

# Effect of N-Acetylcysteine Combined with Lung Rehabilitation Therapy on Exercise Endurance and Quality of Life of Patients with Rheumatoid Arthritis-Related Interstitial Lung Disease

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**Abstract:** *Objective:* To explore the effect of N-acetylcysteine combined with lung rehabilitation therapy on exercise endurance and quality of life in patients with rheumatoid arthritis-related interstitial lung disease (RA-ILD). *Methods:* Fifty-six patients with RA-ILD admitted to Xijing Hospital from May 2022 to January 2024 were randomly divided into two groups: a non-rehabilitation group and a pulmonary rehabilitation group, with 28 patients in each group. Both groups received routine treatment. Additionally, the non-rehabilitation group received N-acetylcysteine treatment, while the lung rehabilitation group received lung rehabilitation treatment in addition to N-acetylcysteine. The improvement in exercise endurance and dyspnea between the two groups after treatment was compared and the quality of life of the patients was observed. *Results:* After treatment, the exercise endurance score in the lung rehabilitation group ( $335.67 \pm 45.29$ ) was higher than that in the non-rehabilitation group ( $P < 0.05$ ). The dyspnea score in the lung rehabilitation group ( $0.72 \pm 0.16$ ) was lower than that in the non-rehabilitation group ( $P < 0.05$ ). Additionally, FVC ( $3.18 \pm 0.58$  L), FEV<sub>1</sub> ( $2.28 \pm 0.56$  L), FEV<sub>1</sub>/FVC ( $69.69 \pm 5.56$ ), and DLCO ( $60.53 \pm 5.92$  mL/mmHg/min) were higher in the lung rehabilitation group compared to the non-rehabilitation group after treatment ( $P < 0.05$ ). *Conclusion:* Lung rehabilitation therapy combined with N-acetylcysteine treatment can effectively improve dyspnea symptoms, lung function, and exercise endurance in patients with RA-ILD. This approach helps to improve patient's quality of life and is beneficial for their prognosis.

**Keywords:** Rheumatoid arthritis-associated interstitial lung disease; N-acetylcysteine; Lung rehabilitation therapy; Exercise endurance; Quality of life

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## 1. Introduction

Rheumatoid arthritis (RA) is a common autoimmune disease characterized by inflammatory reactions throughout the body. As the disease progresses, it can affect not only the joints but also organs such as the lungs, leading to conditions like interstitial lung disease (ILD) and pulmonary fibrosis, which significantly impair lung

function and require early intervention and treatment<sup>[1]</sup>. RA-ILD induces inflammatory responses in the alveoli, often accompanied by excessive secretions, necessitating active expectorant therapy. N-acetylcysteine is a reliable expectorant widely utilized in clinical practice. However, due to substantial lung function impairment in these patients, intensive rehabilitation treatment is also essential<sup>[2]</sup>.

Currently, the clinical community has been actively exploring various lung rehabilitation strategies for RA-ILD patients. Yet, the efficacy of combining N-acetylcysteine with such rehabilitation remains unclear. Therefore, this study enrolled 56 RA-ILD patients admitted to Xijing Hospital between May 2022 and January 2024 to investigate and compare the combined treatment's effects on parameters such as exercise endurance, dyspnea, and quality of life.

## 2. Materials and methods

### 2.1. General information

Fifty-six patients diagnosed with RA-ILD who were admitted to Xijing Hospital from May 2022 to January 2024 were randomly assigned to either the non-rehabilitation group or the lung rehabilitation group, with 28 patients in each group. In the lung rehabilitation group, there were 13 males and 15 females, aged 35 to 68 years (mean age  $51.52 \pm 16.41$  years), with a disease duration ranging from 1 to 6 years (mean duration  $4.35 \pm 1.63$  years). Similarly, the non-rehabilitation group comprised 14 males and 14 females, aged 36 to 68 years (mean age  $51.92 \pm 15.89$  years), with a disease duration of 1 to 6 years (mean duration  $4.21 \pm 1.71$  years). There were no significant differences in baseline characteristics between the two groups ( $P > 0.05$ ). This study was approved by the hospital's Ethics Committee.

### 2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) First-time patients at our hospital able to cooperate with treatment and rehabilitation; (2) Complete lung biopsy confirming the pathological diagnosis of RA-ILD; (3) No other autoimmune diseases; (4) Normal communication abilities without barriers; (5) Signed informed consent forms from both patients and their families.

Exclusion criteria: (1) Concurrent respiratory tract infections; (2) Patients with joint or muscle diseases unable to participate in rehabilitation training; (3) Non-compliance with treatment or withdrawal from the study; (4) Mental disorders; (5) Other organ failures, etc.

### 2.3. Methods

Patients in both groups received routine treatment consisting of sulfasalazine enteric-coated tablets ( $0.25 \text{ g} \times 60$  tablets, Shanghai Xinyi Tianping Pharmaceutical Co., Ltd.), administered at 1.5 to 2 g per dose once daily, and methotrexate tablets ( $2.5 \text{ mg} \times 100$  tablets, Tonghua Maoxiang Pharmaceutical Co., Ltd.), administered at 5 to 10 mg per dose once or twice weekly. In addition to routine treatment, the non-rehabilitation group received N-acetylcysteine treatment: acetylcysteine tablets ( $0.6 \text{ g} \times 20$  tablets, Hainan Zangbang Pharmaceutical Co., Ltd.), 0.6 g orally three times daily for 3 months. The lung rehabilitation group underwent additional lung rehabilitation therapy on top of the non-rehabilitation treatment regimen. During training sessions, medical staff closely monitored patients' vital signs and finger oxygen saturation, halting training immediately upon detection of any abnormalities.

Training included:

(1) Aerobic training: Patients were instructed to warm up by moving limb joints for 5 minutes, followed by

bicycle riding with gradually increased exercise intensity. Heart rate was controlled to increase by 20 to 30 beats/min above resting heart rate. Each session lasted 30 minutes, conducted 3 to 4 times per week over 12 weeks.

- (2) Abdominal breathing training: Patients were guided to relax both physically and mentally while standing or sitting. They were instructed to place their palms on the upper abdomen, inhale slowly to feel the abdomen rise, and exhale slowly through the mouth to fully expel the air. Training sessions lasted 10 to 15 minutes, conducted twice daily (morning and evening) over 12 weeks.

## 2.4. Observation indicators

- (1) Exercise endurance evaluation: Changes in 6-minute walking distance (6MWD) were measured before and after treatment, and improvements in endurance were compared between the two groups<sup>[3]</sup>.
- (2) Dyspnea assessment: The modified Medical Research Council (mMRC) dyspnea scale, ranging from 0 to 4, was used to evaluate dyspnea severity. Scores before and after treatment were compared between the two groups<sup>[4]</sup>.
- (3) Pulmonary function assessment: Levels of forced vital capacity (FVC), forced expiratory volume in the first second (FEV<sub>1</sub>), FEV<sub>1</sub>/FVC ratio, and carbon monoxide diffusion capacity (DLCO) were measured before and after treatment, and changes in lung function were compared between the two groups.
- (4) Quality of life: Patients' quality of life was assessed using the Barthel Index for activities of daily living, with scores ranging from 0 to 100. Higher scores indicated a better quality of life. Scores before and after treatment were compared between the two groups.

## 2.5. Statistical analysis

SPSS 20.0 statistical software was used for data analysis. Measurement data are expressed as mean ± standard deviation (SD), and the *t*-test was applied. Count data are presented as [*n* (%)], and the chi-squared test was used. A significance level of *P* < 0.05 was considered statistically significant.

## 3. Results

### 3.1. Assessment of exercise endurance and dyspnea

After treatment, both the lung rehabilitation group and the non-rehabilitation group showed significantly improved exercise endurance scores compared to before treatment (*P* < 0.05). Similarly, the scores for dyspnea were significantly lower after treatment in both groups (*P* < 0.05). Specifically, the lung rehabilitation group exhibited higher exercise endurance scores compared to the non-rehabilitation group (*P* < 0.05), and a lower degree of dyspnea (*P* < 0.05). Refer to **Table 1** for details.

**Table 1.** Comparison of scores of exercise endurance and dyspnea (mean ± SD)

Group	6MWD (score)		mMRC (score)	
	Before treatment	After treatment	Before treatment	After treatment
Lung rehabilitation group	189.25 ± 25.36	335.67 ± 45.29*	2.89 ± 0.68	0.72 ± 0.16*
Non-rehabilitation group	190.19 ± 25.41	231.52 ± 39.86*	2.92 ± 0.71	1.52 ± 0.13*
<i>t</i>	0.026	15.282	0.041	18.415
<i>P</i>	0.918	< 0.001	0.829	< 0.001

Compared with the same group before treatment, \**P* < 0.05

### 3.2. Pulmonary function assessment

After treatment, both groups showed significantly improved pulmonary function indices compared to before treatment ( $P < 0.05$ ). Moreover, the pulmonary function indices were significantly higher in the pulmonary rehabilitation group compared to the non-rehabilitation group ( $P < 0.05$ ). Refer to **Table 2** for details.

**Table 2.** Comparison of pulmonary function indexes (mean  $\pm$  SD)

Group	FVC (L)		FEV <sub>1</sub> (L)		FEV <sub>1</sub> /FVC		DLCO (mL/mmHg/min)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Lung rehabilitation group	2.23 $\pm$ 0.33	3.18 $\pm$ 0.58*	1.56 $\pm$ 0.25	2.28 $\pm$ 0.56*	58.69 $\pm$ 7.67	69.69 $\pm$ 5.56*	43.56 $\pm$ 8.26	60.53 $\pm$ 5.92*
Non-rehabilitation group	2.25 $\pm$ 0.35	2.86 $\pm$ 0.47*	1.55 $\pm$ 0.26	1.85 $\pm$ 0.52*	58.62 $\pm$ 7.72	62.24 $\pm$ 6.38*	43.54 $\pm$ 8.19	52.52 $\pm$ 6.13*
<i>t</i>	0.074	5.263	0.075	4.589	0.043	4.539	0.058	5.348
<i>P</i>	0.918	0.015	0.829	0.018	0.941	0.017	0.892	0.017

Compared with the same group before treatment, \* $P < 0.05$

### 3.3. Quality of life assessment

Following treatment, the Barthel Index scores reflecting quality of life were significantly higher in both groups compared to before treatment ( $P < 0.05$ ). Additionally, the Barthel Index scores were higher in the lung rehabilitation group compared to the non-rehabilitation group ( $P < 0.05$ ). Refer to **Table 3** for details.

**Table 3.** Comparison of Barthel Index scores (mean  $\pm$  SD)

Group	Barthel Index scores	
	Before treatment	After treatment
Lung rehabilitation group	67.25 $\pm$ 8.56	89.15 $\pm$ 7.63*
Non-rehabilitation group	67.31 $\pm$ 8.49	78.25 $\pm$ 8.36*
<i>t</i>	0.052	5.718
<i>P</i>	0.934	0.005

Compared with the same group before treatment, \* $P < 0.05$

## 4. Discussion

RA-ILD presents a significant risk in patients with rheumatoid arthritis, characterized by a high incidence and often asymptomatic early stages. As the disease progresses, it can lead to diffuse pulmonary lesions and pulmonary fibrosis, severely compromising lung function and posing a threat to patient safety<sup>[5]</sup>. Patients with RA-ILD often exhibit lung inflammatory reactions, characterized by increased alveolar cell exudates and sputum production, necessitating timely expectorant therapy<sup>[6]</sup>. N-acetylcysteine serves as an effective expectorant, facilitating sputum clearance and aiding symptom management, although its ability to improve lung function remains limited. Therefore, combining it with lung rehabilitation therapy becomes crucial to enhancing lung function, improving exercise endurance, promoting daily life activities, and mitigating adverse prognostic outcomes<sup>[7]</sup>.

Lung rehabilitation therapy represents a reliable approach to enhancing lung function. Through structured rehabilitation training, improvements in vital capacity and lung ventilation function can enhance cardiopulmonary function and augment exercise endurance in patients<sup>[8]</sup>. However, the specific impact of combined therapy on RA-ILD patients requires clarification<sup>[8]</sup>. This study aimed to evaluate the specific effects of combined N-acetylcysteine and lung rehabilitation therapy in RA-ILD patients. The findings demonstrated that following treatment, the lung function indices in the lung rehabilitation group were significantly superior to those in the non-rehabilitation group ( $P < 0.05$ ), with lower dyspnea scores ( $P < 0.05$ ). Moreover, the exercise endurance score in the lung rehabilitation group ( $335.67 \pm 45.29$ ) surpassed that in the non-rehabilitation group. Importantly, the Barthel index reflecting quality of life was higher in the lung rehabilitation group post-treatment compared to the non-rehabilitation group. These results underscore the effectiveness of combined lung rehabilitation in enhancing pulmonary ventilation, alleviating dyspnea symptoms, and overall improving pulmonary function and quality of life. Thus, the enhancement in exercise endurance promotes recovery in daily living activities, ultimately enhancing patient quality of life and offering significant clinical utility.

In conclusion, adding lung rehabilitation therapy to N-acetylcysteine treatment effectively improves dyspnea symptoms and lung function in RA-ILD patients. It enhances exercise endurance, promotes quality of life, and contributes to a better prognosis for these patients<sup>[8]</sup>.

## Disclosure statement

The author declares no conflict of interest.

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