

Preoperative physiotherapy in subjects with idiopathic pulmonary fibrosis qualified for lung transplantation: implications on hospital length of stay and clinical outcomes

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Background: Lung transplantation (LTx) candidates with chronic disease are more prone to exercise limitations. Preoperative physiotherapy (PP) can improve exercise tolerance, which in some patients, is severely impaired, often leaving them housebound. The aim of this study was to answer this question: In patients with idiopathic pulmonary fibrosis (IPF) qualifying for LTx, is PP effective in improving postoperative outcomes and reducing length of stay (LOS) after transplantation?

Methods: Six major databases were searched up to December 2015. We did not apply limits to publication date, date, gender, or language. Citations were accepted if they discussed preoperative physiotherapeutic treatment in patients with IPF waiting for LTx.

Results: After the full texts were read, three papers met the inclusion criteria and were included. All of these papers had an observational design. In total, 55 subjects with IPF and awaiting LTx were observed.

Conclusions: The effectiveness of PP in improving postoperative outcomes and reducing LOS following LTx remains unclear, although it appears to benefit IPF patients who qualify for LTx by improving their health status, physical activity levels, and respiratory-related symptoms.

Keywords: Preoperative care; idiopathic pulmonary fibrosis (IPF); treatment outcome; lung transplantation (LTx)

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Introduction

It has been argued that rehabilitation plays an important role in lung transplantation (LTx) candidates, because patients with chronic lung diseases are medically complex and a preoperative program will increase patients' comprehension of their illness (1). In addition, as LTx candidates with chronic disease are more prone to exercise limitations, preoperative physiotherapy (PP) can improve exercise tolerance (1), which in some patients, is severely impaired, often leaving them housebound. Specifically, a rehabilitation program

including supervised aerobic and strengthening exercises can significantly improve symptoms and physical activity levels in idiopathic pulmonary fibrosis (IPF) patients (2). IPF is a chronic progressive disease of unknown etiology that affects mainly adult men; the symptoms of IPF are mainly shortness of breath and cough. Some recent evidence has shown that new drugs may slow the decline in vital capacity (3). LTx is the only treatment that improves the survival of IPF patients, and should be considered 3–6 months after diagnosis (4), because the average survival rate at diagnosis is

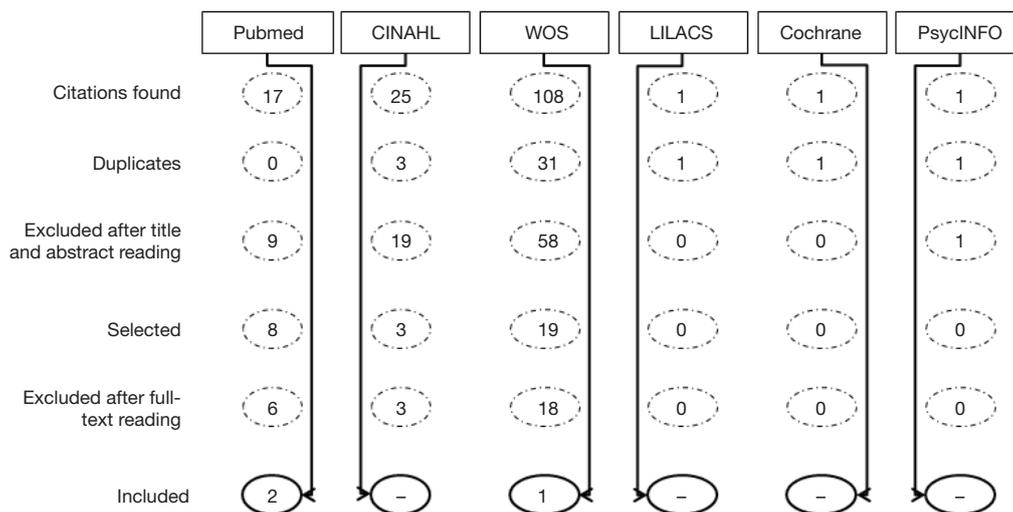


Figure 1 Flow chart. WOS, Web of Science.

about 2–3 years. However, patient selection for LTx remains controversial due to the age of these patients.

One might speculate that PP would reduce postoperative complications and the hospital length of stay (LOS) after LTx. The aim of this study was to answer this question: In patients with IPF qualifying for LTx, is PP effective in improving postoperative outcomes and reducing LOS after transplantation?

Materials and methods

Six major databases, namely PubMed, CINAHL, Web of Science, LILACS, Cochrane Library, and PsycINFO, were searched up to December 2015 using the string: (“Physical Therapy Modalities” OR rehabilitation OR “physical therapy” OR physiotherapy) AND (“Idiopathic Pulmonary Fibrosis” OR “Idiopathic pulmonary fibrosis” AND “lung transplantation”). We did not apply limits to publication date, gender, or language. The search examined the title, abstract, and keyword fields.

Inclusion criteria

Citations were accepted if they discussed preoperative physiotherapeutic treatment in patients with IPF waiting for LTx.

Exclusion criteria

Studies discussing pathologies other than IPF and those

considering physiotherapeutic treatment in patients not undergoing LTx were excluded.

Results

In total, 153 papers were found, and after duplicate removal, 117 citations were screened (*Figure 1*). After the full texts were read, three papers met the inclusion criteria and were included (*Table 1*). All of these papers had an observational design. In total, 55 subjects with IPF and awaiting LTx were observed. Two of the three studies used the SF-36 questionnaire, which seemed to be the most suitable tool for evaluating the health status of IPF patients. The main results obtained in the three studies are shown in *Table 1*.

In a prospective study conducted in 2013, Florian *et al.* (5) found that the motor and respiratory performance of patients on the active list for LTx improved following a 36-session rehabilitation program (90 min, three times per week). The physiotherapy consisted of respiratory exercises, muscle strengthening, and aerobic exercise on a treadmill. The preoperative rehabilitation program also involved a psychiatric evaluation, nutritional counseling, social assistance, and educational lectures.

In another prospective study conducted in 2013, Wickerson *et al.* (6) found that an exercise-based rehabilitation program contributed to improving the physical activity levels in a cohort of candidates for LTx with IPF. In the Wickerson study (6), rehabilitation included stretching and resistance and endurance training (treadmill and cycle ergometer). LTx candidates with ILD were more active on rehabilitation

Table 1 Included studies

Authors, study	Patients/intervention	Outcomes measures	Results	Key points
Florian <i>et al.</i> , 2013 (5), prospective cohort study (evidence level: 1B)	58 subjects (27 with IPF) completed a 36 session rehabilitation program	Walking distance (6MWD) Dyspnea (modified Borg scale) Health status (SF-36 domains)	6MWD increased by 72 mt. (mean distance) Post-exercise dyspnea decreased from 5 to 4 points, and leg fatigue after exercise decreased from 3 to 2 points Significant score increase ($P \leq 0.001$) in physical functioning (20 to 45), vitality (57 to 65), and social functioning (50 to 64) domains	This study showed that a PP program was useful and beneficial in subjects qualified for LTx There was not a control group There was not a separate analysis of the results in the considered diseases The follow-up was quite short (at the end of the rehabilitation program). It would be more intriguing to verify if the results could be maintained in an additional follow-up There was not drop out from the study highlighting that subjects strongly appreciated the program: LTx, dying while awaiting and transplantation refusal were reasons for leave the program LTx candidates in wait list were more active while participating in an exercise-based rehabilitation program The majority of increased physical activity (daily steps) on rehabilitation days was accumulated during the rehabilitation program Total daily physical activity of the study participants may have been underestimated in this study as hip-mounted accelerometers cannot accurately measure nonambulatory activities and therefore may underestimate overall activity. Stationary exercise such as cycling and resistance training done during the rehabilitation program as well as many common household chores that contribute to time spent in moderate-intensity activity may not have been captured
Wickerson <i>et al.</i> , 2013 (6), prospective cross-sectional study (evidence level: 1B)	24 subjects with ILD on long term oxygen therapy (12 with IPF) awaiting LTx (time on wait list 4±3 months) underwent an exercise-based rehabilitation program (90-minute sessions for 3 times/week for at least 4 weeks). A weekly support group was also available for patients and family members	Functional exercise capacity (6MWT)	The 6MWD showed the strongest correlation to daily steps ($r=0.59$, $P<0.01$), isometric quadriceps torque ($r=0.51$, $P<0.01$) and time spent in moderate-intensity physical activity per day ($r=0.56$, $P<0.01$)	
Jastrzebski <i>et al.</i> , 2005 (7), cohort study with limited population (evidence level: 3B)	30 subjects on long term oxygen therapy (16 with IPF)	Measurements were taken at the enrollment in the active list and 1 year after qualification for LTx: health status (SF-36 domains), respiratory function (spirometry), blood oxygenation (ABGs)	Role-physical decreased from 43 to 25 points FEV1 decreased from 37.1% to 33.9% predicted, FVC decreased from 44.0% to 42.2% predicted PaO ₂ decreased from 56.7 to 51.7 mmHg, PCO ₂ increased from 43 to 46.8 mmHg, SaO ₂ decreased from 86.8% to 80.3%	Subjects did not undergo physiotherapy while on active list: this study highlights the disease's severity in this particular class of patients The study showed that SF-36 was a good measurement tool in IPF patients

Evidence's level of the included studies has been graded following the recommendations reported in "Oxford Centre for Evidence-based Medicine-Levels of evidence (March 2009)", available at: <http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/>. IPF, idiopathic pulmonary fibrosis; 6MWD, six-minute walking distance; ILD, interstitial lung disease; 6MWT, six-minute walk test; SF-36, short form-36; LTx, lung transplantation; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; ABGs, arterial blood gas analysis; PaO₂, partial pressure of oxygen; PCO₂, partial pressure of carbon dioxide; SaO₂, oxygen saturation.

than on non-rehabilitation days (daily steps, $3,780 \pm 2,196$ vs. $2,138 \pm 1,353$; $P < 0.001$). During the 90-minute rehabilitation sessions, the number of steps taken comprised 58% of the total daily steps, and the time spent in moderate-intensity activity per day was 4.5 (interquartile range, 1.5–17) min, compared with 2 (1–3.5) min. This finding should be considered when proposing exercise to IPF patients. In fact, due to disease characteristics, IPF patients are prone to exercise limitations.

In IPF patients, Jastrzebski *et al.* (7) reported a positive correlation between the arterial blood gas level and the SF-36 domains general health, emotional functioning, and mental cumulative score. They found that patients with a higher PaO₂ reported better general health, and that the FEV₁ was positively correlated with social functioning and the level of body pain.

Discussion

Patients with IPF are eligible for LTx, which is a viable therapeutic option (4,8), particularly in those with chronic respiratory insufficiency, despite high peri- and postoperative morbidity and mortality rates (9); simultaneously, pulmonary rehabilitation and physiotherapeutic intervention are indicated in patients preparing for LTx (1) to enhance muscular function (9). Skeletal muscle weakness is usually observed, but not inspiratory muscle weakness, so the preoperative training of these muscles may not be specifically indicated (10) unless these patients are already hypercapnic because the presence of hypercapnia indicates respiratory pump failure and is associated with a very poor prognosis (11). A randomized clinical trial by Hulzebos *et al.* suggested that preoperative inspiratory muscle training may reduce the incidence of postoperative pulmonary complications in high-risk patients undergoing coronary artery bypass grafting surgery, even when they are not hypercapnic (12). The use of inspiratory muscle training has been shown in animal studies and human studies to be deleterious, and it may produce injury to the diaphragm, although it may benefit the external intercostal muscles (13–15).

Based on our findings, it is impossible to establish whether PP is effective in improving postoperative outcomes and reducing the LOS after LTx in IPF patients. In fact, we were unable to find any citations addressing our question. Conversely, it was clear that pulmonary rehabilitation and exercise, when appropriate, should be considered as a non-surgical therapeutic option in

IPF patients (1,2,16). Furthermore, it seems that a pre-transplant rehabilitation program may improve physical activity levels in LTx candidates on a waiting list (6). Our initial question remains unanswered because no study has demonstrated the effectiveness of PP in reducing LOS and improving clinical outcomes after LTx in IPF patients. In this regard, the great difficulty in evaluating the course of IPF patients while they are on an active list should be considered. This important issue must be considered while programming health policies and scheduling appropriate and effective rehabilitation treatment for LTx candidates. Additionally, it could be surmised that physical activity in IPF candidates for LTx can be also planned for the home environment although the supervised exercise seems to be more efficacious because the physical activity during rehabilitation can be greater (6). However, as commonly seen in daily practice, those subjects who arrive at LTx in better physical shape are likely to face their postoperative course more successfully. A PP program may facilitate postoperative recovery after LTx; unfortunately, it is not possible to define which elements of PP influence postoperative recovery after LTx, particularly in terms of LOS and clinical outcomes.

Limitations

This study was restricted to a very select population (IPF subjects waiting for LTx); thus, we are aware of the difficulty in answering our initial question, which was based on the assumption that we could find published studies. Despite the small number of citations retrieved, even though six major databases were searched, those selected did strictly fit our search question, meeting the inclusion criteria. Although IPF was the most common condition, the included studies investigated subjects with different diseases; in light of this, it was not possible to relate the findings of this review to various sub-groups. Strictly speaking, the main objective of the study was not satisfied because no citation was found that addressed the selected topic; however, this research has contributed to better understanding of the need to investigate PP from a cost-effectiveness point of view. Ultimately, the only way to answer the question of whether PP is effective in reducing LOS and improving clinical outcomes will be to compare series of patients who underwent LTx and successfully recovered from surgery with subjects who did not attend PP prior surgery but also successfully recovered from LTx.

Conclusions

The effectiveness of PP in improving postoperative outcomes and reducing LOS following LTx remains unclear, although it appears to benefit IPF patients who qualify for LTx by improving their health status, physical activity levels, and respiratory-related symptoms. Our question underlines the importance of investigating physiotherapy in these patients.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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