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*Research article*

# Effect of a Structured Pulmonary Rehabilitation Program on Quality of Life in Post-Tuberculosis Lung Disease: A Prospective Controlled Study

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**Abstract:** Post-tuberculosis lung disease (PTLD) refers to persistent respiratory impairment after completion of anti-tuberculosis therapy, leading to impaired quality of life (QoL) [1,2]. The objective was to evaluate the impact of an individualized pulmonary rehabilitation program on QoL in PTLD, describing changes in functional capacity, symptoms, and inflammatory indices. A prospective controlled interventional study included 37 PTLD patients allocated to a Study Group (SG, n=19) receiving structured rehabilitation or a Control Group (CG, n=18) receiving standard care. Baseline (T1) and follow-up (T2) assessed 6MWD, TUG, dyspnea (mMRC), exertion (Borg CR10), QoL (SGRQ, EUROHIS-QOL-8, WHOQOL-BREF), and inflammatory indices. Within-group tests and difference-in-differences analyses were applied. Groups were comparable at baseline. SG improved significantly in 6MWD (+27 m), TUG (−0.70 s), dyspnea/exertion (mMRC −1.37; Borg −3.42), QoL (SGRQ −19.74; EUROHIS +8.37; WHOQOL-BREF +18.58), and inflammatory indices (all $p<0.001$ except TUG $p=0.007$). CG showed no functional gains and a small 6MWD decline, with only modest symptom and QoL changes. Difference-in-differences favored SG across most outcomes, with large effects for several endpoints. No serious adverse events were recorded. Individualized pulmonary rehabilitation was feasible and safe, improving QoL in PTLD while increasing functional capacity and reducing symptom burden, supporting integration into post-TB care and broader delivery models..

**Keywords:** post-tuberculosis lung disease, pulmonary rehabilitation, quality of life, six-minute walk test, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio

## 1. Introduction

Tuberculosis (TB) remains one of the most lethal infectious diseases worldwide, despite major advances in diagnosis and antimicrobial treatment [1]. Although global efforts in the antibiotic era have primarily focused on improving cure rates, a substantial proportion of TB survivors continue to experience persistent respiratory impairment, profoundly affecting their quality of life (QoL) and increasing long-term mortality risk [2,3]. Post-tuberculosis lung disease (PTLD) encompasses a wide spectrum of chronic respiratory sequelae that persist after microbiological cure, affecting an estimated 18–87% of individuals treated for TB [4].

The global burden of PTLD is considerable. In 2019, approximately 58 million people were estimated to be living with PTLD, with the greatest loss of disability-adjusted

life years occurring in low-income countries [5]. TB survivors have been shown to carry a nearly threefold higher risk of mortality compared with the general population, even after successful completion of anti-tuberculosis therapy [3,6]. Beyond mortality, PTLD-related physical and psychological impairments are associated with reduced functional capacity, diminished economic productivity, and, in severe cases, job loss, further amplifying the societal impact of the disease [7].

The development and severity of post-TB sequelae are influenced by multiple factors. Delayed diagnosis, extensive lung damage at presentation, treatment interruptions, drug-resistant TB, pre-existing undernutrition or inadequate nutritional status during therapy, and inhalational exposures such as tobacco smoke or silica dust have all been identified as contributors to unfavorable long-term pulmonary outcomes. These factors interact to shape the extent of residual lung injury and functional limitation following TB cure [2,8].

From a pathophysiological perspective, PTLD is characterized by a complex interplay between host immune responses and environmental influences, leading to both reversible and irreversible changes in pulmonary structure, function, and immune signaling. Unlike some chronic lung diseases, PTLD is often marked by persistent inflammation and abnormal tissue repair, resulting in fibrosis, scarring, bronchiectasis, or cavitation. Consequently, patients may exhibit restrictive, obstructive, or mixed ventilatory patterns, with symptoms that can emerge or worsen years after completion of TB treatment, in some cases up to six years later [2,7,9].

In this context, the neutrophil-to-lymphocyte ratio (NLR) represents an accessible marker of systemic inflammation and immune imbalance, reflecting the interplay between innate and adaptive immune responses [10]. In post-tuberculosis lung disease, persistent low-grade inflammation contributes to ongoing lung injury, functional limitation, and impaired health-related quality of life. Therefore, NLR provides relevant insight into residual inflammatory burden and its modulation following pulmonary rehabilitation in a pre–post study design [10,11].

Given the heterogeneity of PTLD, several critical challenges remain. It is essential to identify which subgroups of TB survivors are most likely to benefit from interventions aimed at improving physical capacity, mental well-being, and overall QoL. Furthermore, determining which clinical, functional, and biological markers before and after TB treatment can predict response to rehabilitation strategies is crucial. Finally, there is a pressing need to evaluate effective, scalable interventions in TB-endemic settings using assessment tools and therapeutic approaches that are locally acceptable and feasible.

Pulmonary rehabilitation has emerged as a cornerstone intervention in the management of chronic respiratory diseases and represents a promising therapeutic strategy for individuals with PTLD. By addressing dyspnea, exercise intolerance, functional impairment, and psychosocial consequences, pulmonary rehabilitation has the potential to mitigate long-term disability, enhance quality of life, and reduce the broader health and economic burden associated with post-tuberculosis lung disease [7,12].

The platelet-to-lymphocyte ratio (PLR) reflects systemic inflammation and platelet activation, mechanisms increasingly implicated in the pathophysiology of post-tuberculosis pulmonary sequelae. Elevated PLR has been associated with chronic inflammatory activity and disease severity in chronic respiratory disorders. Its assessment alongside functional and quality-of-life outcomes enables evaluation of systemic inflammatory status and response to pulmonary rehabilitation [11].

Post-tuberculosis lung disease (PTLD) represents a major source of long-term morbidity, characterized by persistent respiratory symptoms, reduced functional exercise capacity, and chronic physical limitation despite microbiological cure. Increasing evidence indicates that PTLD substantially impairs health-related quality of life (HRQoL), affecting not only physical functioning but also psychological well-being and social participation. As these patient-perceived outcomes are not fully explained by physiological impairment alone, their systematic assessment is essential for an accurate evaluation of disease burden [7,13].

Pulmonary rehabilitation is increasingly recognized as an effective intervention for individuals with PTLD, with growing evidence demonstrating improvements in functional performance, symptom burden, and HRQoL. Pre–post interventional and controlled studies report clinically meaningful gains in exercise capacity and dyspnea accompanied by significant improvements in quality-of-life scores. These findings support the inclusion of HRQoL as a core outcome in rehabilitation studies, reflecting patient-centered benefits beyond traditional functional endpoints [13,14].

Although pulmonary rehabilitation is well established in chronic respiratory diseases, the largest and most robust body of evidence has been generated in COPD populations. However, PTLD represents a distinct and heterogeneous clinical entity, with sequelae that may include fibro-cicatricial parenchymal changes, bronchiectasis, residual cavitation, small-airway involvement, and ventilation-perfusion abnormalities, frequently resulting in mixed obstructive-restrictive ventilatory defects. This post-infectious structural damage and its inflammatory and functional consequences may differ substantially from COPD pathophysiology, potentially influencing symptom burden, exercise limitation, and health-related quality of life, as well as responsiveness to rehabilitation interventions. Therefore, generating PTLD-specific evidence is necessary to support tailored rehabilitation strategies and patient-centered outcome assessment [2,12].

Validated quality-of-life instruments are critical for capturing the multidimensional effects of pulmonary rehabilitation. The St. George's Respiratory Questionnaire (SGRQ) provides a disease-specific assessment of symptoms, activity limitation, and disease impact and is sensitive to intervention-related changes in chronic respiratory conditions. In contrast, generic instruments such as WHOQOL-BREF and EUROHIS-QOL enable a broader evaluation of physical, psychological, and social domains, facilitating a comprehensive assessment of overall health status and well-being [15–17].

In a pre–post pulmonary rehabilitation study design, the combined use of disease-specific and generic HRQoL scales alongside functional measures (6MWD, TUG) and symptom scores (mMRC, Borg scale) allows a robust and clinically relevant evaluation of treatment effects. This multidimensional outcome framework aligns with current international standards for the assessment and rehabilitation of PTLD and supports a comprehensive evaluation of intervention efficacy [2,12,13].

## 2. Materials and Methods

### 2.1. Study Design and Setting

This prospective controlled interventional study was conducted between March 2025 and December 2025 in the Pneumology Department of the "Victor Babeș" Clinical Hospital of Infectious Diseases and Pneumophthisiology, Craiova, and in the Department of Physical Medicine and Rehabilitation at Filantropia Hospital, Craiova, Romania

Group allocation was not randomized. Participants were assigned to the rehabilitation group (Study Group - SG) or standard care group (Control Group - CG) based on participants' willingness to engage in the pulmonary rehabilitation

program (Figure 1. Diagram of the study) and on practical feasibility, including rehabilitation slot availability during the study period and the participant's ability to attend on-site sessions. Baseline comparability between groups was evaluated using demographic and clinical variables and baseline (T1) outcome measures. To account for non-randomization and potential baseline differences, intervention effects were estimated using difference-in-differences analyses (between-group difference in change from T1 to T2); additional models were adjusted for baseline outcome values (and relevant covariates) where applicable.

The study aimed to evaluate the impact of a tailored pulmonary rehabilitation program on physical performance and quality of life in patients diagnosed with PTLD. Although participants were not randomly assigned, baseline characteristics between groups were comparable, and potential confounding factors were controlled for through statistical adjustments to minimize selection bias and enhance the study's internal validity.

The study protocol was approved by the Ethics Committee of the University of Medicine and Pharmacy of Craiova (Approval No. 9/10.01.2025), and written informed consent was obtained from all participants prior to inclusion in the study.

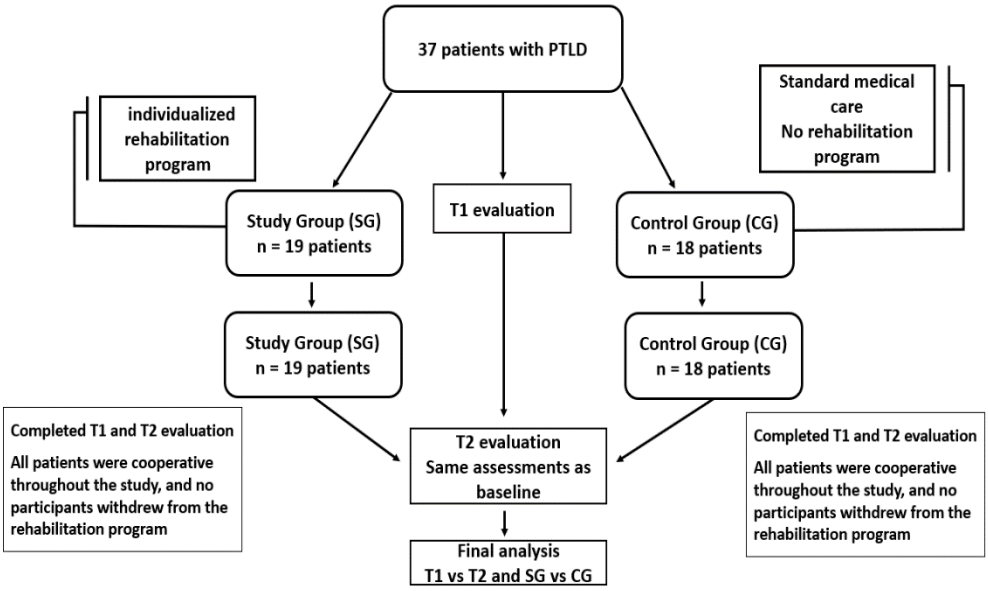


**Figure 1. Diagram of the study**

### 2.2. Study Population and Group Allocation

The present research was conducted on 37 patients diagnosed with PTLD, who had completed anti-tuberculosis treatment and presented persistent respiratory impairment. Patients diagnosed with PTLD were divided into two groups:

- **Study Group (SG)** – 19 patients who participated in an individualized pulmonary rehabilitation program;
- **Control Group (CG)** – 18 patients who received standard medical care without structured pulmonary rehabilitation.

Baseline demographic and clinical characteristics of both groups are presented in **Table 3 (Results)**.

#### 2.2.1. Inclusion and Exclusion Criteria

The inclusion criteria considered for group allocation were:

- age ≥ 18 years;
- documented history of pulmonary tuberculosis with completion of anti-tuberculosis therapy;
- presence of residual pulmonary impairment compatible with PTLD (restrictive, obstructive, or mixed ventilatory pattern);
- clinical stability at the time of enrollment;
- ability to understand and comply with the rehabilitation protocol and assessments.

Exclusion criteria included:

- active tuberculosis or ongoing anti-tuberculosis treatment;
- acute respiratory exacerbation at enrollment;
- severe cardiovascular, neurological, or musculoskeletal conditions limiting participation in physical training;
- refusal or inability to provide informed consent.

### 2.3. Clinical and Functional Assessment

For all patients included in the study, clinical, functional, and laboratory data were analyzed using standardized assessment protocols.

The clinical evaluation included:

- complete general physical examination;
- measurement of anthropometric parameters, including body weight, height, and body mass index (BMI = weight (kg)/height$^2$ (m$^2$));
- respiratory system examination (inspection, palpation, percussion, and auscultation);
- musculoskeletal assessment, including posture, joint mobility, and muscle strength (Manual Muscle Testing, MMT);
- assessment of balance and gait.

#### 2.3.1. Anthropometric Assessment

Anthropometric data were collected by measuring height and body weight, and body mass index (BMI) was calculated using the formula BMI = weight (kg)/height$^2$ (m$^2$). Body weight was recorded using a Fazzini S7350HR electronic scale (0–200 kg, accuracy 100 g). Height was measured using a portable stadiometer with an accuracy of 0.1 mm. Patients were barefoot and wore light clothing. Each measurement was performed three times by the same evaluator, and the mean value was used for analysis.

#### 2.3.2. Physical Performance and Gait Assessment

For gait analysis, the BTS G-WALK wireless system (BTS Bioengineering Corp., Italy) was used. This system includes a tri-axial accelerometer, a magnetic sensor, and a tri-axial gyroscope, allowing functional gait analysis while worn by the patient [23]. All patients received standardized instructions and were familiarized with the equipment prior to testing. Verbal encouragement was provided to promote maximal effort.

Gait and functional performance parameters included:

- Timed Up and Go (TUG) test, assessing functional mobility and balance during transitions [21];
- Symmetry index, evaluating bilateral gait symmetry;
- Six-Minute Walk Test (6MWT), assessing functional exercise capacity and walking cadence [22];
- Walking cadence, reflecting gait efficiency and motor control.

#### 2.3.3. Symptom and Quality-of-Life Assessment

Functional assessment was performed using the following tools:

- Modified Medical Research Council (mMRC) dyspnea scale (5-point ordinal scale used to assess the severity of breathlessness during daily activities. Scores range from 0 to 4, with higher scores indicating greater dyspnea-related functional limitation (0 = dyspnea only with strenuous exercise; 4 = dyspnea when dressing or inability to leave the house)) [18];
- Borg CR10 scale (used to quantify perceived exertion and dyspnea during physical activity. The scale ranges from 0 (no exertion) to 10 (maximal exertion), with higher scores reflecting greater intensity of perceived effort.) [19];
- St. George's Respiratory Questionnaire (SGRQ) (disease-specific instrument for assessing health-related quality of life in patients with chronic respiratory diseases. It consists of 50 items grouped into three domains (Symptoms, Activity, and Impacts). Total and domain scores range from 0 to 100, with higher scores indicating worse health-related quality of life. A change of 4 units or more is considered clinically significant.) [15,20];
- EUROHIS-QOL-8 and WHOQOL-BREF questionnaires (the EUROHIS-QOL-8 consists of 8 items rated on a 5-point Likert scale, yielding total scores ranging from 8 to 40, with higher scores indicating better perceived quality of life. The WHOQOL-BREF includes 26 items distributed across four domains (physical health, psychological health, social relationships, and environment), with domain scores transformed to a 0–100 scale, where higher scores denote better quality of life.) [16,17].

### 2.4. Laboratory Assessment

Laboratory evaluation included routine blood tests, from which inflammatory indices were calculated:

- **Neutrophil-to-lymphocyte ratio (NLR)**;
- **Platelet-to-lymphocyte ratio (PLR)**.

Peripheral venous blood samples were collected from the antecubital vein after an overnight fast and under aseptic conditions at two predefined time points: baseline (T1, prior to initiation of pulmonary rehabilitation) and post-intervention (T2, after completion of the rehabilitation program). A complete blood count was performed using an automated hematology analyzer (MINDRAY BC-6800).

NLR and PLR were calculated from absolute neutrophil, lymphocyte, and platelet counts. Adult reference ranges were applied. Changes between T1 and T2 were used to evaluate systemic inflammatory status and response to pulmonary rehabilitation.

### 2.5. Pulmonary Rehabilitation Program

Patients in the Study Group participated in an individualized pulmonary rehabilitation program adapted to functional status and clinical tolerance. Peripheral oxygen saturation ($SpO_2$) was continuously monitored during exercise sessions using pulse oximetry to ensure patient safety and appropriate exercise intensity.

The rehabilitation program included:

- breathing exercises;
- aerobic training with progressive intensity;
- upper and lower limb strengthening;
- balance and gait training;
- education and counselling [12].

Exercise sessions were performed daily, with a duration of 40–60 minutes per session, over a total period of 2 weeks in-patient (12 supervised sessions) (Table 1).

**Table 1. In-patient rehabilitation program**

**(Dyspnea Borg 3–4/10,** mMRC **1-2/4, SpO2 ≥ 92%. Progress only one variable per session)**

| Session | **Ante Meridiem**<br>(Respiratory therapy + Strength + Balance) | **Post Meridiem**<br>(Aerobic) |
|---|---|---|
| **1** | Respiratory therapy 15–20 min: breathing control, diaphragmatic, thoracic expansion (3×3), thoracic mobility; add huff if secretions.<br>Strength 15–20 min: 1–2 sets×10–12 reps @~30–40% (knee ext/flex, elbow flex/ext), rest 90–120 s.<br>Balance/gait 5–10 min: basic gait drills, direction changes, planned pauses. | Aerobic intervals 20–30 min:<br>- warm-up 5 min;<br>- 8–10 × (1 min easy + 1 min very easy);<br>- cool-down 5 min<br>Breathing reset 3–5 min. |
| **2** | Respiratory therapy 15–20 min: same + pacing cues.<br>Strength: 1–2 sets×10–12 reps, technique + exhale on effort.<br>Balance/gait 5–10 min: as S1 with slightly less support if safe. | Aerobic 20–30 min:<br>-warm-up 5 min;<br>- 7×(2 min easy + 1 min very easy)<br>- cool-down 5 min |
| **3** | Respiratory therapy 15–20 min: add gentle inspiratory holds; thoracic mobility.<br>Strength: progress to 2 sets for main exercises as tolerated.<br>Balance/gait 5–10 min. | Aerobic 20–25 min:<br>-warm-up 5 min;<br>- intervals 2 min easy + 1 min very easy; - - cool-down 5 min |
| **4** | Respiratory therapy ~15 min.<br>Strength:<br>2 sets×10–12 reps; add calf raises + low step-ups if safe.<br>Balance:<br>unstable surface biped stance 3×30–45 s with close guarding. | Aerobic 25–30 min:<br>-warm-up 5 min;<br>-intervals 3 min easy + 1–2 min very easy;<br>- cool-down 5 min |
| **5** | Respiratory therapy ~15 min.<br>Strength: if stable SpO2/dyspnea ≤4, slightly increase resistance; keep 10–12 reps, 2 sets.<br>Balance/gait: progress obstacles/turns. | Aerobic 25–30 min: progress ONE variable. Example 4 × (4 min easy + 2 min very easy).<br>-cool-down 5 min |
| **6** | Respiratory therapy ~15 min.<br>Strength: 2 sets×10–12 reps.<br>Balance: obstacles + weight shifts; unstable surface 4×45 s. | Aerobic ~30 min total: include optional 10 min continuous easy segment if tolerated; otherwise, intervals;<br>-cool-down 5 min |
| **7** | Respiratory therapy: dyspnea control during effort (planned pauses, pursed-lip breathing).<br>Strength: 2–3 sets as tolerated; add band rows (posture/scapular).<br>Balance/gait 5–10 min. | Aerobic 30–35 min: target 12–15 min continuous easy + intervals as needed;<br>-cool-down 5 min |
| **8** | Respiratory therapy ~15 min.<br>Strength: maintain/progress as tolerated.<br>Balance: assisted tandem walk 2×20–30 m; assisted single-leg stance 3×10–15 s/side. | Aerobic to ~35 min total: aim 15–20 min continuous easy + easy recovery;<br>-cool-down 5 min |
| **9** | Respiratory therapy ~15 min.<br>Strength: increase resistance so last 2 reps are moderate, dyspnea ≤4; 2–3 sets.<br>Balance/gait: reinforce safe walking economy. | Aerobic: 20–25 min continuous at Borg 3–4;<br>-cool-down 5 min |
| **10** | Respiratory therapy brief reset 10–15 min as needed.<br>Functional circuit: sit-to-stand 2×8–10; step-ups 2×8/leg; band rows 2×12; calf raises 2×12; paced breathing between sets. | Aerobic 30–40 min total: aim 25–30 min continuous easy if tolerated;<br>-cool-down 5 min |

| | | |
|---|---|---|
| **11** | Respiratory therapy ~10–15 min.<br>Gait conditioning: 10 min alternating 30 s slightly faster + 60 s normal, monitor SpO2. | Aerobic: ~30 min continuous easy; revert to intervals if desaturation/marked dyspnea; cool-down 5 min |
| **12** | Ante Meridiem re-check: response to 6–10 min walk, breathing technique, key functional tasks (optional safe stair trial).<br>Teach home routine + pacing. | Home-transition 20–30 min: easy aerobic + simplified home plan; finalize progression rules. |
| **Short education (2–3 minutes at the end of each session). Example:**<br>**Pacing (energy dosing):** Try to *spread your effort out* instead of doing everything at once. Move at a comfortable pace, take short breaks before you feel very breathless, and split tasks into smaller steps. A simple rule is: if you can't speak in short sentences, slow down and pause.<br>**Anti-breathlessness positions (to ease dyspnea):** When you feel short of breath, use positions that support your upper body and help your breathing muscles work better. Lean forward with your hands supported on your thighs (*hands-on-thighs position*), or sit/stand leaning forward with your forearms resting on a table or countertop. Relax your shoulders and let your neck and jaw soften.<br>**Hydration:** Drink fluids regularly throughout the day (unless your doctor has told you to restrict fluids).<br>Good hydration can help keep mucus thinner and easier to clear, especially if you have a productive cough.<br>**Airway hygiene (if your cough is productive):** If you're bringing up mucus, the goal is to clear it effectively without exhausting yourself. Use gentle, controlled coughing and rest between attempts. If you notice mucus becoming thicker, harder to clear, or changing color with fever or worsening breathlessness, let your clinician know. | | |

Afterwards, the patients followed a **home-training program**, 3 months, under the supervision of a **physiotherapist**, on an **outpatient basis** (Table 2 ).Training intensity and volume were progressively adjusted based on patient tolerance and perceived exertion. Patients in the Control Group received standard medical care and general physical activity advice without structured rehabilitation.

**Table 2. Out-patient kinetic program**

| **Daily home exercise program (20–30 min), 5–6 days/week, 3 months** | |
|---|---|
| **Warm-up + breathing (5 minutes)** | **Breathing control** 1 minute (inhale through the nose, exhale slowly).<br>**Pursed-lip breathing** 1–2 minutes (make the exhale longer than the inhale).<br>**Chest/shoulder mobility** 2 minutes: raise your arms up as you inhale, lower them as you exhale, gentle shoulder rolls. |
| **Simple strength (10–12 minutes)** | Do **1–2 sets**. Reps: **8–12**. Rest: **60–90 sec**. **Exhale on effort.**<br>**Sit-to-stand (from a chair)** 1–2 sets × 8–12 (use your hands on your thighs if needed).<br>**Calf raises** 1–2 sets × 10–15, light support from the chair backrest.<br>**Step-ups on a low step** (if safe) 1 set × 8–10 each leg (slow, controlled).<br>**Wall push-ups** 1–2 sets × 8–12. |
| **Balance (3–5 minutes)** | **Heel-to-toe walking** down a hallway 2 passes (or next to a wall).<br>**Single-leg stand** 2 × 10–20 sec each side (hold on for support if needed). |
| **Easy aerobic (8–15 minutes)** | Choose one: **Walking** indoors/outdoors for 8–15 min at a pace where "I can talk, but I feel I'm working."<br>Or, if you get breathless quickly: intervals of **1 minute normal walk + 1 minute very easy**, repeated **6–8 times**. |
| **Cool-down (2–3 minutes)** | Very slow walking + **pursed-lip breathing** for 1–2 minutes. |

### 2.6. Statistical Analysis

All data were collected from patient observation sheets and entered into a dedicated database. Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 29.0 (IBM Corp., Armonk, NY, USA).

Continuous variables are presented as mean ± standard deviation, while categorical variables are expressed as absolute numbers and percentages. Normality was assessed using the Shapiro–Wilk test. Between-group comparisons were conducted using Welch's t-test or non-parametric alternatives, while within-group changes were analyzed using paired tests. Difference-in-differences analyses were applied. A p-value $< 0.05$ was considered statistically significant.

## 3. Results.

This section presents the experimental findings of the study, including baseline characteristics, within-group and between-group comparisons, and changes in functional, symptomatic, quality-of-life, and inflammatory outcomes following pulmonary rehabilitation.

### 3.1. Baseline Characteristics of the Study Population

Patients with post-tuberculosis lung disease (PTLD) included in this study presented with a heterogeneous clinical profile, ranging from mild exertional dyspnea to marked functional limitation and reduced exercise tolerance. A total of 37 participants were evaluated, of whom 19 were assigned to the Study Group (SG) and 18 to the Control Group (CG).

Baseline demographic and clinical characteristics are summarized in **Table 3**. The two groups were well balanced at baseline, with no statistically significant differences observed for age, anthropometric parameters, disease duration, or ventilatory dysfunction patterns. Restrictive and mixed ventilatory dysfunctions predominated in both groups, while obstructive dysfunction was not observed.

**Table 3. Baseline demographic data**

| Variable | SG (patients) | SG (Mean ± SD) | CG (patients) | CG (Mean ± SD) | p-value |
|---|---|---|---|---|---|
| **Age (years)** | 19 | 46.11 ± 15.19 | 18 | 47.83 ± 11.55 | 0.698 |
| **Weight (kg)** | 19 | 70.42 ± 14.77 | 18 | 70.44 ± 15.2 | 0.996 |
| **Height (m)** | 19 | 1.75 ± 0.11 | 18 | 1.75 ± 0.11 | 0.973 |
| **BMI (kg/m²)** | 19 | 22.86 ± 3.03 | 18 | 23.07 ± 2.04 | 0.806 |
| **Disease duration (months)** | 19 | 11.37 ± 7.18 | 18 | 11.17 ± 6.79 | 0.931 |
| **Ventilatory dysfunction** | 19 | 2 = 11, 3 = 8 | 18 | 2 = 11, 3 = 7 | 1.000 |

Abbreviations: SG = Study Group; CG = Control Group; SD = standard deviation; BMI = body mass index.

Ventilatory dysfunction categories: 1 = obstructive; 2 = restrictive; 3 = mixed.

In SG, male patients predominated (14/19; 73.7%) compared with females (5/19; 26.3%), while in CG male patients also predominated (11/18; 61.1%) compared with females (7/18; 38.9%) (Table 2). When stratified by place of residence, the urban environment predominated in SG (11/19; 57.9%) and in CG (8/18; 44.4%) (Table 4). Venti-

latory dysfunction patterns were reported as restrictive and mixed; obstructive ventilatory dysfunction was not observed in the dataset, which can be explained by the predominance of post-tuberculosis parenchymal fibrosis, lung volume loss, and cicatricial remodeling, leading mainly to restrictive or combined ventilatory impairment rather than isolated airflow obstruction in the absence of significant airway-predominant disease or advanced smoking-related COPD.

Sex- and residence-stratified baseline characteristics are presented in Table 4. Male patients predominated in both groups, and the urban environment was more frequent than rural residence. Across both SG and CG, males showed higher mean weight and height than females, consistent with expected anthropometric differences. Female subgroups were smaller, particularly in the SG, and therefore subgroup distributions should be interpreted with caution. When stratified by place of residence, urban participants tended to be older, whereas rural participants had longer mean disease duration. Anthropometric measures and ventilatory dysfunction patterns were otherwise comparable across strata, with no statistically significant between-group differences within sex or residence categories.

**Table 4. Baseline demographic and clinical characteristics stratified by gender (female/male) and place of residence (urban/rural)**

**Stratification by gender**

| Variable | Study Female (n=5) | Control Female (n=7) | p Female (Study vs Control) | Study Male (n=14) | Control Male (n=11) | p Male (Study vs Control) |
|---|---|---|---|---|---|---|
| **Age (years)** | 44.2 ± 6.72 | 45.57 ± 10.41 | 0.787 | 46.79 ± 17.43 | 49.27 ± 12.48 | 0.682 |
| **Weight (kg)** | 55.0 ± 9.59 | 61.43 ± 14.16 | 0.371 | 75.93 ± 12.23 | 76.18 ± 13.39 | 0.962 |
| **Height (m)** | 1.66 ± 0.15 | 1.7 ± 0.14 | 0.635 | 1.78 ± 0.08 | 1.78 ± 0.09 | 0.938 |
| **BMI (kg/m²)** | 19.96 ± 0.36 | 22.26 ± 2.01 | 0.023 | 23.89 ± 2.88 | 23.58 ± 1.97 | 0.752 |
| **Disease duration (months)** | 7.2 ± 2.68 | 9.29 ± 6.45 | 0.463 | 12.86 ± 7.75 | 12.36 ± 7.03 | 0.869 |
| **Ventilatory dysfunction (counts)** | 2=0, 3=5 | 2=3, 3=4 | 0.31 | 2=11, 3=3 | 2=8, 3=3 | 1.000 |

**Stratification by place of residence**

| Variable | Study Urban (n=11) | Control Urban (n=8) | p Urban (Study vs Control) | Study Rural (n=8) | Control Rural (n=10) | p Rural (Study vs Control) |
|---|---|---|---|---|---|---|
| **Age (years)** | 53.09 ± 8.41 | 53.75 ± 6.36 | 0.848 | 36.5 ± 17.61 | 43.1 ± 12.82 | 0.391 |
| **Weight (kg)** | 67.64 ± 16.7 | 70.0 ± 18.33 | 0.777 | 74.25 ± 11.55 | 70.8 ± 13.21 | 0.563 |
| **Height (m)** | 1.73 ± 0.12 | 1.74 ± 0.12 | 0.88 | 1.77 ± 0.11 | 1.75 ± 0.12 | 0.718 |
| **BMI (kg/m²)** | 22.32 ± 3.3 | 22.88 ± 1.69 | 0.638 | 23.6 ± 2.64 | 23.22 ± 2.36 | 0.755 |
| **Disease duration (months)** | 7.64 ± 2.8 | 7.38 ± 2.56 | 0.835 | 16.5 ± 8.33 | 14.2 ± 7.69 | 0.556 |
| **Ventilatory dysfunction (counts)** | 2=5, 3=6 | 2=5, 3=3 | 0.788 | 2=6, 3=2 | 2=6, 3=4 | 0.867 |

Abbreviations: BMI = body mass index; SD = standard deviation.

Ventilatory dysfunction categories: 1 = obstructive; 2 = restrictive; 3 = mixed.

At baseline, patients exhibited reduced functional capacity, impaired mobility, and substantial symptom burden, reflected by limited six-minute walk distance (6MWD), prolonged Timed Up and Go (TUG) performance, altered gait parameters, and moderate dyspnea. Quality-of-life measures indicated marked impairment across both disease-specific and generic domains.

### 3.2. Within-Group Pre–Post Changes

After completion of the rehabilitation period, within-group (paired) pre–post changes from baseline (T1) to follow-up (T2) were evaluated for functional capacity, mobility, gait parameters, respiratory symptoms, quality of life, and inflammatory indices (Table 3 for SG; Table 4 for CG).

#### 3.2.1. Study Group (SG)

Within-group pre–post changes observed in the Study Group are presented in Table 5.

In the SG, significant improvements were observed across functional, symptomatic, and quality-of-life outcomes. Exercise tolerance increased significantly, as demonstrated by a higher 6MWD at follow-up. Functional mobility improved, with a reduction in TUG time. Gait-related parameters also changed favorably, with an increase in symmetry index and a reduction in stance phase duration. In parallel, symptom burden decreased substantially, with marked reductions in dyspnea severity and perceived exertion during effort.

**Table 5.**

**Within-group (paired) pre–post changes in the Study Group across outcomes**

| Outcome | N (paired) | T1 (mean ± SD) | T2 (mean ± SD) | Mean Δ (T2–T1) | Normality p (Shapiro–Wilk on Δ) | Test | Paired p-value |
|---|---|---|---|---|---|---|---|
| **6MWD (meters)** | 19 | 581.26 ± 66.51 | 608.26 ± 65.09 | 27.00 | 0.037 | Wilcoxon | <0.001 |
| **TUG (seconds)** | 19 | 13.03 ± 0.85 | 12.34 ± 1.14 | −0.70 | 0.002 | Wilcoxon | 0.007 |
| **SI (%)** | 19 | 92.75 ± 4.7 | 96.79 ± 0.66 | 4.05 | <0.001 | Wilcoxon | <0.001 |
| **Stance phase** | 19 | 60.08 ± 1.99 | 58.69 ± 1.97 | −1.39 | 0.018 | Wilcoxon | 0.006 |
| **mMRC** | 19 | 2.0 ± 0.58 | 0.63 ± 0.5 | −1.37 | <0.001 | Wilcoxon | <0.001 |
| **Borg CR10** | 19 | 6.68 ± 1.2 | 3.26 ± 1.15 | −3.42 | <0.001 | Wilcoxon | <0.001 |
| **SGRQ** | 19 | 52.63 ± 13.51 | 32.89 ± 11.95 | −19.74 | 0.111 | Paired t-test | <0.001 |
| **EUROHIS-QOL-8** | 19 | 21.16 ± 4.21 | 29.53 ± 3.85 | 8.37 | 0.016 | Wilcoxon | <0.001 |
| **WHOQOL-BREF** | 19 | 48.37 ± 10.56 | 66.95 ± 9.22 | 18.58 | 0.040 | Wilcoxon | <0.001 |
| **NLR** | 19 | 3.65 ± 1.01 | 2.46 ± 0.58 | −1.19 | 0.076 | Paired t-test | <0.001 |
| **PLR** | 19 | 174.74 ± 37.45 | 141.54 ± 25.49 | −33.20 | 0.001 | Wilcoxon | <0.001 |

Abbreviations: 6MWD = six-minute walk distance; TUG = Timed Up and Go test; SI = symmetry index; mMRC = modified Medical Research Council dyspnea scale; Borg CR10 = Borg Category Ratio 10 scale; SGRQ = St. George's Respiratory Questionnaire; EUROHIS-QOL-8 = EUROHIS Quality of Life 8-item index; WHOQOL-BREF = World Health Organization Quality of Life – Brief version; NLR = neutrophil-to-lymphocyte ratio; PLR = platelet-to-lymphocyte ratio; SD = standard deviation.

#### 3.2.2. Control Group (CG)

Within-group pre–post changes observed in the Control Group are presented in Table 6.

In contrast, the CG showed a different pattern of change over time. Functional performance did not improve, and 6MWD decreased slightly at follow-up. Mobility and gait parameters remained largely unchanged. Although modest reductions in dyspnea and perceived exertion were observed, these changes were smaller in magnitude and were not accompanied by objective improvements in functional capacity

**Table 6.**

**Within-group (paired) pre–post changes in the Control Group across outcomes**

| Outcome | N (paired) | T1 (mean ± SD) | T2 (mean ± SD) | Mean Δ (T2–T1) | Normality p (Shapiro–Wilk on Δ) | Test | Paired p-value |
|---|---|---|---|---|---|---|---|
| **6MWD (m)** | 18 | 581.56 ± 66.08 | 573.17 ± 62.66 | −8.39 | 0.034 | Wilcoxon | 0.009 |
| **TUG (s)** | 18 | 12.73 ± 0.91 | 12.72 ± 0.91 | −0.01 | 0.742 | Paired t-test | 0.916 |
| **SI (%)** | 18 | 94.59 ± 3.42 | 94.29 ± 4.49 | −0.30 | 0.114 | Paired t-test | 0.828 |
| **Stance phase** | 18 | 59.75 ± 2.14 | 59.45 ± 2.22 | −0.30 | 0.077 | Paired t-test | 0.694 |
| **mMRC** | 18 | 1.61 ± 0.61 | 1.22 ± 0.55 | −0.39 | <0.001 | Wilcoxon | 0.008 |
| **Borg CR10** | 18 | 5.0 ± 0.91 | 4.22 ± 0.65 | −0.78 | <0.001 | Wilcoxon | 0.001 |
| **SGRQ** | 18 | 54.5 ± 9.23 | 49.83 ± 8.55 | −4.67 | 0.068 | Paired t-test | 0.010 |
| **EUROHIS-QOL-8** | 18 | 27.83 ± 4.85 | 28.94 ± 4.5 | 1.11 | 0.010 | Wilcoxon | 0.030 |
| **WHOQOL-BREF** | 18 | 53.78 ± 11.13 | 56.11 ± 11.53 | 2.33 | 0.100 | Paired t-test | 0.007 |
| **NLR** | 18 | 3.21 ± 1.05 | 3.23 ± 1.06 | 0.02 | 0.002 | Wilcoxon | 0.777 |
| **PLR** | 18 | 138.12 ± 24.9 | 150.35 ± 34.28 | 12.23 | 0.252 | Paired t-test | 0.150 |

Abbreviations: 6MWD = six-minute walk distance; TUG = Timed Up and Go test; SI = symmetry index; mMRC = modified Medical Research Council dyspnea scale; Borg CR10 = Borg Category Ratio 10 scale; SGRQ = St. George's Respiratory Questionnaire; EUROHIS-QOL-8 = EUROHIS Quality of Life 8-item index; WHOQOL-BREF = World Health Organization Quality of Life – Brief version; NLR = neutrophil-to-lymphocyte ratio; PLR = platelet-to-lymphocyte ratio; SD = standard deviation.

### 3.3. Between-Group Comparisons at Baseline and Follow-Up

Quality-of-life outcomes, representing the primary endpoint of the study, are detailed in Tables 5–7.

Between-group comparisons at baseline (T1) and follow-up (T2) are presented in Table 7.

**Table 7. Outcomes in SG and CG at both assessment moments (T1 and T2)**

| Outcome | T1 Study (mean ± SD) | T1 Control (mean ± SD) | T1 Test | p T1 | T2 Study (mean ± SD) | T2 Control (mean ± SD) | T2 Test | p T2 |
|---|---|---|---|---|---|---|---|---|
| **6MWD (m)** | 581.26 ± 66.51 | 581.56 ± 66.08 | Mann–Whitney | 0.963 | 608.26 ± 65.09 | 573.17 ± 62.66 | Mann–Whitney | 0.091 |
| **TUG (s)** | 13.03 ± 0.85 | 12.73 ± 0.91 | Mann–Whitney | 0.218 | 12.34 ± 1.14 | 12.72 ± 0.91 | Welch t-test | 0.271 |
| **SI (%)** | 92.75 ± 4.7 | 94.59 ± 3.42 | Mann–Whitney | 0.098 | 96.79 ± 0.66 | 94.29 ± 4.49 | Mann–Whitney | 0.005 |
| **Stance phase** | 60.08 ± 1.99 | 59.75 ± 2.14 | Mann–Whitney | 0.582 | 58.69 ± 1.97 | 59.45 ± 2.22 | Welch t-test | 0.280 |
| **mMRC** | 2.0 ± 0.58 | 1.61 ± 0.61 | Mann–Whitney | 0.053 | 0.63 ± 0.5 | 1.22 ± 0.55 | Mann–Whitney | 0.003 |
| **Borg CR10** | 6.68 ± 1.2 | 5.0 ± 0.91 | Mann–Whitney | <0.001 | 3.26 ± 1.15 | 4.22 ± 0.65 | Mann–Whitney | 0.005 |
| **SGRQ** | 52.63 ± 13.51 | 54.5 ± 9.23 | Welch t-test | 0.625 | 32.89 ± 11.95 | 49.83 ± 8.55 | Welch t-test | <0.001 |
| **EUROHIS-QOL-8** | 21.16 ± 4.21 | 27.83 ± 4.85 | Welch t-test | <0.001 | 29.53 ± 3.85 | 28.94 ± 4.5 | Mann–Whitney | 0.760 |
| **WHOQOL-BREF** | 48.37 ± 10.56 | 53.78 ± 11.13 | Welch t-test | 0.139 | 66.95 ± 9.22 | 56.11 ± 11.53 | Mann–Whitney | 0.010 |
| **NLR** | 3.65 ± 1.01 | 3.21 ± 1.05 | Mann–Whitney | 0.188 | 2.46 ± 0.58 | 3.23 ± 1.06 | Mann–Whitney | 0.012 |
| **PLR** | 174.74 ± 37.45 | 138.12 ± 24.9 | Mann–Whitney | 0.006 | 141.54 ± 25.49 | 150.35 ± 34.28 | Mann–Whitney | 0.613 |

Abbreviations: 6MWD = six-minute walk distance; TUG = Timed Up and Go test; SI = symmetry index; mMRC = modified Medical Research Council dyspnea scale; Borg CR10 = Borg Category Ratio 10 scale; SGRQ = St. George's Respiratory Questionnaire; EUROHIS-QOL-8 = EUROHIS Quality of Life 8-item index; WHOQOL-BREF = World Health Organization Quality of Life – Brief version; NLR = neutrophil-to-lymphocyte ratio; PLR = platelet-to-lymphocyte ratio; SD = standard deviation.

### 3.4. Difference-in-Differences Analysis

To further evaluate intervention-related effects over time, difference-in-differences (DiD) analyses were performed (Table 8).

Between-group changes from baseline to follow-up were significantly greater in the SG than in the CG for exercise capacity, dyspnea, perceived exertion, quality-of-life scores, and inflammatory markers, with large effect sizes observed for several outcomes.

No significant between-group DiD effect was observed for stance phase. This parameter may be less responsive to pulmonary rehabilitation over the studied timeframe and is subject to higher inter-individual variability; therefore, the study may have been underpowered to detect small changes in this gait component.

**Table 8. Difference-in-differences analysis: between-group comparison of within-group changes (Δ = T2 − T1), SG vs CG**

| Outcome | Δ Study (mean ± SD) | Δ Control (mean ± SD) | Test on Δ | p-value | Effect size (Cohen's d on Δ) |
|---|---|---|---|---|---|
| **6MWD (m)** | 27.0 ± 16.81 | −8.39 ± 11.36 | Mann–Whitney | <0.001 | 2.454 |
| **TUG (s)** | −0.7 ± 0.82 | −0.01 ± 0.46 | Mann–Whitney | 0.003 | −1.023 |
| **SI (%)** | 4.05 ± 4.83 | −0.3 ± 5.78 | Mann–Whitney | 0.005 | 0.819 |
| **Stance phase** | −1.39 ± 1.55 | −0.3 ± 3.15 | Mann–Whitney | 0.512 | −0.446 |
| **mMRC** | −1.37 ± 0.5 | −0.39 ± 0.5 | Mann–Whitney | <0.001 | −1.965 |
| **Borg CR10** | −3.42 ± 0.77 | −0.78 ± 0.65 | Mann–Whitney | <0.001 | −3.713 |
| **SGRQ** | −19.74 ± 2.26 | −4.67 ± 4.37 | Welch t-test | <0.001 | −4.373 |
| **EUROHIS-QOL-8** | 8.37 ± 1.21 | 1.11 ± 1.28 | Mann–Whitney | <0.001 | 5.832 |
| **WHOQOL-BREF** | 18.58 ± 2.61 | 2.33 ± 2.3 | Mann–Whitney | <0.001 | 6.591 |
| **NLR** | −1.19 ± 0.46 | 0.02 ± 1.53 | Mann–Whitney | 0.003 | −1.086 |
| **PLR** | −33.2 ± 13.27 | 12.23 ± 34.45 | Mann–Whitney | <0.001 | −1.759 |

Abbreviations: Δ = change score (T2 − T1); 6MWD = six-minute walk distance; TUG = Timed Up and Go test; SI = symmetry index; mMRC = modified Medical Research Council dyspnea scale; Borg CR10 = Borg Category Ratio 10 scale; SGRQ = St. George's Respiratory Questionnaire; EUROHIS-QOL-8 = EUROHIS Quality of Life 8-item index; WHOQOL-BREF = World Health Organization Quality of Life – Brief version; NLR = neutrophil-to-lymphocyte ratio; PLR = platelet-to-lymphocyte ratio; SD = standard deviation.

### 3.5. Figures and Safety Outcomes

Changes in outcome measures are visually summarized in Figure 2.

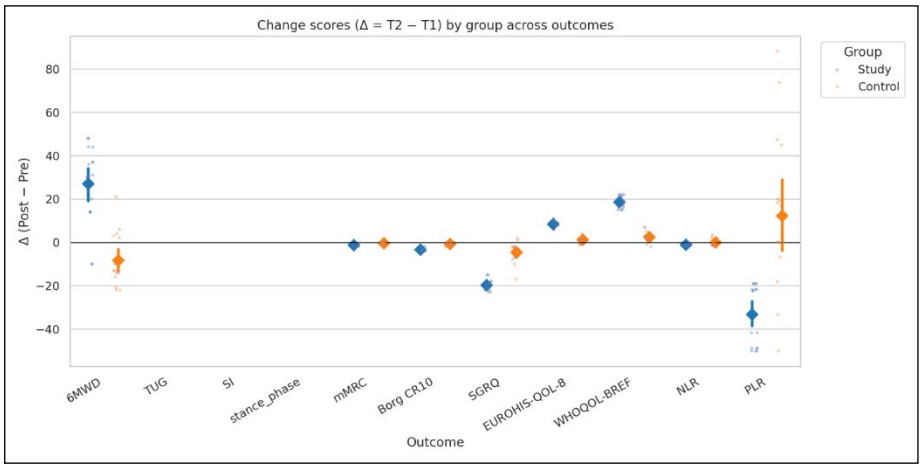


**Figure 2. Change scores (Δ = T2 − T1) by group across outcomes**

All participants in the SG completed the pulmonary rehabilitation program. No serious adverse events related to the intervention were reported. Training intensity and exercise components were adapted according to individual tolerance, allowing continuation of the program despite fluctuating symptoms. These findings support the feasibility, safety, and tolerability of pulmonary rehabilitation in patients with post-tuberculosis lung disease.

## 4. Discussion

Pulmonary rehabilitation represents a cornerstone intervention in the management of chronic respiratory diseases and has increasing relevance for patients with post-tuberculosis lung disease (PTLD) [12]. The findings of the present study support the concept that a structured and individualized pulmonary rehabilitation program can lead to clinically meaningful improvements in functional capacity, respiratory symptoms, quality of life, and systemic inflammation in patients with PTLD [13]. Importantly, these benefits were observed despite the heterogeneous nature of post-tuberculosis sequelae and the presence of restrictive, obstructive, or mixed ventilatory patterns, highlighting the broad applicability of rehabilitation strategies in this population [2,7].

In TB-endemic regions, access to center-based pulmonary rehabilitation may be limited by distance, transportation costs, workforce shortages, and competing social priorities. Home-based or hybrid PR models may therefore be practical alternatives, using standardized exercise prescriptions, education, and self-management components, complemented by periodic in-person assessments and remote follow-up (telephone or tele-rehabilitation where available). Such approaches could improve reach and adherence while preserving safety through structured monitoring and clear escalation criteria [24].

The pulmonary rehabilitation program implemented in this study was multimodal and individualized, combining aerobic training, resistance exercises, balance and gait training, breathing exercises, and patient education. The intervention included a supervised inpatient phase lasting 2 weeks (12 sessions), followed by a structured home-based rehabilitation program over 3 months, a model comparable to pulmonary rehabilitation protocols reported in previous studies in PTLD and other chronic respiratory diseases [12,13]. While the duration of supervised rehabilitation varies widely in the literature, ranging from short-term inpatient programs to longer interventions of 6–8 weeks, existing evidence suggests that even shorter supervised programs can yield clinically meaningful benefits when combined with prolonged home-based training.

In the present study, pulmonary rehabilitation led to a clinically meaningful improvement in exercise capacity. The Study Group exhibited a mean increase in six-minute walk distance (6MWD) of +27 m, whereas the Control Group demonstrated a mean decline of −8.4 m over the same period. These findings are consistent with previous studies in PTLD and other chronic respiratory diseases, which report improvements in 6MWD ranging from approximately 20 to 50 m following structured pulmonary rehabilitation, values generally considered clinically relevant. The absence of improvement and the slight functional decline observed in the Control Group support existing evidence that residual functional impairment may persist or progress in PTLD in the absence of targeted intervention [12,13,16].

Functional mobility followed a similar pattern. Timed Up and Go performance improved in the Study Group, with a mean reduction of −0.7 s, while the Control Group showed virtually no change (−0.01 s). Comparable improvements in TUG have been reported in pulmonary rehabilitation studies and are interpreted as reflecting en-

hanced balance, lower-limb strength, and efficiency of transitional movements. Together, these results indicate that pulmonary rehabilitation positively influences both endurance and mobility-related functional domains in PTLD.

Instrumented gait analysis revealed rehabilitation-related improvements that extend beyond traditional functional tests. In the Study Group, gait symmetry increased by +4.05%, while a slight deterioration (−0.3%) was observed in the Control Group. Additionally, stance phase duration decreased by −1.39% in rehabilitated patients, compared with a negligible change (−0.3%) in controls. Similar trends toward improved gait symmetry and efficiency have been described in rehabilitation studies involving chronic respiratory and post-infectious pulmonary conditions, supporting the concept that structured exercise training can normalize gait patterns altered by chronic dyspnea and deconditioning.

The use of the BTS G-WALK wearable system represents a key methodological strength of the present study for the assessment of functional outcomes in PTLD. Unlike conventional functional tests that primarily quantify performance through time or distance, instrumented gait analysis provides objective, quantitative, and reproducible measures of spatiotemporal gait parameters, offering deeper insight into locomotor control and movement efficiency. The ability of BTS G-WALK to detect subtle functional changes complements traditional assessments such as the 6MWT and TUG and enhances the clinical relevance of functional outcome evaluation in pulmonary rehabilitation research [23].

Pulmonary rehabilitation was also associated with substantial reductions in symptom burden. Dyspnea severity, assessed using the mMRC scale, decreased by **−1.37 points** in the Study Group, compared with a smaller reduction of **−0.39 points** in the Control Group. Similarly, perceived exertion during effort, evaluated using the Borg CR10 scale, showed a pronounced reduction in the Study Group (**−3.42 points**) versus modest improvement in controls (**−0.78 points**). Reductions of this magnitude are consistent with previous pulmonary rehabilitation studies and reflect meaningful improvements in daily functional tolerance and symptom perception.

Quality-of-life outcomes demonstrated some of the largest rehabilitation-related gains. In the Study Group, SGRQ scores improved by −19.7 points, markedly exceeding the minimal clinically important difference, while the Control Group showed a smaller improvement (−4.7 points). Generic quality-of-life instruments showed a consistent pattern, with EUROHIS-QOL-8 increasing by +8.37 points and WHOQOL-BREF by +18.6 points in the Study Group, compared with minimal changes in controls. Similar improvements in both disease-specific and generic quality-of-life domains have been reported in the literature and underscore the broad impact of pulmonary rehabilitation on physical, psychological, and social well-being [17,18].

The concurrent improvement across disease-specific and generic quality-of-life scales highlights the essential role of these instruments in capturing patient-centered outcomes, as functional gains do not always translate proportionally into perceived benefits. The inclusion of quality-of-life scales therefore provides a comprehensive evaluation of rehabilitation efficacy and reflects the real-world impact of pulmonary rehabilitation in PTLD.

Pulmonary rehabilitation is a relatively low-technology intervention that primarily relies on training, education, and behavior change strategies, suggesting a favorable cost profile. In PTLD, improvements in functional capacity and HRQoL may translate into reduced symptom-related visits, fewer exacerbation-related admissions, and improved ability to perform daily activities and work, supporting the plausibility of cost-effectiveness. Nevertheless, dedicated health-economic studies are required to quantify incremental costs and benefits in PTLD populations [25].

In addition to functional and patient-reported outcomes, pulmonary rehabilitation was associated with favorable changes in systemic inflammatory markers. The Study Group demonstrated a mean reduction in NLR of −1.19 and a decrease in PLR of −33.2, whereas the Control Group showed no improvement in NLR (+0.02) and a tendency toward increased PLR (+12.2). Although data on inflammatory responses to pulmonary rehabilitation in PTLD remain limited, similar reductions have been reported in other chronic respiratory populations, suggesting a potential systemic anti-inflammatory effect of structured exercise interventions [10,11].

Overall, the present findings are consistent with and extend previous literature by demonstrating that pulmonary rehabilitation in PTLD yields quantified and clinically meaningful gains across multiple domains, including exercise capacity (+27 m 6MWD), mobility (−0.7 s TUG), gait symmetry (+4.05%), dyspnea (−1.37 mMRC points), quality of life (−19.7 SGRQ points), and systemic inflammation (−1.19 NLR). In contrast, patients receiving standard care alone exhibited minimal improvement or functional decline, reinforcing the role of structured pulmonary rehabilitation as a key component of post-tuberculosis care.

**Several limitations** should be acknowledged. First, the study was non-randomized, which may introduce selection bias and residual confounding despite baseline comparability. Although we assessed baseline differences and applied difference-in-differences and baseline-adjusted analyses, unmeasured confounders cannot be fully excluded. In addition, the relatively small sample size and the non-randomized design limit the generalizability of the findings and preclude definitive causal inferences. Subgroup analyses (e.g., by ventilatory pattern) were not performed due to the limited sample size, which would have substantially reduced statistical power and increased the risk of spurious findings; larger studies should evaluate whether responses differ across ventilatory phenotypes. Additionally, the absence of long-term follow-up restricts conclusions regarding the durability of rehabilitation benefits over time. While inflammatory markers were included as exploratory outcomes, their clinical interpretation in the context of PTLD rehabilitation warrants further investigation. Future studies should aim to incorporate larger, randomized cohorts, longer follow-up periods, and a broader range of physiological and patient-reported outcomes.

Future studies should include adequately powered randomized controlled trials with longer-term follow-up to evaluate durability of benefits and capture clinically relevant endpoints. In addition, formal cost-effectiveness analyses (including direct and indirect costs) are needed to inform implementation in resource-limited settings. Finally, further work should validate inflammatory indices and candidate biomarkers as prognostic markers and as measures of response to rehabilitation, ideally using standardized sampling, prespecified outcomes, and external validation cohorts.

## 5. Conclusions

This study confirms that post-tuberculosis lung disease is associated with persistent functional impairment, respiratory symptoms, reduced exercise tolerance, and compromised quality of life, even after successful completion of anti-tuberculosis treatment. The baseline characteristics of the study population highlight the heterogeneity of PTLD, with restrictive, obstructive, and mixed ventilatory patterns contributing to diverse clinical presentations and functional limitations.

The findings demonstrate that an individualized pulmonary rehabilitation program produces clinically and statistically significant benefits in patients with PTLD. Improvements were observed across multiple domains, including functional capacity (as reflected by increased six-minute walk distance and improved mobility), symptom burden (reduced dyspnea and perceived exertion), gait and balance parameters,

and health-related quality of life. These changes indicate that pulmonary rehabilitation effectively addresses both the physical and psychosocial dimensions of post-tuberculosis sequelae.

Importantly, the magnitude of improvement in the rehabilitation group exceeded that observed in the control group across most outcomes, supporting a true intervention effect rather than spontaneous recovery or regression to the mean. The observed benefits occurred despite the presence of residual structural lung damage and variable ventilatory dysfunction patterns, underscoring that meaningful functional and quality-of-life gains can be achieved even when complete physiological normalization is not possible.

The results further emphasize that quality-of-life outcomes represent a central and clinically relevant endpoint in PTLD management. Improvements in patient-reported outcomes were closely aligned with functional gains, reinforcing the concept that pulmonary rehabilitation enhances real-life functioning and patient adaptation, beyond changes measurable by isolated physiological parameters.

From a clinical and public health perspective, these findings support the systematic assessment of patients at the end of tuberculosis treatment for post-TB sequelae and the early integration of pulmonary rehabilitation into post-TB care pathways. Expanding access to rehabilitation services and adopting standardized functional and quality-of-life assessments may contribute to reducing long-term disability, improving social reintegration, and mitigating the broader socioeconomic impact of PTLD.

In conclusion, pulmonary rehabilitation represents a key therapeutic strategy in the comprehensive management of post-tuberculosis lung disease. By shifting the focus from microbiological cure alone toward long-term functional recovery and patient-centered outcomes, rehabilitation has the potential to transform post-TB care into a model centered on recovery, participation, and sustained quality of life.

## 6. Patents

This section is not mandatory but may be added if there are patents resulting from the work reported in this manuscript.

**Supplementary Materials:** no.

**Author Contributions:** Conceptualization, M.V.P. and M.R.T.; methodology, G.M.A.; software, M.0.; validation, M.V.P., G.M.A. and M.R.T.; formal analysis, M.O.; investigation, M.V.P.; resources, M.O.; data curation, M.R.T.; writing—original draft preparation, M.V.P.; writing—review and editing, M.O.; visualization, G.M.A.; supervision, M.R.T.; project administration, M.V.P.

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**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study

**Data Availability Statement:** Data are available upon reasonable request.

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**Conflicts of Interest:** The authors declare no conflict of interest

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