

Jiang H and Chi F. (2023) COMPARATIVE ANALYSIS OF MICROMETASTASIS INDICATORS AND PROGNOSIS IN FITNESS AND ATHLETIC PATIENTS WITH NON-SMALL CELL LUNG CANCER POST PULMONARY LOBECTOMY VERSUS SEGMENTECTOMY. Revista Internacional de Medicina y Ciencias de la Actividad Física y el Deporte vol. 23 (93) pp. 59-73

DOI: <https://doi.org/10.15366/rimcafd2023.93.005>

ORIGINAL

COMPARATIVE ANALYSIS OF MICROMETASTASIS INDICATORS AND PROGNOSIS IN FITNESS AND ATHLETIC PATIENTS WITH NON-SMALL CELL LUNG CANCER POST PULMONARY LOBECTOMY VERSUS SEGMENTECTOMY

Hongqian Jiang¹, Fusheng Chi^{1*}

¹ Department of Thoracic Surgery, The People's Hospital of China Medical University, Shenyang 110016, China.

E-mail: 13940363979@163.com

Recibido 11 de agosto de 2022 **Received** August 11, 2022

Aceptado 12 de octubre de 2023 **Accepted** October 12, 2023

ABSTRACT

Objective: To analyze the impact of fitness and athletic lifestyle on micrometastasis indicators and prognosis in patients with non-small cell lung cancer (NSCLC) undergoing pulmonary lobectomy and segmentectomy.

Methods: This retrospective analysis included 40 NSCLC patients, all of whom were fitness enthusiasts or athletes, treated at our institution from January 2020 to December 2021. These patients were divided into two groups: a lobectomy group and a segmentectomy group, each comprising 20 patients. We compared treatment outcomes, clinical indicators (operative time, intra-operative blood loss, chest drainage, length of hospital stay), micrometastasis indicators (CK20mRNA, CK19mRNA, CEAmRNA, lunxmrna) in peripheral blood, lung function (forced vital capacity, forced expiratory volume in 1 second), postoperative complications, and quality of life (physical, psychological, social, environmental) for both groups before and 6 months' post-therapy. **Results:** ① No significant difference in healing effect between the two groups ($P>0.05$). ② The segmentectomy group showed reduced chest drainage and hospitalization time compared to the lobectomy group ($P<0.05$), with no significant difference in surgery time and intra-operative blood loss ($P>0.05$). ③ No significant difference in pre-therapy micrometastasis indicators between the groups ($P>0.05$). Post-therapy, both groups showed similar levels of CEAmRNA ($P>0.05$). ④ Pre-therapy lung function was comparable between groups

($P > 0.05$), but post-therapy, the segmentectomy group had better lung function ($P < 0.05$). ⑤ No significant difference in postoperative complication rates ($P > 0.05$). ⑥ The segmentectomy group exhibited superior quality of life post-therapy in all aspects. **Conclusion:** Both pulmonary lobectomy and segmentectomy are effective in treating NSCLC in fitness and athletic patients. Lobectomy showed better outcomes in altering tumor micrometastasis indicators post-surgery, while segmentectomy was more favorable for postoperative lung function, chest drainage, and hospital stay. The choice of procedure should be tailored to the patient's individual condition, considering their active lifestyle and physical demands.

KEYWORDS: Pulmonary lobectomy; Segmentectomy; Non-small cell lung cancer; Micrometastasis indicator; Prognosis

1. INTRODUCTION

Non-small cell lung cancer (NSCLC) represents a significant health challenge globally, and its management often requires surgical interventions such as pulmonary lobectomy and segmentectomy. These procedures, while effective, can have varying impacts on patients, particularly those leading an athletic lifestyle (Li et al., 2021; Popat et al., 2021). The physical demands and health dynamics of athletic patients necessitate a nuanced understanding of how surgical choices affect their outcomes, especially in terms of micrometastasis indicators and overall prognosis (Gong et al., 2021; H et al.).

Athletic individuals typically exhibit enhanced lung capacity and efficiency, traits that are crucial in their performance and overall health. Surgical intervention, therefore, must be optimized to preserve these attributes as much as possible. Additionally, the physiological resilience and recovery capabilities of this group might differ significantly from the general population, influencing their response to surgery and postoperative recovery (Bertaglia et al., 2021; Donington et al., 2018).

This study aims to analyze the changes in micrometastasis indicators and the prognostic implications of pulmonary lobectomy versus segmentectomy in athletic patients diagnosed with NSCLC. Considering their unique physiological characteristics, this research seeks to provide a comparative evaluation of these surgical approaches, focusing on various clinical outcomes. These include operative time, intra-operative blood loss, chest drainage, length of hospital stay, changes in lung function, occurrence of postoperative complications, and quality of life assessments (Chen et al., 2019; Passiglia et al., 2020).

By specifically focusing on athletic patients, this research addresses a gap in the current understanding of NSCLC surgical outcomes in this population. The findings aim to guide clinicians in making more informed surgical decisions

and tailoring postoperative care to better suit the needs of patients who engage in regular athletic activities (Johnson, Pennell, & Borghaei, 2018; Van Laar, van Amsterdam, van Lindert, de Jong, & Verhoeff, 2020). This approach is pivotal for ensuring not just the effectiveness of the cancer treatment, but also the preservation of the patient's quality of life and ability to return to their athletic endeavors.

2. Athletic Patient Data and Methods

2.1 Patient Data

A total of 40 Athletic patients suffering from non-small cell lung carcinoma treating in our institution during the period from January 2020 to December 2021 were taken as the study subjects for retrospective analysis. These 40 Athletic patients were classified into two groups of 20 Athletic patients in each group: i.e. the controlling group and the observing group. In the controlled group, there were 12 men and 8 women; the minimum age was 44 years and the maximum was 76 years, with a mean measurement of (55.66 ± 6.11) years; the minimum tumour diameter was 1 cm and the maximum tumour diameter was 2 cm, and the average measured data was (1.54 ± 0.31) cm; there were 10 cases of adenocarcinoma, 7 cases of squamous cell carcinoma and 3 cases of other pathological types; there were 12 cases occurring in the right lung and 8 cases in the left lung.

There were 13 males and 7 females in the observation group; the youngest was 43 years old, while the oldest was 77 years old and the average measured data was (55.67 ± 6.12) years old; the minimum diameter of the tumors was 1 cm, the maximum diameter was 2 cm, and the average measured data was (1.55 ± 0.32) cm; there were 11 cases with adenocarcinoma, 6 cases with squamous cell carcinoma and 3 cases with other pathological types; there were 13 cases occurring in the right lung and 7 cases in the left lung. The above data between groups were evaluated by statistical software, and there was no difference, with $P > 0.05$.

Inclusion criteria of the Athletic patients: (1) Athletic Patients met the relevant clinical medical diagnostic criteria for non-small cell lung cancer; (2) All Athletic patients were confirmed by intraoperative pathological examination; (3) Athletic Patients with clear indications for surgical treatment. Exclusion criteria: (1) Athletic Patients combined with other malignant tumor diseases; (2) Patients with severe cognitive impairment; (3) Athletic Patients had received chemotherapy and radiotherapy before surgery.

2.2 Methods

The control group (performed by pulmonary lobectomy): Athletic Patients received general anesthesia and then were performed unilateral ventilation of

the contralateral lung, and at the same time Athletic patients obtained a decubitus position in healthy side, and the upper limb of the operation side was suspended. The incision was made at the intersection of the 8th intercostal part and the anterior axillary midline of the patients' body to perform thoracoscopy for patients, and then 1-3 operative cannula incisions were made. The operating hole of retractor was made around the posterior axillary line of the 7th and 8th intercostal part of the patients' body.

A small incision was made at the anterior and posterior axillary line of the 6th intercostal part of the patients' body to place a surgical instrument needle to process wedge resection for the lung lobes, and then the specimens were taken out and sliced for examination. The upper lobe of the left lung was treated by traction with noninvasive lung forceps, and the mediastinal pleura under the aortic arch was cut by ultrasonic scalpel. After the vascular sheath was separated, the upper lobe artery branches were disconnected by disposable endoscope. The lung lobe tissues were lifted up after the lung lobe traction again, to fully free the upper lobe bronchus, and then the upper lobe bronchus was closed and disconnected.

Observation group (performed by segmentectomy): After anesthesia, the patients' posture, specific incision location, surgical placement, pulmonary arteriovenous and bronchial separation treatment were consistent with those of the control group. Then the intersegmental fissure was closed and disconnected along the plane of the segment surface, and the distance between the resection scope and the edge of the tumor was kept at more than 2 cm. The frozen pathological examination of the resection margin was rapidly carried out after resection. If the result was positive, lung lobe needed to be resected again, and if it was negative, then systematic lymph gland was cleaned and submitted for examination. After that, the chest was rinsed with warm saline and then number 28 intrathoracic drain was placed, and the chest was closed gradually if no abnormality was confirmed.

2.3 Evaluation Criteria

The treatment effects of both groups were compared. The clinical indicators (operative time, intra-operative blood loss, chest drainage and length of stay) of the two groups were compared. The positive rates of tumor micrometastasis indicators (CK20mRNA, CK19mRNA, CEAmRNA and LunxmRNA) in peripheral blood for both groups before and after 6 months of therapy were compared. The lung functions (forced vital capacity, forced expiratory volume in 1 second) for both groups before and after 6 months of therapy were compared. The occurrence of postoperative complications was compared for both groups. The quality of life (physical, psychological, social and environmental) for both groups before and after 6 months of therapy were compared. The treatment effects of both groups: The judgment basis of

treatment effects was according to the tumor disease judgment standard formulated by the World Health Organization. It was divided into complete remission, partial remission, disease progression, and stable lesion. Among them, complete remission was that there were no lesions in the lung and no metastasis of the tumor found after the relevant medical imaging examination.

The partial remission was that the lesion area in the lung was reduced by more than 30% after the relevant medical imaging examination. Disease progressed was that the lesion area in the lung was reduced after relevant medical imaging examination, and the reduction degree was less than 30%. The stable lesion was that the lesions in the lungs have not improved after the relevant medical imaging examination, and even had the situations of increased area or metastasis. Total effectiveness rate = full remission rate + partial remission rate + disease progression rate. Tumor micrometastasis indicators in peripheral blood (CK20mRNA, CK19mRNA, CEA mRNA and LunxmrRNA): 4ml venous blood samples of patients in fasting state was collected and mixed with heparin, then the samples were shaken well and performed relevant operations according to the instructions of Trizol kit. And total RNA was extracted after cell lysis.

Lung functions (forced vital capacity, forced expiratory volume in 1 second): The relevant data results were measured according to the lung function test apparatus.

Postoperative complications: The complications included pulmonary infection, atelectasis and arrhythmia.

Quality of life (physical, psychological, social and environmental): According to the integrated quality of living assessment questionnaire, each area is scored out of 100. The upper the mark, the greater the quality of living of the patient.

2.4 Statistical methods

All index data were included in spss23.0. The count data were expressed in the form of % and χ^2 was used to verify. The measurement data were expressed in the form of $\bar{x} \pm s$ and t-value was used to verify. $P < 0.05$ was the inspection standard.

3. Results

3.1 Comparison of the treatment effects of the two groups of patients

There were no discrepancies in the data indicators comparing the therapeutic effects of the observed and controlled groups with $P > 0.05$, as illustrated in Table 1 and Figure 1

Table 1: Comparison of treatment effects between the two groups (%)

GROUP	COMPLETE REMISSION	PARTIAL REMISSION	DISEASE PROGRESSION	STABLE LESION	TOTAL EFFECTIVE RATE OF TREATMENT
OBSERVATION GROUP	2 (10.00)	10 (50.00)	4 (20.00)	4 (20.00)	16 (80.00)
CONTROL GROUP	1 (5.00)	10 (50.00)	4 (20.00)	5 (25.00)	15 (75.00)
X ²					0.143
P					0.705

Total effective rate of treatment

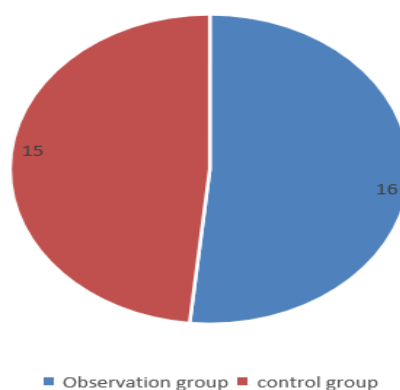


Figure 1: Comparison of treatment effects between the two groups

3.2 Comparing the clinical indicators of both groups (operating time, intra-operative blood loss, chest drainage and length of hospital stay)

The data indicators of chest drainage and hospital stay in the observed group were below those of the controlled group, and there was a discrepancy, $P < 0.05$; however, there was no discrepancy in the data indicators of operating time and intra-operative blood loss between the observed group and the controlled group, $P > 0.05$, see Table 2 and Figure 2.

Table 2: Comparing the clinical indicators of both groups (operative time, intra-operative blood loss, chest drainage and length of hospital stay)

GROUP	OPERATION TIME (MINUTES)	INTRAOPERATI VE BLOOD LOSS (ML)	THORACIC DRAINAGE VOLUME (ML)	LENGTH OF STAY (DAYS)
OBSERVATION GROUP	140.44 ± 5.55	156.66 ± 10.22	122.22 ± 4.44	7.77 ± 0.55
CONTROL GROUP	141.45 ± 5.56	156.77 ± 10.23	144.33 ± 6.66	9.89 ± 0.11
T	0.575	0.034	12.353	16.903
P	0.569	0.973	0.000	0.000

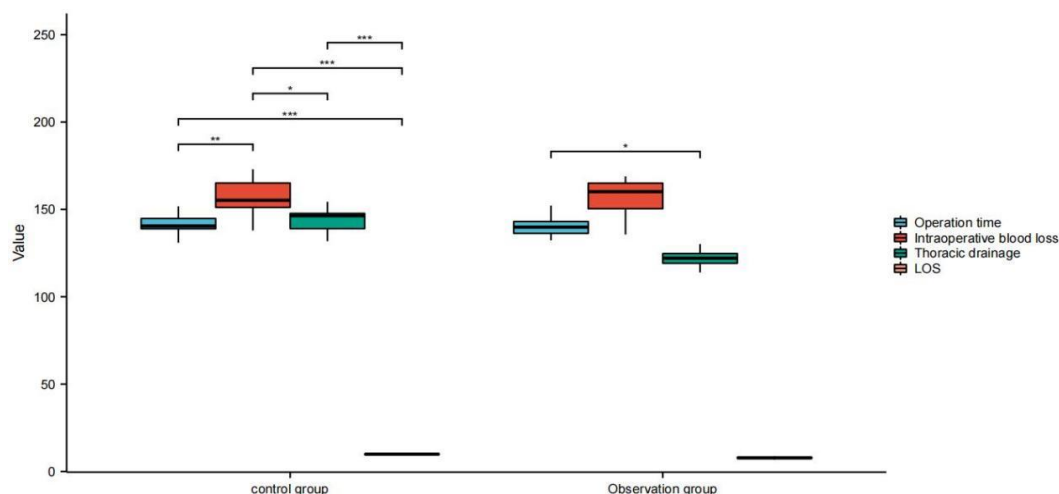


Figure 2: Comparison of clinical indicators (operation time, intraoperative blood loss, thoracic drainage and length of stay) of both groups

3.3 Comparison of positive rates of tumor micro metastasis indicators (CK20mRNA, CK19mRNA, CEAm RNA and LunxmRNA) in peripheral blood of both groups before therapy and after 6 months of therapy

There was no discrepancy in comparing the data index of the positive rate of tumor micro metastasis indicators in peripheral blood between observed group and controlled group before therapy, with $P > 0.05$; after 6 months of therapy, the positive rates of CK20mRNA, CK19mRNA and Lunxm RNA in the controlled group were below those in the observed group, and the data differed, $P < 0.05$. There was no discrepancy between the data indicators of CEAm RNA positivity in the observed and controlled groups after 6 months of therapy, $P > 0.05$, see Table 3 and Figure 3.

Table 3: Comparison of the positive rates of tumor micrometastasis indicators (CK20mRNA, CK19mRNA, CEAmRNA and LunxmRNA) in peripheral blood for both groups before and after 6 months of therapy were compared. (%)

GROUP	CK20MRNA		CK19MRNA		CEAMRNA		LUNXMRNA	
	Before treatment	6 months of treatment	Before treatment	6 months of treatment	Before treatment	6 months of treatment	Before treatment	6 months of treatment
OBSERVATION GROUP	11.55 ± 4.55	6.66 ± 1.11	13.33 ± 4.44	7.77 ± 2.22	9.44 ± 0.55	5.55 ± 0.33	13.67 ± 4.33	6.66 ± 1.44
CONTROL GROUP	11.56 ± 4.53	4.55 ± 1.02	13.36 ± 4.43	5.66 ± 1.11	9.45 ± 0.56	5.53 ± 0.33	13.69 ± 4.32	5.55 ± 1.22
X²	0.007	6.260	0.021	3.802	0.057	0.192	0.015	2.630
P	0.994	0.000	0.983	0.001	0.955	0.849	0.988	0.012

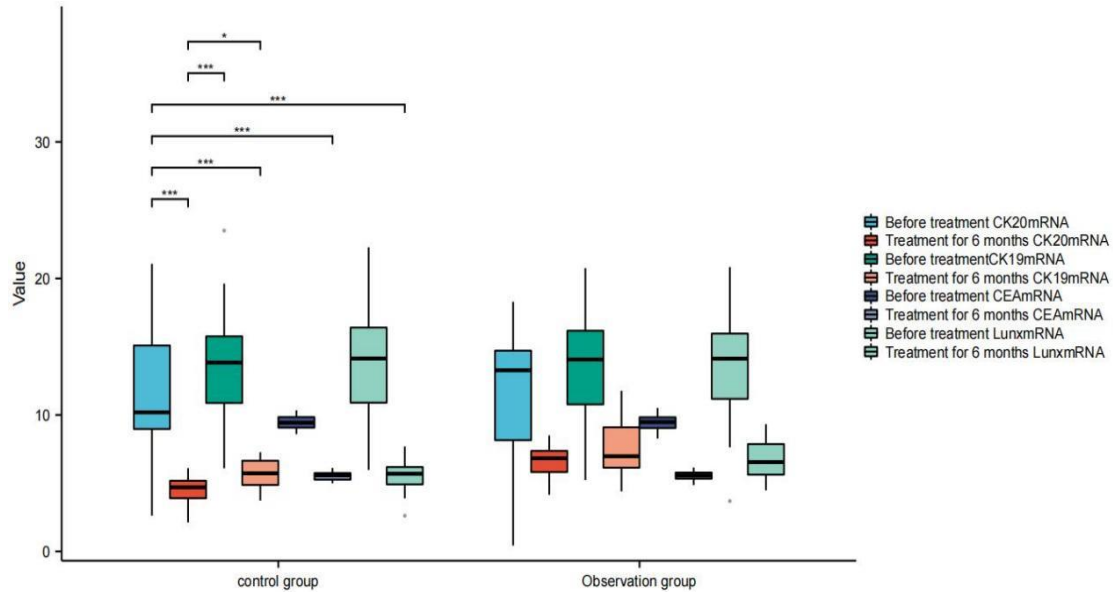


Figure 3: Comparison of the positive rates of tumor micrometastasis indicators (CK20mRNA, CK19mRNA, CEAmRNA and LunxmRNA) in peripheral blood for both groups before and after 6 months of therapy were compared.

3.4 Comparison of the lung functions (forced vital capacity, forced expiratory volume in 1 second) for both groups before and after 6 months of therapy were compared

There was no discrepancy between the observed group and the controlled group in the data indicators of forced vital capacity and first second forced expiratory volume before therapy, $P > 0.05$; however, the forced vital capacity and first second forced expiratory volume of the observed group were above the controlled group after 6 months of therapy and there was a discrepancy in the data, $P < 0.05$, see Table 4 and Figure 4.

Table 4: Comparison of lung functions (forced vital capacity, forced expiratory volume in 1 second) for both groups before and after 6 months of therapy were compared.

GROUP	FORCED VITAL CAPACITY		FORCED EXPIRATORY VOLUME IN 1 SECOND	
	Before treatment	6 months of treatment	Before treatment	6 months of treatment
OBSERVATION GROUP	91.22 ± 3.33	81.22 ± 3.11	92.22 ± 4.44	86.66 ± 3.33
CONTROL GROUP	91.23 ± 3.35	76.44 ± 2.22	92.23 ± 4.45	78.22 ± 3.11
T	0.009	5.594	0.007	8.284
P	0.992	0.000	0.994	0.000

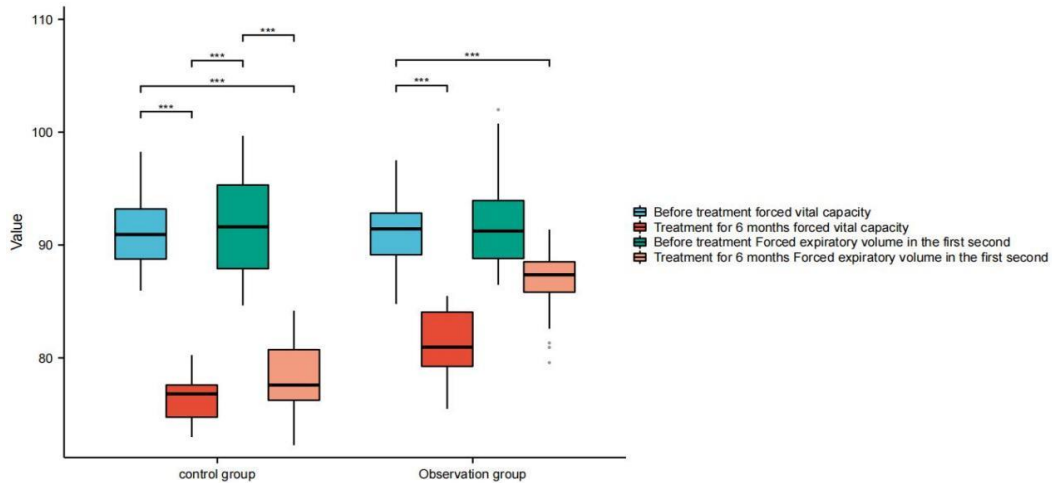


Figure 4: Comparison of lung functions (forced vital capacity, forced expiratory volume in 1 second) for both groups before and after 6 months of therapy were compared

3.5 Comparison of the occurrence of postoperative complications for both groups

There was no discrepancy in comparing the data index of postoperative complication rate between the observed group and the controlled group, with $P > 0.05$, see Table 5 and Figure 5

Table 5: Comparison of the occurrence of postoperative complications for both groups (%)

Group	Pulmonary Infection	Atelectasis	Arrhythmia	Complication Rate
Observation Group	1 (5.00)	1 (5.00)	1 (5.00)	3 (15.00)
Control Group	1 (5.00)	2 (10.00)	1 (5.00)	4 (20.00)
X^2				0.173
P				0.677

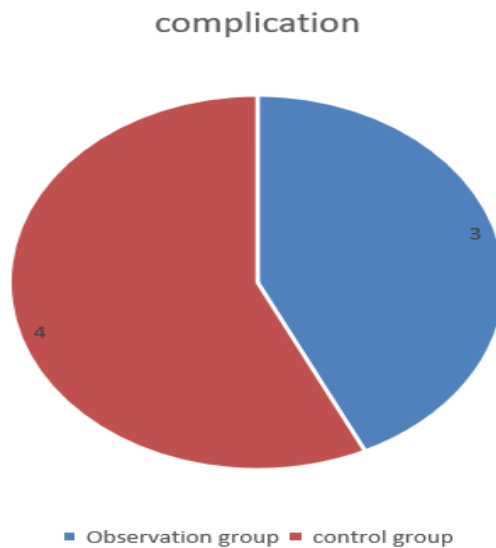


Figure 5: Comparison of postoperative complication rates for both groups

3.6 Comparison of the quality of living for both groups before and after 6 months of therapy (physical, psychological, social and environmental)

The quality of living indicators of the observed group was above the controlled group after 6 months of therapy and there was a discrepancy in the data, $P < 0.05$, see Table 6 and Figure 6.

Table 6: Comparison of the quality of living for both groups of patients after 6 months of therapy (physical, psychological, social and environmental)

GROUP	PHYSIOLOGY	PSYCHOLOGY	SOCIETY	ENVIRONMENT
OBSERVATION GROUP	70.44 ± 2.22	70.56 ± 2.33	70.65 ± 2.11	70.98 ± 2.13
CONTROL GROUP	65.55 ± 1.22	65.67 ± 2.11	65.22 ± 1.35	65.23 ± 1.11
T	8.633	6.957	9.694	10.706
P	0.000	0.000	0.000	0.000

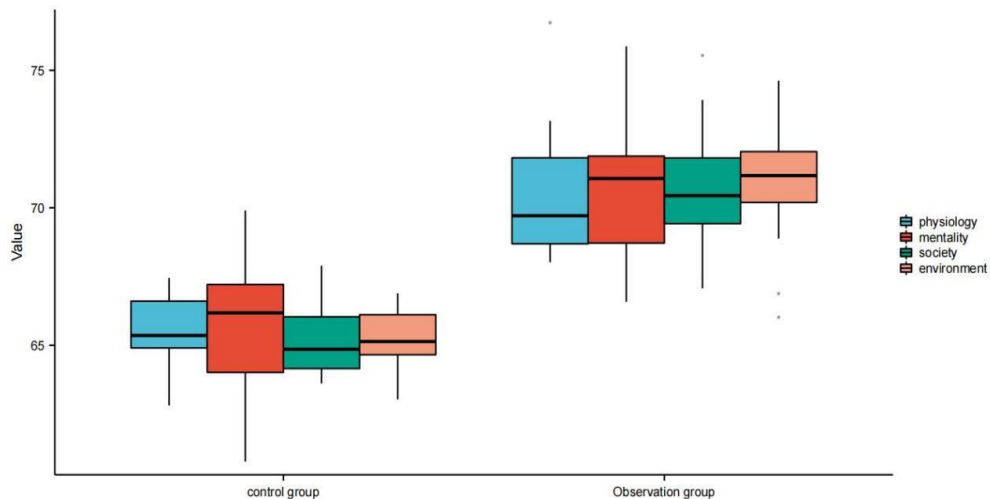


Figure 6: Comparison of the quality of life of the two groups of patients after 6 months of treatment (physical, psychological, social and environmental)

4. Discussion

There are many ways to treat non-small cell lung cancer, such as radiotherapy, chemotherapy and surgery. Among them, surgical treatment is conducive to removing tumor tissues and providing favorable conditions for other related treatment, so surgical treatment has been used frequently in clinic (Hayashi et al., 2022; Mennezier, Olland, Mascaux, & Falcoz, 2021). Thoracotomy is the main way to treat non-small cell lung cancer, which can directly contact with the lesion tissues and completely remove the lesions. However, this surgical method will bring greater body trauma to patients, and the risk of the incidence of complications after surgery is higher (Seto et al., 2022; Zou et al., 2022). Since thoracoscopic technology has been widely used in the treatment of clinical diseases, the degree of trauma brought to patients

by surgical treatment has been reduced, and the risk of the incidence of postoperative complications has also been reduced (Huang et al., 2021; Mitchell et al., 2020). The pulmonary lobectomy performed based on thoracoscopy is beneficial to obtain the exact therapeutic effect, but this surgical method will have a certain impact on the lung functions of patients, while segmentectomy performed based on thoracoscopy can effectively remove the lesion tissues and effectively preserve the healthy lung tissues (Gao et al., 2022; Lococo, Chiappetta, Cesario, & Margaritora). This study mainly analyzes the specific efficacy of the above two surgical treatment methods.

With the continuous development and improvement of the current medical technology, the exploration of the structure of lung in body is more and more in-depth in clinic, and some studies have shown that the resection of the lesion lung segment can ensure the integrity of the patients' normal lung tissues to the greatest extent, and can effectively protect the lung function for patients with non-small cell lung cancer (Imai et al., 2021; Ryska et al., 2018). There are also relevant literature data showing that there is a close relationship between the prognostic effect of patients with non-small cell lung cancer and tumor cell metastasis indicators, in which tumor micrometastasis indicators in peripheral blood play a very important role in determination (Kodama et al., 2022; shimoyama et al.).

Tumor micrometastasis refers to that during the occurrence and development of malignant tumor, the adhesion between the cells is significantly reduced, and the tumor cells that have fallen off will be scattered along with lymph, blood and bone marrow in various organs and tissues inside the patients, and cannot be found after routine physical examination (Kiriú et al., 2019; Sun et al., 2020). Therefore, exploring the expression changes of tumor micrometastasis indicators in peripheral blood is the key factor to judge the prognosis of the disease. In this study, the data showed that the data indexes of treatment effects, operation time, intraoperative blood loss, positive rate of CEAmRNA after 6 months of therapy and postoperative complication rate of the observed group and the controlled group were compared showing that $P > 0.05$ (De Silva & Jang, 2015).

The forced vital capacity, forced expiratory volume in the first second, and quality of life in the observed group after 6 months of therapy were greater than those in the controlled group, with $P < 0.05$, while the index data of thoracic drainage volume and length of stay in the observed group were lesser than those in the controlled group. The positive rates of CK20mRNA, CK19mRNA, and LunxmRNA in the controlled group were lesser than those in the observed group after 6 months of therapy, with $P < 0.05$ (Gharib, 2020).

According to this data, peripheral blood tumor micrometastasis indicators can be utilized to predict a patient's prognosis for non-small lung

carcinoma, and specific surgical method can be selected according to various indicators and actual conditions of patients (Kojima et al., 2020; Lim et al., 2018). Among them, pulmonary lobectomy has a relatively low risk of micrometastasis, and the reasons may lie in that this surgical method can relatively and completely remove the lesion tissues to reduce the risk of tumor spread (Ma et al., 2020; Morita et al., 2022), while segmentectomy cannot completely rule out the possibility that there are still primary lesions, but it is conducive to effectively protecting the body's lung function, and reducing the irritation caused by surgical treatment to the body to the greatest extent (Cirenajwis, Lauss, Planck, Vallon-Christersson, & Staaf, 2020; Ostheimer et al., 2019).

5. Conclusion

In the context of fitness and athletic patients with non-small cell lung cancer (NSCLC), both pulmonary lobectomy and segmentectomy demonstrate significant therapeutic effectiveness. The study highlights that lobectomy is more advantageous in modifying tumor micrometastasis indicators in peripheral blood post-surgery. Conversely, segmentectomy shows a more favorable impact on postoperative lung function, chest drainage, and length of hospital stay. These findings are particularly relevant for patients engaged in regular physical activity, where lung function and rapid recovery are crucial. The decision between lobectomy and segmentectomy should be individualized, taking into account the patient's overall physical health, athletic demands, and specific clinical characteristics of NSCLC. This tailored approach ensures optimal treatment efficacy while supporting the unique health needs and lifestyle of fitness and athletic patients.

Reference

- Bertaglia, V., Reale, M. L., Bironzo, P., Palesandro, E., Mariniello, A., Leone, G., . . . Rapetti, S. (2021). Italian survey on the clinical management of non-small cell lung cancer patients during the COVID-19 pandemic: A lesson for the second wave. *Critical Reviews In Oncology/hematology*, *157*, 103189.
- Chen, L., Smith, D. A., Somarouthu, B., Gupta, A., Gilani, K. A., & Ramaiya, N. H. (2019). A Radiologist's Guide to the Changing Treatment Paradigm of Advanced Non–Small Cell Lung Cancer: The ASCO 2018 Molecular Testing Guidelines and Targeted Therapies. *American Journal of Roentgenology*, *213*(5), 1047-1058.
- Cirenajwis, H., Lauss, M., Planck, M., Vallon-Christersson, J., & Staaf, J. (2020). Performance of gene expression–based single sample predictors for assessment of clinicopathological subgroups and molecular subtypes in cancers: a case comparison study in non-small cell lung cancer. *Briefings In Bioinformatics*, *21*(2), 729-740.
- De Silva, M. T., & Jang, S. R. (2015). Competitive exclusion and coexistence in

- a Lotka–Volterra competition model with Allee effects and stocking. *Letters in Biomathematics*. doi:<https://doi.org/10.30707/LiB2.1DeSilva>
- Donington, J. S., Kim, Y. T., Tong, B., Moreira, A. L., Bessich, J., Weiss, K. D., . . . Zweig, J. (2018). Progress in the management of early-stage non–small cell lung cancer in 2017. *Journal of Thoracic Oncology*, 13(6), 767-778.
- Gao, Z., Xu, y., Zu, J., Wang, x., Sun, C., Qiu, s., . . . Ma, K. (2022). The time window for the reversal of differentiation from aggregation to recovery in a non small cell lung cancer patient with pre-existing vitiligo using anti programmed cell death-1 therapy: a case report *Front immunol.* 13, 946829.
- Gharib, M. R. (2020). Comparison of robust optimal QFT controller with TFC and MFC controller in a multi-input multi-output system. *Reports in Mechanical Engineering*, 1(1), 151-161.
- Gong, K., Zhou, H., Liu, H., Xie, T., Luo, Y., Guo, H., . . . Xie, L. (2021). Identification and integrate analysis of key biomarkers for diagnosis and prognosis of non-small cell lung cancer based on bioinformatics analysis. *Technology in Cancer Research & Treatment*, 20, 15330338211060202.
- H, A.-L., Ferreira, C., baldotto, C., Mathias, C., Castro, g.-J., & Coudry, R. Next generation sequencing of circulating tumor DNA for metabolic non small cell lung cancer: a discussion on its implementation in the Brazilian clinical practice *Future oncol* 2021. 17(2), 205-213.
- Hayashi, K., Suzuki, O., Shiomi, H., Nakai, M., Fujiwara, K., Nakanishi, E., . . . Hirata, H. (2022). Stereotactic ablative radiotherapy using CyberKnife for stage I non-small-cell lung cancer: a retrospective analysis. *Anticancer Research*, 42(1), 321-327.
- Huang, R. S., Severson, E., Haberberger, J., Duncan, D. L., Hemmerich, A., Edgerly, C., . . . Williams, E. (2021). Landscape of biomarkers in non-small cell lung cancer using comprehensive genomic profiling and PD-L1 immunohistochemistry. *Pathology and Oncology Research*, 27, 592997.
- Imai, H., Onozato, R., Kaira, K., Kawashima, S., Masubuchi, K., Nagashima, T., . . . Minato, K. (2021). Course of postoperative relapse in non-small cell lung cancer is strongly associated with post-progression survival. *Thoracic Cancer*, 12(20), 2740-2748.
- Johnson, M., Pennell, N. A., & Borghaei, H. (2018). “My Patient Was Diagnosed With Nontargetable Advanced Non–Small Cell Lung Cancer. What Now?” Diagnosis and Initial Treatment Options for Newly Diagnosed Patients With Advanced NSCLC. *American Society of Clinical Oncology Educational Book*, 38, 696-707.
- Kiriu, T., Yamamoto, M., Nagano, T., Koyama, K., Katsurada, M., Tamura, D., . . . Nishimura, Y. (2019). Prognostic value of red blood cell distribution width in non-small cell lung cancer treated with anti-programmed cell death-1 antibody. *in vivo*, 33(1), 213-220.
- Kodama, T., Arimura, H., Shirakawa, Y., Ninomiya, K., Yoshitake, T., &

- Shioyama, Y. (2022). Relapse predictability of topological signature on pretreatment planning CT images of stage I non-small cell lung cancer patients before treatment with stereotactic ablative radiotherapy. *Thoracic Cancer*, 13(15), 2117-2126.
- Kojima, H., Terada, Y., Yasuura, Y., Konno, H., Mizuno, T., Isaka, M., . . . Ohde, Y. (2020). Prognostic impact of the number of involved lymph node stations in patients with completely resected non-small cell lung cancer: a proposal for future revisions of the N classification. *General Thoracic and Cardiovascular Surgery*, 68, 1298-1304.
- Li, Y., Sun, C., Tan, Y., Zhang, H., Li, Y., & Zou, H. (2021). ITGB1 enhances the radioresistance of human non-small cell lung cancer cells by modulating the DNA damage response and YAP1-induced epithelial-mesenchymal transition. *International journal of biological sciences*, 17(2), 635.
- Lim, J. U., Yeo, C. D., Rhee, C. K., Kim, Y. H., Park, C. K., Kim, J. S., . . . Lee, S. H. (2018). Overall survival of driver mutation-negative non-small cell lung cancer patients with COPD under chemotherapy compared to non-COPD non-small cell lung cancer patients. *International Journal of Chronic Obstructive Pulmonary Disease*, 2139-2146.
- Lococo, F., Chiappetta, m., Cesario, a., & Margaritora, S. Non small cell lung cancer with pathological complete response after induction therapy followed by surgical response: which is the pattern of failure and which are the future perspectives? . *Eur J cardiothoracic surg*, 58(2), 407.
- Ma, Y., Ou, J., Lin, T., Chen, L., Wang, J., Qiao, D., . . . Chang, R. (2020). Phenotypic analysis of tumor-infiltrating lymphocytes from non-small cell lung cancer and their potential application for adoptive cell therapy. *Immunopharmacology and Immunotoxicology*, 42(4), 319-329.
- Menecier, B., Olland, A., Mascaux, C., & Falcoz, P.-E. (2021). Re: Two centres' experience with lung cancer resection in patients with advanced non-small-cell lung cancer following treatment with immune checkpoint inhibitors: safety and clinical outcomes. In (Vol. 60, pp. 1306-1307): Oxford University Press.
- Mitchell, K. G., Nelson, D. B., Corsini, E. M., Correa, A. M., Erasmus, J. J., Hofstetter, W. L., . . . Sepesi, B. (2020). Surveillance after treatment of non-small-cell lung cancer: a call for multidisciplinary standardization. *Innovations*, 15(1), 57-65.
- Morita, Y., Saijo, A., Nokihara, H., Mitsuhashi, A., Yoneda, H., Otsuka, K., . . . Nishioka, Y. (2022). Radiation therapy induces an abscopal effect and upregulates programmed death-ligand 1 expression in a patient with non-small cell lung cancer. *Thoracic Cancer*, 13(7), 1079-1082.
- Ostheimer, C., Evers, C., Palm, F., Mikolajczyk, R., Vordermark, D., & Medenwald, D. (2019). Mortality after radiotherapy or surgery in the treatment of early stage non-small-cell lung cancer: a population-based study on recent developments. *Journal of Cancer Research and Clinical Oncology*, 145, 2813-2822.

- Passiglia, F., Bertolaccini, L., Del Re, M., Facchinetti, F., Ferrara, R., Franchina, T., . . . Pilotto, S. (2020). Diagnosis and treatment of early and locally advanced non-small-cell lung cancer: The 2019 AIOM (Italian Association of Medical Oncology) clinical practice guidelines. *Critical Reviews In Oncology/hematology*, 148, 102862.
- Popat, S., Navani, N., Kerr, K. M., Smit, E. F., Batchelor, T. J., Van Schil, P., . . . McDonald, F. (2021). Navigating Diagnostic and Treatment Decisions in Non-Small Cell Lung Cancer: Expert Commentary on the Multidisciplinary Team Approach. *The Oncologist*, 26(2), e306-e315.
- Ryska, A., Buiga, R., Fakirova, A., Kern, I., Olszewski, W., Plank, L., . . . Thallinger, C. (2018). Non-small cell lung cancer in countries of Central and Southeastern Europe: Diagnostic procedures and treatment reimbursement surveyed by the Central European Cooperative Oncology Group. *The Oncologist*, 23(12), e152-e158.
- Seto, K., Shimizu, J., Masago, K., Araki, M., Katayama, R., Sagae, Y., . . . Kuroda, H. (2022). Sensitivity to dabrafenib and trametinib treatments in patients with non-small-cell cancer harboring BRAF compound mutations: A pooled analysis of BRAF p. V600E-positive advanced non-small-cell lung cancer. *Cancer Genetics*, 266, 1-6.
- shimoyama, R., Nakagawa, K., ishikura, s., Wakabayashi, m., Sasaki, T., Yoshioka, h., . . . Watanabe, s. A multi institutional randomized phase III trial comparing posterior radiation to observation after adjust chemotherapy in patients with pathological N2 stage III non small cell lung cancer: Japan Clinical Oncology Group study jcog1916 (j-port study). *JPN J Clin oncol*, 51(6), 999-1003.
- Sun, C., Anraku, M., Kawahara, T., Karasaki, T., Kitano, K., Nagayama, K., . . . Nakajima, J. (2020). Prognostic significance of low pectoralis muscle mass on preoperative chest computed tomography in localized non-small cell lung cancer after curative-intent surgery. *Lung Cancer*, 147, 71-76.
- Van Laar, M., van Amsterdam, W. A., van Lindert, A. S., de Jong, P. A., & Verhoeff, J. J. (2020). Prognostic factors for overall survival of stage III non-small cell lung cancer patients on computed tomography: A systematic review and meta-analysis. *Radiotherapy and Oncology*, 151, 152-175.
- Zou, D., Ye, W., Hess, L. M., Bhandari, N. R., Ale-Ali, A., Foster, J., . . . Harris, M. (2022). Diagnostic value and cost-effectiveness of next-generation sequencing-based testing for treatment of patients with advanced/metastatic non-squamous non-small-cell lung cancer in the United States. *The Journal of Molecular Diagnostics*, 24(8), 901-914.