

# Short Term Effect of Supervised Pulmonary Rehabilitation Program after Lung Transplantation Surgery on Quality of Life and Exercise Capacity; the First Report of Iranian Experience

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## Abstract

**Background:** The role of exercise based rehabilitation following lung transplantation (LT) is gradually being recognized. This is the first investigation in pulmonary rehabilitation after LT in Iran.

**Materials and Methods:** A prospective before-and-after trial was designed in the tertiary referral center of Masih Daneshvari hospital. Measurements before and after intervention included Body Mass Index (BMI), Health Related Quality Of Life (HRQOL) score using St. George Respiratory Questionnaire (SGRQ), functional exercise capacity and desaturation during six minute walking test (6MWT). Pulmonary rehabilitation sessions included a series of 1 to 1.5 hours of education and exercise training that were carried out three times in a week continued for eight weeks.

**Results:** A total number of 16 subjects {men (n=10), female (n=6)} were studied (mean age: 36.8 ± 12.5 years). 6MWT distances before and after intervention were 324 ± 139.7 m and 418.9 ± 133.4 m respectively (p<0.001). Oxygen desaturations before and after intervention were 5.08 ± 4.31 and 4.08 ± 2.8 percent respectively (p=0.053). The SGRQ scores before and after intervention were 58.15 ± 16.45 and 34.78 ± 13.93 respectively (p<0.001). BMI before and after intervention were 19.12 ± 6.42 and 20.89 ± 6.17 respectively (P<0.001).

**Conclusion:** Rehabilitation program including supervised exercise after successful LT could improve functional exercise capacity, HRQOL scores and BMI.

**Keywords:** Rehabilitation program; Lung transplantation surgery; Quality of life; Exercise capacity

## Introduction

Lung transplantation (LT) surgery is an established treatment that has opened new horizons for patients with end-stage lung diseases [1]. With the advent of modern surgical techniques and increased clinical experiences, patient's survival has been improved [2]. Despite near-normal lung function following LT, impaired functional capacity is frequently reported in numerous studies [3,4]. This underscores the role of extra pulmonary factors including abnormalities of peripheral circulation and peripheral muscle wasting in patients undergoing LT [5].

Pulmonary rehabilitation is a multidisciplinary program that has been widely applied for patients with chronic respiratory diseases. Nowadays, using of such multidisciplinary tasks has been increased before and after thoracic surgical interventions including pneumonectomy and single or double lung transplantation [6,7]. Rehabilitation program has been suggested to decrease the presence of transplantation comorbidities such as poor nutrition, corticosteroid or immunosuppressant induced myopathy, prolonged intensive care unit (ICU) or hospital admission, episodes of rejection resulting to reduced muscle mass and the impaired functional capacity [8]. According to European Respiratory Society (ERS)

definition in 2013, pulmonary rehabilitation programs include the education, exercise therapy and behavioral changes [6] that have been employed to increase patients' quality of life and functional capacity. It has been shown that following the LT, the subjects increased participation in daily physical activity might have benefits to improve their exercise capacity and reduce the risk of development of co- morbidities [9]. Thanks to a large number of studies in the last decade, our knowledge about the effects of rehabilitation after LT and its mechanism to increase the functional capacity of organ recipients has been increased. The aim of the current research was to investigate the short term results of the progressive exercise-base rehabilitation after successful LT surgery in a referral center in Iran. As far as we know, this study is the first investigation on pulmonary rehabilitation after LT in Iranian patients.

## Material and Methods

This study was designed as a prospective before-and-after trial in the tertiary referral center for respiratory diseases of Masih Daneshvari hospital. This study is derived from a greater investigation of rehabilitation among patients referred to the pulmonary rehabilitation unit of Masih Daneshvari hospital in Tehran, Iran. The study was approved by the ethical committee of National Research Institute of Tuberculosis and Lung Diseases (NRITLD) (code: IR.sbmu.NRITLD.REC.1394.202). Written informed consent was obtained from each patient prior to the participation.

All patients who underwent single or bilateral lung transplantation surgery in the setting of lung transplantation group of Masih Daneshvari hospital were enrolled in the study. Subjects were eligible if they were medically stable, could be discharged from hospital and agreed to participate in the outpatient exercise based rehabilitation.

Before the rehabilitation, a brief medical and surgical history of each participant was taken. Age, gender, underlying disease, single or double lung transplantation and complications during or after surgery were considered in their history.

Measurements before and after intervention included Body mass index (BMI), Health related quality of life (HRQOL) score, functional exercise capacity and desaturation during exercise.

BMI is calculated from body mass (in kilogram: kg) divided on the square of the body height (in meter: m), and expressed in  $\text{kg}/\text{m}^2$ .

HRQOL was measured using the Persian translation of St. George Respiratory Questionnaire (SGRQ). This questionnaire has been translated into Farsi and validated by Fallah-Tafti et al. [10]. The questionnaire consists of 50 questions and 76 items of evaluation and has been designed in three sections including sequence and intensity of respiratory complaints, activities restricted to social activities and psycho-social issues [10]. Each section is scored from 0 to 100 where 0 is considered as the best health situation of all choices and 100% is considered as the worst. The scores of all questions in each

section were summed and the total score for the questionnaire was calculated by adding the section's scores.

To study the functional exercise capacity, 6MWT was performed for all patients in a corridor according to American Thoracic Society (ATS) guideline [11]. The test was conducted along a 30-meter flat and straight corridor while hemoglobin oxygen saturation ( $\text{SpO}_2$ ) was recorded continuously every 30 seconds automatically using WEIMMANN OXYCOUNT mini Puls oxymeter-Germany. Each patient relaxed for at least 20 min before the test. At the start of the test, patients' heart rate, blood pressure, and  $\text{SpO}_2$  were measured using a pulse oxymeter probe putting on their right index finger. Patients were asked to walk as long as possible for six minutes. At the end of six minutes, their heart rate, blood pressure, oxygen saturation and the distance covered during six minutes (in meter) were documented.

All eligible subjects attended an outpatient supervised pulmonary rehabilitation program designed specifically for lung transplant recipients at the pulmonary rehabilitation unit of Masih Daneshvari hospital.

Pulmonary rehabilitation sessions included a series of 1 to 1.5 hours of supervised educational and exercise training sessions that were performed three times in a week and continued for eight weeks. Educational sessions included supervised breathing retraining, relaxed diaphragmatic breathing, symmetric chest expansion, education of airway clearance techniques, self-paced activity remodeling education and nutritional and psychological recommendations. Supervised exercise training program comprised of warm up, aerobic exercise (stationary cycling and treadmill walking), resistance training and stretching exercises. Warm up included stations of open and closed kinetic chain exercises including both upper and lower extremity (straight leg rise, leg abductions, knee extension, semi squat) and calisthenics workouts (wall push-up) for 10 repetition and two to three sets. Aerobic exercise included 20-40 minute stationary cycling and treadmill walking with the intensity of slow rising up to 4-6/10 by modified Borg Scale. Resistance training consisted of six stations of upper and lower extremity workouts using free weights and elastic bands, 10 to 18 repetitions for two to three sets. Stretching exercise consisted of static stretching of major muscle groups for 20 to 30 seconds, two to three time, including hamstring, calf, triceps and pectoralis major with caution. In the case of oxygen desaturation during exercise training, supplementary oxygen was prescribed via nasal cannula until  $\text{SpO}_2 \geq 88\%$ . A trained sports and exercise medicine specialist closely monitored all sessions.

## Statistical Analysis

Data were entered into SPSS 16.0 and were analyzed using descriptive statistics and paired sample T tests. The statistically significant criterion was set at  $P \leq 0.05$ . Data are presented as mean  $\pm$  standard deviation (minimum, maximum).

## Results

Between November 2014 and June 2015, sixteen subjects (men (n=10), female (n=6)) were eligible to enrol in our investigation. Subjects had a mean age of  $36.8 \pm 12.5$  years (Minimum=18 and Maximum=62). Ten patients had received bilateral lung transplantation and six subjects had received single lung transplantation. Pre transplant diagnoses were as follow: Bronchiectasis (n=7), Idiopathic pulmonary fibrosis (n=5), Cystic fibrosis (CF) (n=2), microlithiasis (n=1) and emphysema (n=1). Mean waiting time to start supervised pulmonary rehabilitation program was  $42.9 \pm 16.35$  days (Minimum=20 and Maximum=72).

The 6MWT distance improved from  $324 \pm 139.7$  m before the rehabilitation to  $418.9 \pm 133.4$  m after eight weeks. This was statistically significant ( $p < 0.001$ ). Oxygen desaturation during 6MWT that was done before and after eight weeks of rehabilitation were  $5.08 \pm 4.31$  and  $4.08 \pm 2.8$  percent respectively and was not statistically significant ( $p = 0.053$ ). The SGRQ total scores before and after eight weeks of rehabilitation were  $58.15 \pm 16.45$  and  $34.78 \pm 13.93$  respectively and was statistically significant ( $p < 0.001$ ). BMI, before and after eight weeks of rehabilitation, were  $19.12 \pm 6.42$  and  $20.89 \pm 6.17$  respectively and the difference was statistically significant (0.001). The results are summarized in the **Table 1**.

**Table 1:** Measurements difference before and after 8 weeks of rehabilitation (\*significant difference) analyzed using descriptive statistics and paired sample T tests. Measurements included BMI, SGRQ total score, 6MWT distance and desaturation during 6MWT. The statistically significant criterion was set at  $P \leq 0.05$ . Data are presented as mean  $\pm$  standard deviation (minimum, maximum).

	Basic	After 8 weeks	P Value
SGRQ total score	58.15 $\pm$ 16.45	34.78 $\pm$ 13.93	<0.001*
6MWT	324 $\pm$ 139.7	418.9 $\pm$ 133.4	<0.001*
Desaturation during 6MWT	5.08 $\pm$ 4.31	4.08 $\pm$ 2.8	p=0.053
BMI	19.12 $\pm$ 6.42	20.89 $\pm$ 6.17	P=0.001*

## Discussion

In this investigation, it has been shown that supervised exercise-based pulmonary rehabilitation program significantly increases the exercise capacity, quality of life and BMI of patients following successful lung transplantation surgery. The National Research Institute of Tuberculosis and Lung Diseases (NRITLD), is the referral center for lung transplantation since the year 2000, when the first single-lung transplantation surgery was successfully performed [12]. Furthermore, the rehabilitation unit of the center is the only well-equipped center for noninvasive ventilation and pulmonary

rehabilitation in Iran. Considering to the NRITLD lung transplantation group policy and based on the reports of survival of patients in the waiting list for LT [13], candidates for LT in the waiting list as well as the organ recipients must routinely be enrolled in the pulmonary rehabilitation consultation as a mandatory part of the medical management.

Rehabilitation program has been widely accepted as a part of practical managements before and after LT in more economically developed countries [14]. Unfortunately, due to the absence of a control group, many of studies on the effects of rehabilitation after LT do not show enough clinical evidences. In a randomized trial, Langer, et al. showed that the exercise training performed after LT and following the hospital discharge can significantly increase quadriceps muscle force, functional exercise capacity, health-related quality of life and improve the ability to carry out daily physical activities [15].

According to the latest ERS statement on the field of walking tests, a clinically important change in 6MWT distance can occur if the distance walked increases by 30 meters [11,16]. In this study, a large distance was gained (mean 94 meters). In a study by Munro et al. the distance walked increased by 129 meters [17]. This large distance can be explained by a different patient population (younger CF patients) and less debility of the patients before LT. In a part of the current investigation, the effect of the rehabilitation during 6MWT on SPO<sub>2</sub> desaturation was evaluated in the LT subjects. An obvious decrease in SPO<sub>2</sub> desaturation after supervised rehabilitation was seen, although this change was not statistically significant. In the previously published statements, the role of rehabilitation on desaturation during 6MWT is still inconclusive [6,18]. To evaluate the effect of rehabilitation on the quality of life following LT, the generic SF-36 questionnaire is commonly used. Here, SGRQ was used as a lung specific questionnaire. Kugler, et al. showed that compared to SF-36 questionnaire, SGRQ significantly has better scores for transplant recipients at six months [19]. It is obvious that both questionnaires are validated in patients before and after LT [20].

Here, the effect of rehabilitation was studied on the patients BMI after LT. In a longitudinal four years follow-up on body composition in lung transplant patients, it was shown that BMI and fat free mass (FFM) increased after two years of LT [21]. It is unclear that the increase of BMI after pulmonary rehabilitation is due to the effect of rehabilitation or a result of the nature of LT.

As far as we know, the effect of rehabilitation on muscle wasting (i.e. sarcopenia) and BMI after LT has not been investigated. Moreover, the importance of the weight gain after LT is inconclusive. Yusen et al. showed that the weight gain after LT is a common problem that may be a result of the patient's physical activity [9]. Forli et al. showed that this weight gain may accompany metabolic comorbidities such as diabetes mellitus, hypertension and cardiovascular diseases [22]. However, Ihle et al. showed a significant relation between the higher quality of life score of BMI ( $21.0$ - $25.2$  kg/m<sup>2</sup>) and a 6MWT  $\geq 430$  m [23]. It seems that the importance of

rehabilitation following LT should be further investigated on the patients' weight.

A limitation of the current study included the small number of the patients. However, in the period of this investigation, it was tried to include all lung transplant recipients that were successfully discharged from the hospital after surgery. Besides, in this study, there was no independent control group. This limitation has also been reported in a similar investigation by Munro, et al. [17]. In our transplantation team, pulmonary rehabilitation program is considered as a mandatory part of patient's care before and after LT and eligibility for transplantation. Another limitation is that, although we have measured the BMI during eight weeks, the effect of the rehabilitation on sarcopenia has not been assessed. Sarcopenia is a syndrome characterized by progressive loss of skeletal muscle mass and correlated with physical disability and quality of life. It is unclear that the weight gain observed in the LT recipients after rehabilitation is due to increase of their fat or fat-free mass. To answer this question, it is necessary to address the direct or indirect analysis of body composition and BMI, simultaneously, in a prospective longitudinal study in LT recipients.

In conclusion, the results of this report showed that eight weeks supervised and structured pulmonary rehabilitation program including educational and exercise-training sessions after successful LT could improve functional exercise capacity, HRQOL scores and BMI. In order to determine the longer effect of pulmonary rehabilitation following LT, further prospective and longitudinal trials are essential.

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