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Effects of Pulmonary Rehabilitation on Respiratory Muscle Strength and Functional Capacity of Patients Following Lung Transplantation

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Abstract

Lung Transplantation has become an established treatment option for patients with a wide variety of end-stage lung diseases, with the aim to improve quality of life and survival. Prior studies illustrated respiratory muscle function impairment in patients who undergo lung transplantation. The study objective was to evaluate the effects of a pulmonary rehabilitation program on respiratory muscle strength, functional capacity and health related quality of life in patients following Lung transplantation. Six patients, 4 male and 2 female, who had undergone lung transplantation, 7-18 months prior to the study, participated in the pulmonary rehabilitation program and were evaluated before and after intervention. This program consisted of three main pulmonary rehabilitation components: a) Endurance exercises; (b) Strength exercises; and (c) Stretch exercises. The physical activities were provided twice a week, for 4 months. The results obtained after the pulmonary rehabilitation program showed no significant change in the functional capacity ability of the patients measured by the six-minute walk test. The maximal inspiratory pressure and maximal expiratory pressure values showed no significant change. The physical work capacity measured by the peak oxygen consumption (VO2 peak) showed no significant change. The post lung transplantation patients reported significantly higher health-related quality of life scores in physical health, emotional health and social functioning domains. Therefore, the pulmonary rehabilitation program in these patients did not improved functional capacity, respiratory muscle strength, physical work capacity, but improved health-related quality of life.

Keywords: Lung transplantation; Pulmonary Rehabilitation; Maximal Inspiratory Pressure, 6-Minute Walk Test

Abbreviations: 6MWT: 6-Min Walk Test; PR: Pulmonary Rehabilitation; MIP: Maximal Inspiratory Pressure; MEP: Maximal Expiratory Pressure; LT: Lung Transplantation; ILD: Interstitial Lung Disease; COPD: Chronic Obstructive Pulmonary Disease; IPF: Idiopathic Pulmonary Fibrosis; FVC: Forced Vital Capacity; CPET: Cardiopulmonary Exercise Test; VE: Ventilatory Equivalents; IMT: Inspiratory Muscle Training; SD: Standard Deviation; MVV: Maximum Voluntary Ventilation; FEV: Forced Expiratory Volume; ATS/ERS: American Thoracic Society/European Respiratory Society; HRQoL: Health-Related Quality of Life

Introduction

Lung transplantation has become an established treatment option for patients with a wide variety of end-stage lung diseases, with the aim to improve quality of life and survival [1]. Nevertheless, exercise intolerance, functional disability and peripheral muscle weakness often persist following LT [2,3]. Moreover, prior studies illustrated respiratory muscle function impairment in patients who undergo LT [4,5].

Pulmonary rehabilitation is widely recognized as an important component of care for patients with Chronic Obstructive Pulmonary Disease (COPD), Interstitial Lung Disease (ILD) and Idiopathic Pulmonary Fibrosis (IPF) as it improves dyspnea, exercise tolerance, and quality of life, while reducing health care resource utilization [6-11].

The goal of PR following LT is to enhance the physiological and functional benefits following the surgery [2,12]. Aerobic endurance exercise training has been shown to improve exercise performance in LT recipients and reduce transplant-related morbidities [13,14].

Indeed, many lung transplant centers require recipients to attend an outpatient rehabilitation program [15,16]. Despite their widespread implementation, very few studies have described or evaluated PR programs following LT. Furthermore, no formal guidelines exist with respect to the optimal methods of exercise training or the educational components of PR for patients recovering from LT.

Therefore the aim of the present study was to evaluate the effects of a PR program on respiratory muscle strength and functional capacity of patients more than one year following LT.

Material and Methods

Subjects

Six patients, 4 male and 2 female, who had undergone LT, 7-18 months prior to the study were recruited from the outpatient clinic of the Pulmonary Institute, Rabin Medical Center, Beilinson Hospital, Petach Tikva, Israel. None of the patients were participating in any additional regular exercise or sport activity.

Inclusion criteria:

1) At least four months post-LT

2) Able to perform pulmonary function tests

3) Clinically stable for at least one month.

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Exclusion criteria:

1) Unstable cardiovascular disease

2) Required supplemental oxygen

3) Cor pulmonale

4) Poor compliance.

Patient characteristics are summarized in **Table 1**.

Study design

All six patients were assigned to receive PR for four months. All tests were recorded at baseline before training, and at 4 months, at end of training period. The study protocol was approved by the institutional ethics committee and informed consent was obtained from all subjects.

Tests

Spirometry: Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV1) and Maximum Voluntary Ventilation (MVV) were measured three times on a computerized spirometer according to standard techniques and American Thoracic Society/ European Respiratory Society (ATS/ERS) guidelines (Zan 530: Oberthulba, Wurzburg, Germany) [17,18]. All the measured parameters were presented as the percent of predicted (% pred) values of the European Community for coal and Steel [19]. MVV was presented as L/min.

Cardiopulmonary Exercise Test (CPET) (VO2 peak Test): The cardiopulmonary exercise test (CPET) was performed according to established guidelines [20-23]. All tests were supervised by a physician. Patients were instructed to take their usual medications as prescribed. A 10-15 W/min ramp protocol was performed on an electromagnetically braked cycle ergometer (Ergoline -800S) to the patient's maximal subjective exertion level and respiratory exchange ratio (RER ≥ 1.1) [20]. During the test, 12-lead electrocardiogram, blood pressure, pulse oximetry (SpO2) and breath-by-breath respiratory gas exchange were recorded and monitored (Zan 600, Oberthulba). All peak cardiopulmonary data were calculated and the analysis was based on the average of the last 30 s of the test. The anaerobic threshold was determined by the dual methods approach, using the V-slop method combining ventilatory equivalents (VE/VO2 and VE/VCO2) [20]. Predicted values of peak oxygen consumption (VO2 peak) were determined according to Jones et al. [24] based on prospective data of 100 subjects (50 males and 50 females) from the general population aged 15-71 years.

Six-Minute Walk Test (6MW): The 6MWT test was set according to ATS guidelines [25]. The distance the patient was able to walk in 6 min was determined in a measured 35 meter corridor at the pulmonary unit within the hospital. The patients were instructed to walk at their fastest pace and cover the longest possible distance over 6 min under the supervision of a physiotherapist. The test was performed twice and the best result was recorded.

Respiratory muscle strength: Inspiratory muscle strength was assessed by measuring the MIP at residual volume and the expiratory muscle strength was assessed by measuring the MEP at total lung capacity, using the technique proposed by Black and Hyatt [26-30]. Mouth pressures were measured by an electronic pressure transducer (MicroRPM; Micromedical, Kent, UK). Assessments were repeated at least three times (30 s recovery between attempts), and the value obtained from the best effort was recorded.

Health-Related Quality of Life (HRQoL): Health-related quality of life was measured by the Hebrew Short –Form (SF-36) Questionnaire [31], which has been used widely in many studies and health service institutions. The most popular generic HRQoL instrument is the SF-36. The SF-36 features physical and mental summary scores and a 4-point change in the SF-36 is considered clinically significant.

The intervention programs

An experienced senior physiotherapist monitored participation in the PR program and supervised the exercise classes.

Pulmonary Rehabilitation (PR) exercise training program

Participants received a four-month PR program which consisted of two supervised 60-minute exercise classes each week in our rehabilitation center at the Pulmonary Institute. The program followed recent exercise guidelines prescribed for patients with chronic lung disease [8-11].

The exercise training program consisted of the three main PR components

(a) Endurance: Each session of the endurance exercise training involved 20-30 minutes of free walking, treadmill walking, stationary cycling, and stair climbing. For participants who were unable to tolerate continuous endurance exercises, interval training was used instead.

(b) Strength exercise training for the upper and lower limbs consisted of 5 individual exercises (step-ups, squats, free weights), with three sets of 10 repetitions. The progression of training load was based on each patient's individual tolerance.

(c) Stretch and range of motion exercise training included major muscle groups: the calves, hamstrings, quadriceps, biceps, neck, shoulders and trunk.

Data analysis

All clinical and physiological parameters were presented as mean ± standard deviation (SD). Patient's baseline characteristics, all parameters were presented as changes (delta) from baseline to post-intervention

PR (n=6)	
Age (years)	57.3 ± 11.5
Male/Female	4/2
Time from Transplantation (months)	14 ± 4.4
Basic lung disease	
Fibrosis	2
Bronchiectasis	1
Scleroderma	1
Emphysema	2
Type of Transplantation	
SLT	3
DLT	3
Diaphragm Injury	
Right	2
left	1
BMI (index)	25.9 ± 4
Weight (kg)	75.6 ± 16.5
Height (cm)	170.2 ± 12.4

Abbreviations: BMI: Body Mass Index; DLT: Double Lung Transplantation; SLT: Single Lung Transplantation. Data presented as means and standard deviations at the following measures: Age, Time from transplantation, BMI, Weight and Height. All other measures are presented as frequencies.

Table 1: Patient characteristics of Training Group.

Pulmonary Function Tests	Pre-rehabilitation (T0)	Post-rehabilitation (∆T1-T0)
FVC% predicted	72 ± 15.2	2.1 ± 17.9
FEV1% predicted	66.5 ± 14.3	1 ± 15.7
MVV (L/Min)	64 ± 23.4	2.1 ± 24.5
VO2 peak % predicted	61.3 ± 10.1	-2 ± 10.4
Abbreviations: MVV: Maximal Voluntary Ventilation; FVC: Forced Vital Capacity; FEV1: Forced Expiratory Volume in 1 sec; VO2 peak: Values of Peak Oxygen Consumption; T0: Baseline; T1: After 4 months of intervention. Data presented as means and standard deviations.		

Table 2: Comparison of pulmonary function and VO2 peak pre and post-pulmonary rehabilitation.

	Pre-rehabilitation(T0)	Post-rehabilitation(∆T1-T0)
MIP (cmH2O)	95.3 ± 27.2	-1.5 ± 30.7
MEP (cmH2O)	108.8 ± 31.9	0.5 ± 29.6
6MWT(m)	581.8 ± 79.8	6.2 ± 75
Abbreviations: MIP: Maximal Inspiratory Pressure; MEP: Maximal Expiratory Pressure; 6MWT: 6-minutes-walk test; T0: Baseline; T1: After 4 months of intervention. Data presented as means and standard deviations.		

Table 3: Comparison of respiratory muscle strength and functional capacity pre and post-pulmonary rehabilitation.

SF-36 Domains	Pre- pulmonary rehabilitation	post-pulmonary rehabilitation	The difference in the HRQL values between pre-PR and post-PR
physical functioning	75.8	77.5	1.7
physical health	**50**	**83.3**	**33.3**
emotional health	**33.3**	**72.2**	**38.9**
vitality- energy/fatigue	60	55	-5
mental health/ emotional well-being	74	74.7	0.7
social functioning	**70.8**	**81.3**	**10.5**
pain	76.3	74.6	-1.7
general health	59.2	53.3	-5.9
Categories with the highest difference in the quality of life between pre and Post-pulmonary Rehabilitation (PR) in post LT patients are in **bold.**			

Table 4: Summary of the SF-36 questionnaire average scores pre and post-pulmonary rehabilitation (PR) in post LT patients.

Results

No adverse events were observed during the PR program. The participants did not practice any other exercise training or sports activity at home while participating in the study and none of the participants were hospitalized.

Spirometry and VO2 peak: After 4 months of training, there was no significant change in FEV1, FVC, MVV and VO2 peak values (Table 2).

Respiratory muscle strength: After 4 months of training there was no significant increase in MIP and MEP values (Table 3)

6MWT: After 4 months of training, there was no significant increase in the 6MWT distance (Table 3).

Health-related quality of life: A summary of the SF-36 questionnaire results and comparisons pre and post-PR are shown in (Table 4).

In the **physical health** domain of the SF-36, the difference in the HRQoL values between pre-PR and post-PR was 33.3. It can be classified as an improvement with work or activities.

In the **emotional health** domain of the SF-36, the difference in the HRQL values between pre-PR and post-PR was 38.9. It can be classified as an improvement with work performance due to emotional health.

In the **social functioning** domain of the SF-36, the difference in the HRQL values between pre-PR and post-PR was 10.5. It can be classified as an improvement with social activities due to health and emotional health.

Discussion

In the present study, we examined the before and after training effects of a 4-month PR program on inspiratory muscle strength, functional capacity, physical work capacity and HRQoL in post-LT patients. To the best of our knowledge, no previous studies of PR programs in patients following LT have investigated respiratory muscle strength, before and after training. The majority (5/6) participants were more than one year (14 ± 4.4 months) post-LT. The PR program was well tolerated by all patients.

Following four months of PR we found no significant increase in FEV1, FVC, MVV, MIP, MEP, VO2 peak and 6MWT values.

The importance of incorporating an exercise training program in the management of LT patients is emphasized in the latest update (2013) on PR in the American Thoracic Society/European Respiratory Society guidelines [27]. However, the quality of the evidence supporting this recommendation is low to moderate [28], and does not consider new experimental studies published in recent years. Moreover, the dosing and types of exercises that are most effective in this population have not been clearly defined, due to the wide variability in training protocols. Considering these facts and that the most recent review on this topic only critically assessed the VO2 peak values in a subgroup of LT recipients [29], merits the contribution of our current study in updating the evidence on exercise training in adult LT recipients.

An evidence-informed clinical approach article [30], reported that MIP and Maximal Expiratory Pressure (MEP) values, lower-extremity muscle force, and 6MWTdistance continued to improve at 12 and 18 months after the LT procedure. The VO2 peak test value however, reached its highest predicted value at 6 months after the LT procedure and did not change at 12 or 18 months after the LT procedure.

It is likely that the baseline level of respiratory muscle performance before admission to LT may be a factor conditioning the change after training. Thus, despite the interesting results of our study, lack of such data is a drawback.

The results of our study consequently emphasize the importance for routine screening for weakness of inspiratory muscles in patients who are candidates for LT, particularly in patients who have a history of chronic respiratory illness as COPD, with well-established respiratory muscle weakness.

We found significantly higher ratings differences in HRQL values between pre-PR and post-PR were detected in 3 of the 8 health domains: physical health (higher score by 33.3 points), emotional health (higher score by 38.9 points) and social functioning (higher score by 10.5 points). Together, these results could indicate positive improvement following participation in a PR program in patients post LT.

The first limitation of this case series study was the small number of participants combined with the high variability between patients following LT who participated in this PR program.

Second, although MIP values reflect the respiratory muscle strength better than MEP, no studies to date have been conducted to determine a cutoff value for MIP that requires inspiratory muscle training in patients following LT. Therefore, future studies should identify a cutoff MIP value that requires IMT during a PR program.

Conclusion

In conclusion, in our small case series, the majority (5/6) were more than 12 months after the LT which may explain why there was no significant increase in the FEV1, FVC, MVV, MIP, MEP, VO2 peak and 6MWT values after participating in the PR program. The HRQoL in our LT patients was higher in the following domains of the SF-36 questionnaire: social functioning, physical health, and emotional health.

Conflicts of Interest

None of the authors have financial or other potential conflicts of interest to disclose.

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