

# Does Preoperative Rehabilitation Influence the Quality of Life in Patients Who Are Candidates for Lung Transplant?

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## Abstract

**Objectives:** Lung transplant is an excellent therapeutic option for patients with advanced/end-stage pulmonary disease. The purpose of this review was to define whether preoperative rehabilitation influences quality of life in patients who are candidates for lung transplant.

**Materials and Methods:** This was a scoping review conducted by searching 4 primary databases from inception until January 2022. Three keywords, "lung transplantation," "preoperative rehabilitation," and "quality of life," were matched using the Boolean operator AND. In each database, the following fields were searched: PubMed (all fields), Scopus (title, abstract, keywords), Cochrane Library (title, abstract, keywords), and Web of Science (topic). Filters were applied for age (adult only) and language (English only). No filters were applied for gender, publication date, and subject. The search process was completed in January 2022.

**Results and Conclusions:** We retrieved 57 citations from these databases. After removal of duplicates, 41 documents were screened for eligibility. Two articles were included in the final analysis: 1 was a systematic review, and 1 was an observational prospective study. The rehabilitative interventions were mainly focused on motor and breathing exercises and were integrated by education programs. Preoperative rehabilitation was effective at improving quality of life and mood status and reducing dyspnea

in patients waiting for lung transplant. In addition, the 6-minute walking distance increased after patients participated in preoperative rehabilitation. Preoperative rehabilitation was composed of different types of exercise with variable duration (3-20 weeks) and frequency (3-6 times per week). Patients on the active wait list for lung transplant should be encouraged to attend preoperative rehabilitation in order to preserve and improve their quality of life.

**Key words:** *Exercise capacity, Lung transplantation, Physiotherapy, Pulmonary rehabilitation, Rehabilitative intervention*

## Introduction

Lung transplant (LTx) is an excellent therapeutic option for patients with advanced/end-stage diseases such as idiopathic pulmonary fibrosis, cystic fibrosis, end-stage septic lung disease, and pulmonary hypertension.<sup>1-5</sup> The expected benefits after LTx are the increased rate of patient survival and improved quality of life,<sup>6</sup> as quality of life is particularly reduced in patients with end-stage lung diseases.<sup>7</sup> In addition, long-term pharmacological treatment with corticosteroids can result in muscle atrophy and consequent peripheral muscle dysfunction affecting the limbs.<sup>8</sup> Meanwhile, inactivity and deconditioning represent additional negative factors that influence exercise capacity and physical function in patients with lung disease. Although respiratory function can improve after LTx, the negative effects of the chronic underlying disease may continue, mostly in the musculoskeletal and cardiopulmonary systems.<sup>9</sup>

Preoperative rehabilitation can contribute to enhancing exercise capacity, reducing dyspnea, and improving muscle strength and thereby positively influence patients' quality of life<sup>10,11</sup> and facilitate favorable physical and psychological conditioning

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for patients before surgery.<sup>12</sup> Enhancing muscle strength aerobic capacity preoperatively also allows patients to become accustomed to exercise, especially considering that the waiting time on the active list can vary.<sup>13</sup>

In a previously published review that investigated the possible effects of preoperative rehabilitation in patients with idiopathic pulmonary fibrosis who were candidates for LTx, it was not possible to demonstrate the effectiveness of preoperative rehabilitation, because of the absence of comparative studies of LTx candidates who did or did not attend preoperative rehabilitation.<sup>14</sup>

The purpose of this review was to define whether preoperative rehabilitation influences the quality of life in patients who are candidates for LTx.

## Materials and Methods

This was a scoping review,<sup>15</sup> conducted by searching 4 primary databases, namely, PubMed, Scopus, Cochrane Library, and Web of Science.

### Search strategy

Databases were searched from inception to January 2022. Three keyword entries, “lung transplantation,” “preoperative rehabilitation,” and “quality of life,” were matched using the Boolean operator AND. In each database the following fields were searched: PubMed (all fields), Scopus (title, abstract, keywords), Cochrane Library (title, abstract, keywords), and Web of Science (topic). Filters were applied for age (adult only) and language (English only). No filters were applied for gender, publication date, and subject. The search process was completed in January 2022.

### Inclusion and exclusion criteria

To be included, citations were required to be published in English and to describe preoperative rehabilitation in patients waiting for LTx. For the purpose of this review, we sought to include randomized controlled trials, observational studies, and case reports. All citations that lacked descriptions of preoperative rehabilitation in patients waiting for LTx and/or were published in languages other than English were not eligible for inclusion. Abstracts, conference proceedings, editorials, letters to editor, and study protocols were also not eligible for inclusion.

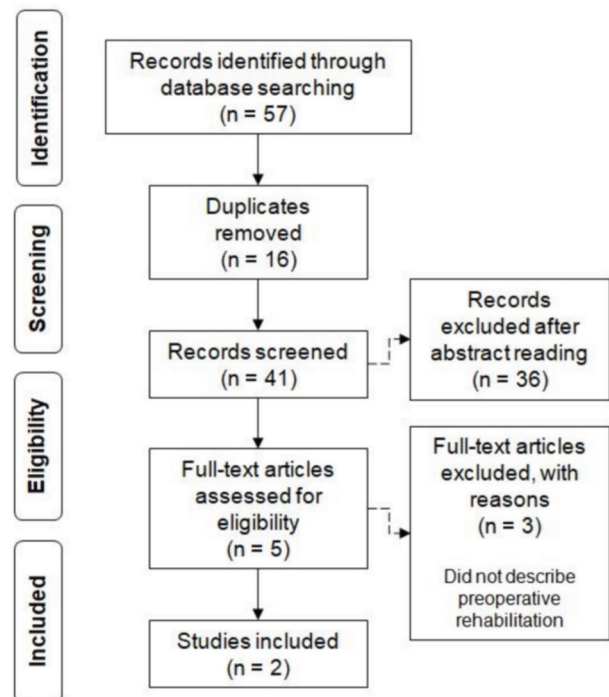
## Selection process

From the retrieved citations, duplicates were removed, and the remaining documents were screened for eligibility according to the content of the abstracts. Subsequently, for those documents with abstracts that met the inclusion criteria, the full text of each article was also screened for the inclusion criteria, and confirmed articles were considered eligible for the final analysis. We followed the PRISMA Guidelines<sup>16</sup> for this review. The studies gathered from the literature by these methods were further evaluated through an open, standardized process by 3 independent reviewers who had evaluated and agreed on the results.

## Results

From the searched databases, we retrieved 57 citations. After removal of duplicates, 41 documents were screened for eligibility. Two articles were included in the final analysis, as shown in Figure 1. One study was a systematic review,<sup>17</sup> and the other was an observational prospective study.<sup>11</sup> There were 1344 patients, of whom 48% were men, that constituted the cohort of the included studies. The systematic review included 6 studies that evaluated the correlation between preoperative rehabilitation and quality of life in LTx candidates.<sup>17</sup>

Figure 1. Study Flow Diagram



The rehabilitative interventions were mainly focused on motor and breathing exercises and were integrated by education programs, as shown in Table 1. Preoperative rehabilitation was shown to be effective at improving quality of life and mood status and reducing dyspnea in patients waiting for LTx. The 36-Item Short Form Health Survey developed for

the RAND Medical Outcomes Study, the EuroQuol EQ-5D health-value descriptive system, the St. George's Respiratory Questionnaire, the Quality of Well-being Scale, the modified Medical Research Council Dyspnea Scale, and the Beck Depression Inventory were the questionnaires and evaluation tools that were used among the included studies. In

**Table 1.** Characteristics and Main Findings of Included Studies

Source	Study Design	Intervention	Main Findings
Hoffman et al <sup>17</sup>	Systematic review of 6 studies that included 1305 (aged ≥18 y) candidates for LTx who attended preoperative pulmonary rehabilitation (men, n = 618).	Stretching, resistive training, aerobic exercise, breathing exercises, muscle strengthening exercises, Nordic walking, endurance training, assisted cough, and education (anatomy, physiology, stress reduction techniques, home oxygen systems).	<ul style="list-style-type: none"> <li>• SF-36 mental health component score: 47 ± 11 to 45 ± 12 (<math>P &lt; .05</math>) in 345 patients.</li> <li>• SGRQ: 65 ± 14 to 69 ± 11 (<math>P &lt; .05</math>) in 345 patients.</li> <li>• EQ-5D: 0.55 ± 0.24 to 0.47 ± 0.27 (<math>P &lt; .05</math>) in 345 patients.</li> <li>• 6-MWD during rehabilitation was 15 m higher than in a subset of 196 patients at listing (<math>P &lt; .002</math>).</li> <li>• Significant improvements in different domains of SF-36: physical functioning/social functioning/mental health (<math>P = .001</math>) and vitality (<math>P &lt; .001</math>) in 58 patients, and 6-MWD increased from 367 ± 136 m to 439 ± 114 m (<math>P = .001</math>).</li> <li>• SF-36 mental health component score: 47 ± 11 to 45 ± 12 (<math>P &lt; .05</math>) in 345 patients.</li> <li>• SGRQ: 65 ± 14 to 69 ± 11 (<math>P &lt; .05</math>) in 345 patients.</li> <li>• EQ-5D: 0.55 ± 0.24 to 0.47 ± 0.27 (<math>P &lt; .05</math>) in 345 patients.</li> <li>• 6-MWD during rehabilitation was 15 m higher than in a subset of 196 patients at listing (<math>P &lt; .002</math>).</li> <li>• Significant improvements in different domains of SF-36: physical functioning/social functioning/mental health (<math>P = .001</math>) and vitality (<math>P &lt; .001</math>) in 58 patients, and 6-MWD increased from 367 ± 136 m to 439 ± 114 m (<math>P = .001</math>).</li> <li>• 6-MWD increased by 35 ± 28 m in 30 patients who attended interval training. In another group, 6-MWD increased by 36 ± 42 m in 30 patients who attended continuous training. There were no significant differences between groups (<math>P = .89</math>).</li> <li>• Significant improvements of SF-36 cumulative score: 27.2 ± 8.2 to 29.9 ± 9.1 (<math>P &lt; .05</math>) in 22 patients.</li> <li>• Significant improvements in SF-36 physical health component score (<math>P &lt; .001</math>) in 811 patients, and 6-MWD significantly increased by 55.9 ± 58.3 m (<math>P &lt; .001</math>).</li> <li>• Significant improvements in QWB (<math>P = .005</math>) in 9 patients. Of these, 4 attended an education program, and their 6-MWD increased from 277.4 ± 190.5 to 350.7 ± 132.3 m (<math>P &lt; .03</math>). The remaining 5 patients were provided with the same education program plus exercise, and their 6-MWD increased from 232.1 ± 87.3 to 299.9 ± 161 m (<math>P &lt; .03</math>).</li> </ul>
Pehlivan et al <sup>11</sup>	Observational prospective study conducted among 39 patients (25 men, 14 women) with a mean age 36.9 ± 13.4 y.	Patient education, breathing exercises (breathing control, dyspnea-coping methods, and bronchial hygiene techniques), aerobic exercises (stationary bike, treadmill walking, and arm ergometer workouts), and strengthening exercises.	<ul style="list-style-type: none"> <li>• 6-MWD: 301.50 ± 107.67 to 355.76 ± 112.15 m (<math>P = .001</math>).</li> <li>• mMRC dyspnea score: 3.91 ± 1.01 to 2.96 ± 0.91 (<math>P &lt; .001</math>).</li> <li>• BDI: 16.07 ± 11.39 to 13.00 ± 10.46 (<math>P = .004</math>).</li> <li>• SF-36 physical function score: 17.89 ± 19.85 to 34.07 ± 25.23 (<math>P = .01</math>).</li> <li>• SF-36 emotional role score: 29.48 ± 42.40 to 76.81 ± 40.05 (<math>P = .02</math>).</li> </ul>

**Abbreviations:** 6-MWD, 6-minute walking distance; BDI, Beck Depression Inventory; EQ-5D, EuroQuol 5D health-value descriptive system; LTx, lung transplant; mMRC, modified Medical Research Council; QWB, Quality of Well-Being scale; SF-36, Medical Outcomes Study 36-item Short Form Health Survey; SGRQ, St. George's Respiratory Questionnaire

addition, the 6-minute walking distance increased after patients participated in preoperative rehabilitative programs, as shown in Table 1. Preoperative rehabilitation was composed of different types of exercise with variable duration. Aerobic exercise (ergometer or treadmill), muscle strengthening exercises (arms and legs), endurance training, and breathing exercises were the most commonly described techniques.

In addition, stretching (arms, legs, hips muscles), education, and Nordic walking constituted other components of the preoperative programs (Table 1). Duration of programs varied from 3 to 20 weeks, and frequency varied from 3 times per week to as often as 5 to 6 times per week.<sup>11,17</sup>

## Discussion

The aim of the present review was to define whether preoperative rehabilitation can influence the quality of life in patients waiting for LTx. This is an interesting and, as we have found here, infrequently covered topic. In fact, only a few studies have investigated the effects of preoperative rehabilitation in LTx recipients.<sup>10,11,17-22</sup> Review of the studies showed that duration, type, and frequency of preoperative rehabilitation varied, and it was provided in an outpatient setting, including preoperative programs at home.

In this regard, the worldwide COVID-19 pandemic has forced patients to stay home and perhaps reduced the possibilities to attend preoperative rehabilitation. Subsequently, home-based rehabilitation has attracted greater interest, and initial experiences are providing encouraging data.<sup>23</sup> A study conducted among 23 patients (mostly male) waiting for LTx found that an 8-week mixed preoperative rehabilitation program (that included home-based exercises) was effective at reducing dyspnea perception after 8 weeks ( $P < .001$ ).<sup>24</sup> More specifically, another study conducted among 78 patients (mostly male) provided the basis for further development of telerehabilitation in LTx candidates.<sup>25</sup> An 8-week telerehabilitation program has also been found to be feasible and safe for LTx recipients.<sup>26</sup> Differences that characterize preoperative rehabilitation programs have been discussed elsewhere, and it is commonly accepted that, in response to the lack of novel guidelines for optimal exercise plans for LTx candidates, preoperative rehabilitation should be provided in accordance with the established

recommendations generally associated with outpatient programs.<sup>27</sup> Mobility is crucial, because ambulatory capacity and physical activity are prerequisites for lung transplant/retransplant eligibility.<sup>28</sup>

## Multidisciplinary in lung transplant

The first successful LTx procedures date back to the 1980s with the pioneering experiences at the Toronto Lung Transplant Centre.<sup>29,30</sup> Review of the early history of the LTx field shows that transplant surgeons did, in fact, recognize the importance of both preoperative and postoperative rehabilitation to facilitate optimal preoperative conditions for patients and to expedite postoperative recovery.<sup>30-32</sup>

More importantly, during the complex pathway that begins at patient selection and placement on active wait lists, multidisciplinary is a cornerstone.<sup>33</sup> Optimal surgical outcomes require support from many disciplines, and our predecessors recognized this notion early in our history and understood the importance of such a complex and multifaceted procedure, particularly with regard to rehabilitation.<sup>29,32</sup> Furthermore, multidisciplinary can be today enhanced by international cooperation among centers and stimulated even in those developing countries that are starting LTx programs where preoperative rehabilitation is not available because of its related costs.<sup>34</sup> Patients receiving LTx are expecting to restore their quality of life, and some can even get involved in sports activities or adventurous travels safely.<sup>35,36</sup>

## Limitations

Although the search was conducted among a substantial number of databases, a primary limitation of the present study was the small number of citations included in the final analysis. Despite this constraint, we are confident that the information we have retrieved would not be enhanced by extending our searches to include additional databases.

Another primary limitation was the heterogeneous nature of the treatments provided to LTx candidates during preoperative rehabilitation. Despite this variability, our primary scope was to understand whether preoperative rehabilitation can influence the quality of life in patients waiting for LTx. The results we have presented in this review have allowed us to respond to our research question positively.

## Conclusions

Although preoperative rehabilitation for patients waiting for LTx is commonly recognized as a crucial intervention to promote active mobility and preserve both motor and respiratory functions, this topic is not covered extensively in the literature. With the present review, we found that preoperative rehabilitation programs include patient education, and these programs are primarily focused on motor and respiratory exercises. Patients waiting on active list for LTx should be encouraged to attend preoperative rehabilitation in order to preserve and improve their quality of life. Contextually, LTx centers that are not prepared yet to provide preoperative rehabilitation should deserve more attention to this specific rehabilitative treatment because patients arriving at transplantation in better conditions are most likely to succeed postoperatively.

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