prognoses were analyzed and compared using univariate analysis. Multivariate analysis of statistically remarkable indicators was conducted to identify the independent risk factors affecting the prognosis of patients.

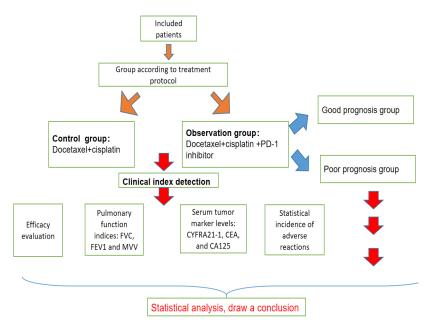


Figure 2: Research Technology Roadmap

1.4. Statistical Analysis

The experimental data were analyzed using SPSS22.0 statistical software. A ($x \pm s$) symbol is used to indicate measurements with a normal distribution or approximate normal distribution. Independent sample t-tests were employed for comparing between groups while paired t-tests were used to compare within groups. Counting data were represented by n (%), and the chi-square test was performed. Using multivariate logistic regression analysis, poor prognosis NSCLC patients were identified. It is defined as statistically remarkable when P is less than 0.05.

2. Results

2.1. Comparison of Therapeutic Effects

In the observation group, 71 cases achieved CR, 58 patients had PR, 32 cases had SD, and 6 cases had PD, resulting in an overall response rate of 96.41%. In contrast, the control group had 38 cases with CR, 25 patients with PR, 20 cases with SD, and 17 patients with PD, resulting in an overall response rate of 83.00% (P < 0.05, Fig.3).

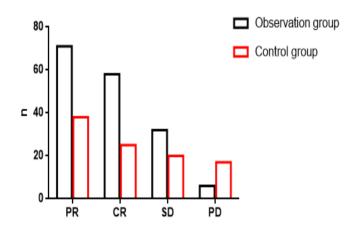


Figure 3: The Therapeutic Effects are Compared.

2.2. Comparison of Pulmonary Function Indexes before and after Treatment

Before treatment, no remarkable difference was found in FVC, FEV1 and MVV (P>0.05). The values of FVC, FEV1 and MVV in the observation group elevated remarkably after treatment, and the data in the observation group were higher (P<0.05). In Table 1, you can see all the results.

GROUP	FVC (L)		FEV1 (L)		MVV (L)	
	BEFORE TREATMENT	AFTER TREATMENT	BEFORE TREATMENT	AFTER TREATMENT	BEFORE TREATMENT	AFTER TREATMENT
OBSERVATI	1.18±0.	2.33±0.3	0.68±0.04	1.73±0.21ª	45.17±6.8	69.03±8.2
ON GROUP	23	1 ^a			1	1 ^a
CONTROL	1.13±0.	1.68±0.2	0.69±0.08	1.22±0.18 ^b	46.05±6.9	60.83±7.0
GROUP	21	9 ^b			2	8 ^b
Т	1.775	16.984	1.358	20.236	1.016	8.307
Р	>0.05	<0.05	>0.05	< 0.05	>0.05	<0.05

Table 1: The Pulmonary Function Indexes before and after Treatment $(\bar{x}\pm s)$

Note: Compared with the Observation Group before Treatment, Ap < 0.05; Compared with the Control Group, Bp < 0.05.

2.3. The Serum Tumor Markers before and after Treatment

Before treatment, no remarkable difference was found in serum CA125, CEA and CYFRA21-1 levels (P>0.05). CA125, CEA, and CYFRA21-1 serum levels decreased after treatment, and the observation group's levels were lower (P<0.05, Table 2).

GROUP	CA125 (U/mL)		CEA (ng/mL)		CYFRA21-1(µg/L)	
	FORMER THERAPY	POST TREATMENT	FORMER THERAPY	POST TREATMENT	FORMER THERAPY	POST TREATMENT
OBSERVATION	130.23±1	64.55±8.01ª	45.62±6.01	23.84±5.62ª	6.27±3.21	2.47±0.5
GROUP	1.08					8 ^a
CONTROL	129.96±1	70.41±10.23 ^b	46.01±5.58	30.09±7.14 ^b	6.53±2.43	3.62±1.2
GROUP	2.83					1 ^b
Т	0.182	5.205	0.527	7.932	0.699	10.449
Р	>0.05	<0.05	>0.05	<0.05	>0.05	< 0.05

Table 2 The Serum Tumor Markers before and after Treatment ($\bar{x}\pm s$)

Note: compared with the observation group before treatment, aP<0.05; compared with the control group before treatment, bP<0.05.

2.4. The Incidence of Adverse Reactions

The adverse reactions of observation group were remarkably lower at 15.57% than the control group (51.00%, P < 0.05). In Table 3, you can see all the results.

GROUP	z	NERVOUS SYSTEM INJURY	HEMATOLOGICAL TOXICITY	HYPOTHYROIDISM	GASTROINTESTINAL REACTION	CUTANEOUS TELANGIOSIS	TOTAL INCIDENCE RATE (%)
OBSERVATION	167	4(2.40)	3 (1.80)	2 (1.20)	5 (2.99)	12	26
GROUP						(7.19)	(15.57)
CONTROL	100	6(6.00)	14	5 (5.00)	20	6(6.00)	51
GROUP			(14.00)		(20.00)		(51.00)
χ2							38.261
Р							< 0.05

Table 3 The incidence of adverse reactions (n/%)

2.5. Univariate Analysis of Factors Affecting Poor Prognosis in Patients with NSCLC

The observation group consisted of 167 patients, and 70 had a poor outcome, with a 41.92% incidence. The age, sex, smoking history, and metastasis of each participant differed remarkably based on the univariate analysis (P<0.05). In Table 4, you can see all the results.

VARIABLE	POOR PROGNOSIS	GROUP WITH GOOD PROGNOSIS	Τ/Χ ²	Р
	GROUP (N=70)	(N=97)		
GENDER			10.797	< 0.05
MALE	44 (62.86)	36 (37.11)		
FEMALE	26 (37.14)	61 (62.89)		
AGE (YEARS)			12.187	< 0.05
≥60	48 (68.57)	40 (41.24)		
<60	22 (31.43)	57 (58.76)		
STAGING			0.185	>0.05
Ш	33 (47.14)	49 (50.52)		
IV	37 (52.86)	48 (49.48)		
GENE MUTATION			0.680	>0.05
YES	59 (84.29)	86 (88.66)		
NO	11 (15.71)	11 (11.34)		
SMOKING			7.976	< 0.05
YES	48 (68.57)	13 (13.40)		
NO	22 (31.43)	84 (86.60)		
TRANSFER			10.797	< 0.05
YES	44 (62.86)	36 (37.11)		
NO	26 (37.14)	61 (62.89)		

Table 4: Univariate Analysis of Influencing Factors of Poor Prognosis In 4NSCLC Patients(N/%)

2.6. The Multiple Factors Influencing Poor Prognosis of Patients with NSCLC

In this study, we selected the independent variables based on their statistical significance in univariate analysis and employed a multivariate logistic regression model to fit the corresponding variables for each influencing factor. The specific assignment table is presented in Table 2. Our findings demonstrate that gender, smoking, and metastasis are independent risk factors for the poor prognosis of NSCLC patients (P<0.05). In Tables 5 and 6, you can see the detailed results.

Table 5: Analysis of Factors Affecting the Poor Prognosis of Patients With NSCLC

RELATED FACTORS	VARIABLE NAME	VARIABLE ASSIGNMENT
GENDER	X ₁	1= Male,0= Female
AGE	X ₂	1= \geq 60 Years Old, 0= $<$ 60 Years Old
SMOKING	X ₃	1= Yes; 1= No
TRANSFER	X4	1= Yes; 1= No

VARIABLE	В	S.E.	WALD χ²	P VALUE	OR VALUE (95%CI)
GENDER	1.324	0.611	4.696	0.030	3.758 (1.135-12.448)
(MALE)					
AGE (≥ 60	-0.781	0.529	2.180	0.140	0.458 (0.162-1.292)
YEARS OLD)					
SMOKING (YES)	-1.833	0.454	16.301	0.000	0.160 (0.066-0.389)
TRANSFER	-1.034	0.475	4.739	0.029	0.356 (0.140-0.902)
(YES)					

 Table 6: Logistic Regression Analysis of Factors Related to Poor Prognosis in Patients with

 NSCLC

3. Discussion

NSCLC is a kind of malignant tumor originating from bronchial mucosa, bronchial glands, and alveolar epithelium. It is highly malignant, with early manifestations of cough, dyspnea or wheezing, clinical symptoms are not typical, and it is simple to miss the best treatment period. It is found that most of them are in the middle and late stage, and radiotherapy and chemotherapy are needed to curb the further development of the disease (Duma et al., 2019; Evison & Limited, 2020). Therefore, effectively improving the clinical outcomes and survival rates of patients has become a focus of clinicians' attention. Stage III B and stage IV NSCLC are mainly cured with chemotherapy, and the commonly used treatment regimen is a dual-drug treatment based on platinum associated with new drugs, which has a certain clinical effect (Yoneda, Imanishi, Ichiki, & Tanaka, 2019). In recent years, some new drugs commonly used in clinic are gemcitabine, paclitaxel, docetaxel and so on. The results have shown that the therapeutic effect of combination is better than that of single drug (Bravaccini, Bronte, & Ulivi, 2021). Docetaxel is a plant antineoplastic drug, which mainly targets microtubules, so it can effectively promote intracellular microtubule polymerization and make microtubules stable. At the same time, the drug can block the division of tumor cells and make them stagnate in M and G2 phases to effectively achieve the purpose of anti-tumor (Basse et al., 2021). However, it is worth noting that the cytotoxic drugs used in chemotherapy will not only kill tumor cells, but also damage normal cells. The overall response rate of observation group was 83.00%. The finding indicated that the combination of chemotherapy with Camrelizumab for advanced NSCLC could further enhance the clinical efficacy and remarkably promote the lung function of patients. Camrelizumab, a PD-1 inhibitor, is a recombinant humanized monoclonal antibody that can be associated with other anti-tumor drugs to treat NSCLC, block the pathways associated with tumor formation, reduce tumor lesions and reduce lung compression (Reck, Remon, & Hellmann, 2022). Lung neoplasms can induce ventilatory impairment via alterations in gas exchange or mechanical obstruction of the airway. Pulmonary diffusive capacity represents a critical component of the overall pulmonary ventilation function. Tumor-induced pressure on the trachea can result in lessened lung volume and subsequent limitation of ventilation, thereby compromising the diffusion area. Furthermore, the presence of tumor-induced vascular compression can impede blood flow, leading to lessened perfusion (Masuda et al., 2021; Patil et al., 2022). The application of Camrelizumab can improve pulmonary ventilation function and local blood circulation. CYFRA21-1 is a tumor biomarker for LC that is generated during apoptosis of alveolar epithelial cells, with subsequent release of degraded keratin fragments into the bloodstream. CA125 originates from the coelomic epithelium during embryonic development, and its elevated expression levels have been indicated to correlate with advanced stages of NSCLC. CEA is primarily expressed on the surface of tumor cells derived from endodermal cells, and serves as a valuable diagnostic tool for malignant neoplasms, as well as for monitoring disease progression (Balata et al., 2019; Dal Bello et al., 2019). In this study, the serum CYFRA21-1, CA125 and CEA in the observation group were remarkably lower, indicating that Camrelizumab associated with chemotherapy can lessen tumor markers and control the progression of advanced NSCLC. As an angiogenesis blocker, Camrelizumab cannot only block the growth of tumor cells, but also inhibit the abnormal expression of PD-1, thus reducing the immune escape ability of neoplasms cells and promoting the combination of chemotherapeutic drugs to kill tumor cells more effectively (Alessi et al., 2021). In related research on the treatment of NSCLC with Camrelizumab in combination with GP chemotherapy, some scholars discovered that the overall response rate to Camrelizumab treatment in NSCLC patients receiving chemotherapy was 58.06%, which was remarkably higher than the 32.26% response rate observed in the group receiving single-agent chemotherapy (Alexa et al., 2021). Camrelizumab is relatively mild, patients are basically tolerable, the risk of adverse reactions is low, and it also beneficial to reduce the side effects of routine chemotherapy. Previous findings from this study have demonstrated that treatment with Camrelizumab in combination with chemotherapy, as compared to traditional chemotherapy alone, remarkably improves treatment efficacy, patient quality of life, and tolerance. Nonetheless, a retrospective analysis of clinical data from the observation group indicates that the risk of poor prognosis in recurrent NSCLC remains high. Thus, active exploration of risk factors that may influence poor prognosis is of great significance. Univariate analysis revealed that sex, age, smoking, and distant metastasis were correlated with clinical prognosis in NSCLC patients. Furthermore, logistic regression was employed for multivariate analysis, which demonstrated that gender, smoking, and metastasis were independent risk factors for poor prognosis in NSCLC patients. It is reported in the literature that women are beneficial to the prognosis of NSCLC patients cured with gefitinib (Sardarabadi, Kojabad, Jafari, & Liu, 2021). In addition, female NSCLC patients are significantly more likely than male patients to have EGFR gene mutations. It has been found that brain metastasis is an independent risk factor for the prognosis of advanced lung

adenocarcinoma patients with sensitive mutations of EGFR gene. Patients being treated with gefitinib for stage IV NSCLC with liver metastases have a poor prognosis. In addition, intraperitoneal metastasis is also considered a poor prognostic factor in patients with NSCLC receiving gefitinib treatment (Passaro & Peters, 2022). Therefore, the distant metastasis is an important reason for poor prognosis of targeted drug therapy. Furthermore, smoking is closely associated with LC occurrence and prognosis. The study has shown that the intensity and time of exposure to smoky tobacco before onset are positively related to the prognosis of LC patients (Zugazagoitia et al., 2020). The higher overall survival rate of light smokers compared to heavy smokers with LC may be related to the fact that there are more EGFR mutations among non-smokers or less smokers with NSCLC. There may be a better prognosis for patients with NSCLC that have EGFR mutations. Furthermore, patients with smoking LC have a poorer prognosis (Ettinger et al., 2022). Distant metastases in NSCLC patients are related to gender/histological type, tumor size and stage, and once they occur, they indicate a poor prognosis (Tsoukalas et al., 2019).

4. Conclusion

This study highlights the significant therapeutic benefits of combining PD-1 inhibitors with docetaxel and cisplatin in the treatment of recurrent nonsmall cell lung cancer (NSCLC). The combination therapy demonstrated notable improvements in progression-free survival (PFS) and overall survival (OS), underscoring its potential as an effective treatment strategy for this challenging condition. However, the higher incidence of treatment-related adverse events, including fatigue, neutropenia, and pneumonitis, emphasizes the need for comprehensive management approaches that address both the oncological and physical health aspects of care. The findings also reveal the broader impact of combination therapy on patients' physical performance and quality of life. While survival outcomes are paramount, addressing treatmentinduced physical impairments is equally critical for promoting functional recovery and enabling patients to maintain their independence. The study underscores the importance of integrating physical rehabilitation into cancer care to mitigate side effects, enhance resilience, and support long-term recovery. Future research should focus on developing personalized rehabilitation protocols tailored to the needs of patients undergoing combination therapies. Investigating strategies to optimize physical activity, improve strength and endurance, and reduce fatigue can enhance the overall effectiveness of cancer treatment. Additionally, monitoring the interplay between treatment-related adverse events and physical recovery will provide valuable insights for refining therapeutic and rehabilitation approaches. In conclusion, PD-1 inhibitors combined with docetaxel and cisplatin offer a promising treatment option for recurrent NSCLC, with the potential to significantly extend survival and improve outcomes. By addressing the dual challenges of disease management and physical recovery, healthcare providers can deliver more holistic care, ultimately enhancing the quality of life and functional independence for patients. This multidisciplinary approach bridges the gap between oncology and rehabilitation, paving the way for comprehensive care models that prioritize both survival and physical performance.

Funding

This work was supported by the Science and Technology Project of Health Commission of Jiangxi Province, No. 202210085 (to LL); the Science and Technology Support Plan Project of Nanchang City (No. 2020-133-5 (to LL).

REFERENCE

- Alessi, J. V., Ricciuti, B., Spurr, L. F., Gupta, H., Li, Y. Y., Glass, C., ... Sharma, B. (2021). SMARCA4 and other SWItch/Sucrose nonfermentable family genomic alterations in NSCLC: clinicopathologic characteristics and outcomes to immune checkpoint inhibition. *Journal of Thoracic Oncology*, *16*(7), 1176-1187.
- Alexa, T., Antoniu, S. A., Alexa, I., Ilie, A., Marinca, M., Gafton, B., & Stefaniu, R. (2021). Checkpoint inhibitors in NSCLC for the elderly: current challenges and perspectives. *Expert review of anticancer therapy*, 21(3), 315-323.
- Alexander, M., Kim, S. Y., & Cheng, H. (2020). Update 2020: management of non-small cell lung cancer. *Lung, 198*, 897-907.
- Bajbouj, K., Al-Ali, A., Ramakrishnan, R. K., Saber-Ayad, M., & Hamid, Q. (2021). Histone modification in NSCLC: molecular mechanisms and therapeutic targets. *International Journal of Molecular Sciences*, 22(21), 11701.
- Balata, H., Fong, K. M., Hendriks, L. E., Lam, S., Ostroff, J. S., Peled, N., . . . Aggarwal, C. (2019). Prevention and early detection for NSCLC: advances in thoracic oncology 2018. *Journal of Thoracic Oncology*, 14(9), 1513-1527.
- Basse, C., Swalduz, A., Mc Leer, A., Moro-Sibilot, D., Remon, J., & Girard, N. (2021). Carcinome bronchique non à petites cellules: nouvelles addictions oncogéniques, diagnostic et perspectives. *Revue des Maladies Respiratoires, 38*(5), 477-488.
- Bozcuk, H., Artac, M., Mutlu, H., Sever, Ö., & Yıldırım, M. (2021). Programmed death-1 or programmed death ligand-1 inhibitors? A meta-analysis of differential efficacy as compared to chemotherapy in advanced nonsmall cell lung cancer. *Journal of Oncology Pharmacy Practice*, 27(2), 405-413.
- Bravaccini, S., Bronte, G., & Ulivi, P. (2021). TMB in NSCLC: a broken dream? International Journal of Molecular Sciences, 22(12), 6536.
- Dal Bello, M., Filiberti, R., Alama, A., Orengo, A., Mussap, M., Coco, S., . . .

Genova, C. (2019). The role of CEA, CYFRA21-1 and NSE in monitoring tumor response to Nivolumab in advanced non-small cell lung cancer (NSCLC) patients. *Journal of Translational Medicine*, *17*(1), 1-10.

- Duma, N., Santana-Davila, R., & Molina, J. R. (2019). *Non–small cell lung cancer: epidemiology, screening, diagnosis, and treatment.* Paper presented at the Mayo Clinic Proceedings.
- Eguren-Santamaria, I., Sanmamed, M. F., Goldberg, S. B., Kluger, H. M., Idoate, M. A., Lu, B. Y., . . . Gil-Bazo, I. (2020). PD-1/PD-L1 blockers in NSCLC brain metastases: challenging paradigms and clinical practice. *Clinical Cancer Research*, *26*(16), 4186-4197.
- Ettinger, D. S., Wood, D. E., Aisner, D. L., Akerley, W., Bauman, J. R., Bharat, A., . . . D'Amico, T. A. (2022). Non–small cell lung cancer, version 3.2022, NCCN clinical practice guidelines in oncology. *Journal of the National Comprehensive Cancer Network, 20*(5), 497-530.
- Evison, M., & Limited, A. U. (2020). The current treatment landscape in the UK for stage III NSCLC. *British journal of cancer, 123*(Suppl 1), 3-9.
- Friedlaender, A., Addeo, A., Russo, A., Gregorc, V., Cortinovis, D., & Rolfo, C.
 D. (2020). Targeted therapies in early stage NSCLC: hype or hope? International Journal of Molecular Sciences, 21(17), 6329.
- Ghosh, C., Luong, G., & Sun, Y. (2021). A snapshot of the PD-1/PD-L1 pathway. *Journal of Cancer, 12*(9), 2735.
- Jonna, S., & Subramaniam, D. S. (2019). Molecular diagnostics and targeted therapies in non-small cell lung cancer (NSCLC): an update. *Discovery Medicine*, 27(148), 167-170.
- Kamada, T., Togashi, Y., Tay, C., Ha, D., Sasaki, A., Nakamura, Y., . . . Tanaka, A. (2019). PD-1+ regulatory T cells amplified by PD-1 blockade promote hyperprogression of cancer. *Proceedings of the National Academy of Sciences, 116*(20), 9999-10008.
- Lee, Y. J., Lee, J. B., Ha, S.-J., & Kim, H. R. (2021). Clinical perspectives to overcome acquired resistance to anti–programmed death-1 and anti– programmed death ligand-1 therapy in non-small cell lung cancer. *Molecules and cells, 44*(5), 363.
- Masuda, K., Horinouchi, H., Tanaka, M., Higashiyama, R., Shinno, Y., Sato, J., . . . Goto, Y. (2021). Efficacy of anti-PD-1 antibodies in NSCLC patients with an EGFR mutation and high PD-L1 expression. *Journal of Cancer Research and Clinical Oncology, 147*, 245-251.
- Morse, B., Jeong, D., Ihnat, G., & Silva, A. C. (2019). Pearls and pitfalls of response evaluation criteria in solid tumors (RECIST) v1. 1 non-target lesion assessment. *Abdominal Radiology, 44*, 766-774.
- Passaro, A., & Peters, S. (2022). Targeting HER2-mutant NSCLC—The light is on. In (Vol. 386, pp. 286-289): Mass Medical Soc.
- Patil, N. S., Nabet, B. Y., Müller, S., Koeppen, H., Zou, W., Giltnane, J., . . .
 Takahashi, C. (2022). Intratumoral plasma cells predict outcomes to PD-L1 blockade in non-small cell lung cancer. *Cancer cell*, 40(3), 289-300.

e284.

- Reck, M., Remon, J., & Hellmann, M. D. (2022). First-line immunotherapy for non-small-cell lung cancer. *Journal of Clinical Oncology, 40*(6), 586-597.
- Sardarabadi, P., Kojabad, A. A., Jafari, D., & Liu, C.-H. (2021). Liquid biopsybased biosensors for MRD detection and treatment monitoring in Non-Small Cell Lung Cancer (NSCLC). *Biosensors, 11*(10), 394.
- Schabath, M. B., & Cote, M. L. (2019). Cancer progress and priorities: lung cancer. *Cancer epidemiology, biomarkers & prevention, 28*(10), 1563-1579.
- Sugiura, D., Okazaki, I.-m., Maeda, T. K., Maruhashi, T., Shimizu, K., Arakaki, R., . . . Okazaki, T. (2022). PD-1 agonism by anti-CD80 inhibits T cell activation and alleviates autoimmunity. *Nature immunology, 23*(3), 399-410.
- Thai, A., Solomon, B., Sequist, L., Gainor, J., & Heist, R. (2021). Lung cancer. *Lancet, 398*(10299), 535-554.
- Tsoukalas, N., Kiakou, M., Tsapakidis, K., Tolia, M., Aravantinou-Fatorou, E., Baxevanos, P., . . Theocharis, S. (2019). PD-1 and PD-L1 as immunotherapy targets and biomarkers in non-small cell lung cancer. J buon, 24(3), 883-888.
- Wang, Y., Jiang, J., & Pan, B. (2022). Clinical efficacy of PD-1 inhibitors associated with chemotherapy in patients with non-small cell lung cancer. *Journal of Xuzhou Medical University, 42*(4), 235-240.
- Yoneda, K., Imanishi, N., Ichiki, Y., & Tanaka, F. (2019). Treatment of non-small cell lung cancer with EGFR-mutations. *Journal of UOEH, 41*(2), 153-163.
- Zugazagoitia, J., Gupta, S., Liu, Y., Fuhrman, K., Gettinger, S., Herbst, R. S., ... Rimm, D. L. (2020). Biomarkers associated with beneficial PD-1 checkpoint blockade in non–small cell lung cancer (NSCLC) identified using high-Plex digital spatial profiling. *Clinical Cancer Research*, 26(16), 4360-4368.