

PULMONARY REHABILITATION PROGRAMS IN LUNG TRANSPLANT: A LITERATURE REVIEW

Programas de reabilitação pulmonar em transplante de pulmão: uma revisão de literatura

Programas de rehabilitación respiratoria en trasplante de pulmón: una revisión de literatura

Review Article

ABSTRACT

Objective: To analyze, using a literature review, Pulmonary Rehabilitation (RP) Programs in lung transplant. **Methods:** A literature review in July 2014 in Ebsco Host, Periódicos Capes, BVS and Science Direct data bases using descriptors in English (“lung transplantation”, “lung transplant” AND/OR “rehabilitation”) and Portuguese (“reabilitação” AND/OR “transplante pulmonar”). The eligibility criteria were interventional studies of PR before and/or after lung transplant; participants who were candidates to lung transplant or lung transplant recipients; studies that applied any kind of PR program (hospital-based, home-based or outpatient) and articles published in English, Spanish or Portuguese. Literature reviews, guidelines and case reports were excluded. The search process yielded 46 articles of which two were duplicated. After title and abstract screening 13 articles remained for full text reading. Six studies met the inclusion eligibility and were included in the review. **Results:** The studies involved patients with Chronic Obstructive Pulmonary Disease, Cystic Fibrosis, Pulmonary Hypertension, Interstitial Lung Disease and Pulmonary Fibrosis. Pulmonary function, exercise capacity, quality of life (QoL) and quadriceps force were evaluated. Most interventions were outpatient programs with three months duration, three times a week and session with at least one hour. Protocols included physical training, educational approach and just one included nutritional, psychiatric and social assistant follow-up. The studies presented significant change in the six-minute walking distance, QoL and quadriceps force after PR programs. **Conclusion:** This review showed the benefits of the PR in the QoL and exercise capacity contributing to the Health Promotion of the patients.

Descriptors: Rehabilitation; Transplantation; Physical Therapy Specialty

RESUMO

Objetivo: Analisar, através de uma revisão de literatura, programas de Reabilitação Pulmonar (RP) em transplante de pulmão. **Métodos:** Revisão de literatura realizada em julho de 2014 nas bases de dados Ebsco Host, Periódicos Capes, BVS e Science Direct, com os descritores em inglês (“lung transplantation”, “lung transplant” e/ou “pulmonary rehabilitation”) e em português (“reabilitação” e/ou “transplante pulmonar”). Os critérios de elegibilidade foram estudos de intervenção de RP antes e/ou depois do transplante pulmonar; estudos com qualquer tipo de programa de RP (hospitalar, domiciliar ou ambulatorial); e artigos em inglês, espanhol ou português. Excluíram-se as revisões de literatura, guidelines e estudos de caso. Encontraram-se 46 artigos, sendo dois duplicados. Após a leitura dos títulos e abstracts, selecionaram-se 13 para leitura completa. Seis estudos cumpriram os critérios de elegibilidade e foram incluídos na revisão. **Resultados:** Os estudos envolviam pacientes com doença pulmonar obstrutiva crônica, fibrose cística, hipertensão pulmonar, doença intersticial pulmonar e fibrose pulmonar. Avaliaram-se a função pulmonar, capacidade ao exercício, qualidade de vida (QV) e força de quadriceps. A maioria das intervenções era em programas ambulatoriais com 3 meses de duração, 3 vezes/semana e, pelo menos, uma hora. Os protocolos incluíam treinamento físico e abordagem educativa, e apenas um incluiu seguimento da nutrição, da psiquiatria e do serviço social. Os estudos demonstraram mudanças significativas na distância percorrida em seis minutos, na QV e na força de quadriceps após programas de RP. **Conclusão:** Esta revisão mostrou os benefícios da RP na QV e capacidade de exercício, contribuindo para a promoção da saúde desses pacientes.

Descritores: Reabilitação; Transplante; Fisioterapia.

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RESUMEN

Objetivo: Analizar a través de una revisión de literatura los programas de Rehabilitación Respiratoria (RR) en trasplante de pulmón. **Métodos:** Una revisión de literatura en julio de 2014 en las bases de datos Ebsco Host, Periodicos Capes, BVS y Science Direct con los descriptores en inglés ("lung transplantation", "lung transplant" AND/OR "pulmonary rehabilitation") y en Portugués ("reabilitação" e/ou "transplante pulmonar"). Los criterios de elección fueron: estudios de intervención con RR antes y/o después del trasplante de pulmón; participantes que eran candidatos al trasplante o trasplantados; estudios que aplicaron cualquier tipo de programa de RR (hospitalario, domiciliario o ambulatorio) y artículos publicados en inglés, español o portugués. Fueron excluidas las revisiones de literatura, las guías y los estudios de casos. El proceso de búsqueda resultó en 46 artículos de los cuales dos eran duplicados. Tras la revisión de los títulos y resúmenes, trece artículos permanecieron para la lectura del texto completo. Seis estudios cumplieron los criterios de inclusión y fueron incluidos en la revisión. **Resultados:** Los estudios fueron realizados con pacientes con Enfermedad Pulmonar Obstructiva Crónica (EPOC), Fibrosis Quística, Hipertensión Pulmonar, Enfermedad Pulmonar Intersticial y Fibrosis Pulmonar. Fueron evaluadas la función pulmonar, la capacidad de ejercicio, la calidad de vida (CV) y la fuerza del cuádriceps. La mayoría de las intervenciones fue de carácter ambulatorio con tres meses de duración, tres veces a la semana y sesiones de por lo menos una hora. Los protocolos incluyeron el entrenamiento físico, el abordaje educativo y solamente uno incluyó el seguimiento nutricional, psiquiátrico y del trabajo social. Los estudios presentaron cambios significativos en la distancia recorrida en seis minutos, la CV y la fuerza de cuádriceps después de los programas de RR. **Conclusión:** Esta revisión mostró los beneficios de la RR en la CV y capacidad de ejercicio contribuyendo para la Promoción de la Salud de estos pacientes.

Descriptores: Rehabilitación. Trasplante. Fisioterapia.

INTRODUCTION

Lung transplant is a therapeutic option accepted worldwide for the treatment of advanced lung diseases as Chronic Obstructive Pulmonary Disease; Idiopathic Pulmonary Fibrosis (IPF); Cystic fibrosis; alpha-1-antitrypsin (alpha-1) deficiency; idiopathic pulmonary arterial hypertension; pulmonary fibrosis (non-IPF); bronchiectasis and sarcoidosis^(1,2). A total number of 3.272 lung transplant was done in the world in 2009⁽³⁾. In 2013, 47.647 lung transplants were registered worldwide. Of these, 45,697 (95.9%) patients underwent primary lung transplantation and 1,950 underwent lung re-transplantation⁽⁴⁾.

In Brazil, about seven hundred were performed and there are patients requiring lung transplant who do not

even were referred to a transplant center once there are just seven active centers in the country⁽²⁾. In the last 5 years, the number of small-volume centers (<10 adult lung transplants per year) decreased, whereas high-volume centers (≥ 30 adult lung transplants per year) increased. Subsequently, the proportion of transplants being performed at high-volume centers increased⁽⁴⁾.

The success for a lung transplant depends on a very strict selection of candidates⁽⁵⁾ as well as a preparation of the patient involving medication, economic, psychosocial and physical aspects, so that he/she may have a satisfactory survival and improve quality of life (QoL)^(6,7).

In this context, the Pulmonary Rehabilitation (PR) is, nowadays, an important intervention in the pre⁽⁸⁾ and post-surgery of lung transplant⁽⁹⁾. It is a multidisciplinary program based on a thorough patient assessment followed by patient-tailored therapies that include, but are not limited to, exercise training, education, and behavior change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviors⁽¹⁰⁾. It aims to enhance the functional capacity^(11,12), to reduce the frequency of the exacerbations⁽¹³⁾ and hospital admission of patients with chronic lung disease⁽¹⁴⁾ and, principally, to improve their QoL^(11,15,16).

Although different studies show the benefits of the PR in COPD^(11,12,15,17) and others respiratory chronic diseases⁽¹⁰⁾ regarding inpatient or outpatient treatment^(18,19), somewhat is known about the physical training repercussions in candidates to lung transplant or lung transplant recipients^(8,9). Investigating PR programs in lung transplant may give a support to describe this treatment as an important allied before and after the surgery contributing to the health promotion of the patients which is the process of enabling people to increase control over, and to improve their health⁽²⁰⁾. The PR programs are included in this context once it promotes the empowerment⁽²¹⁾ of the patients teaching them how to lead with the disease and to control their health through the exercise training before and after the transplant.

Health promotion actions declared years ago are also important nowadays as build healthy public policy, create supportive environments, strengthen community action and develop personal skills⁽²²⁾ which are also part of the PR programs. Health promotion moves beyond a focus on individual towards a wide range of social and environmental interventions. The strategies for prevention and control of chronic respiratory diseases aims to identify cost-effective interventions, upgrade standards and accessibility of care at different levels of the health care system⁽²⁰⁾. A lung transplant is an strategy of controlling chronic respiratory diseases and the PR can be an important tool to give the

necessary support during the process of the pre and post-surgery⁽¹⁰⁾.

The aim of this study was to analyze, using a literature review, Pulmonary Rehabilitation Programs in lung transplant.

METHODS

The search process was performed in Ebsco Host, Journals of Capes, BVS and Science Direct electronic databases in July 2014 using specific words in English (“lung transplantation”, “lung transplant” AND/OR “pulmonary rehabilitation”) and in Portuguese (“*reabilitação*” AND/OR “*transplante pulmonar*”). Four reviewers conducted an independent title and abstract screening followed by an agreement reached between them on the selection of studies. All reviewers carried out the full text reading to identify articles to be included in the review.

It was included studies that described the PR as a treatment to lung transplant recipients or candidates to lung transplant. The studies had to meet the following criteria: (1) be published between 2008 and 2014 due the scarcity of publications about this subject; (2) interventional studies with PR before and/or after the lung transplant; (3) groups of participants who were candidates to lung transplant or lung transplant recipients; (4) studies that applied any kind of PR program (hospital-based, home-based or outpatient) and (5) articles published in English, Spanish or Portuguese. Review articles, guidelines, case reports, articles for which full text was not obtained and the duplicate articles were excluded.

The literature search process yielded 46 articles of which two were duplicated, leaving 44 manuscripts. After screening the title and the abstract, 13 articles remained; of them, 7 were excluded leaving a total of six remaining for full text reading. All of these met the inclusion criteria and were finally included in the review. Figure 1 shows the selection process of the articles included in the review.

The six articles included were deeply read by all reviewers aiming to identify the clinical and socio-demographics characteristics from the investigated patients, the methodological aspects of the studies, the characteristics and the protocols applied in the PR programs and the benefits achieved by the patients with PR programs.

RESULTS

Six articles were included in this literature review^(8,9,23-26). The age of the investigated patients varied from 18 years⁽⁸⁾ to more than 65 years⁽²⁶⁾ and it was identified almost the same number of man and woman when analyzing the total

patients from the studies. The most prevalent diagnosis in the articles were the COPD^(8,23-26), the Cystic Fibrosis^(8,24-26), the Pulmonary Hypertension^(8,24-26), the Interstitial Pulmonary Disease^(8,23,24) and the Pulmonary Fibrosis^(9,25,26). Three studies were realized with lung transplant recipients^(8,24,25) and three with candidates to lung transplant^(9,23,26). Table I presents the socio-demographics and clinical data from the patients of each study.

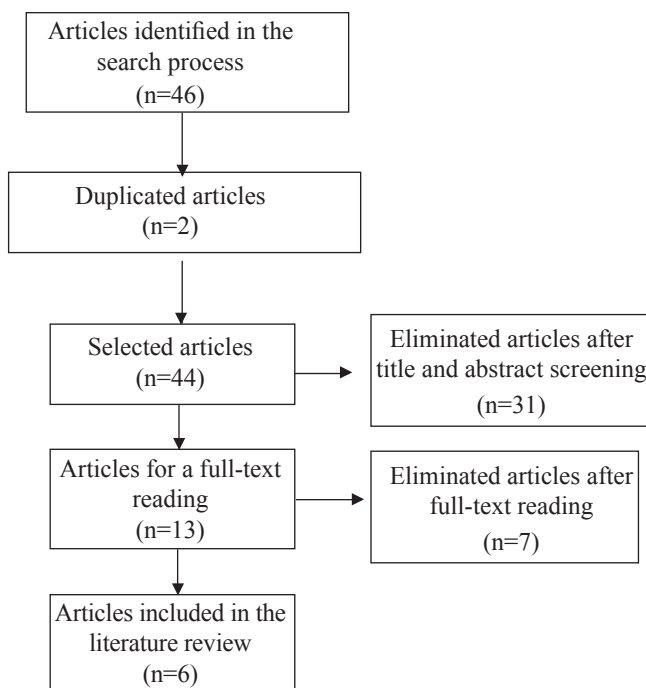


Figure 1 - The selection process of the articles included in the review.

The evaluation of the patients were principally through the pulmonary function^(8,9,23-25), exercise capacity with the Six Minute Walking Test (6MWT)^(8,9,23-26) and the QoL using the generic questionnaire Short-Form 36 (SF-36) in most studies^(8,9,24,26). Quadriceps force was also investigated in some researches^(23,24). In most studies the PR program had 3 months duration^(9,23-25) with the sample varying from 19⁽²⁵⁾ to 345 patients registered in one retrospective study⁽²⁶⁾. Table II describes in detail the methodological aspects of each manuscript.

Table III presents the characteristics of the PR programs applied in each study. Most of them were outpatient program^(9,23,24,26) although some were realized in hospital setting. The frequency of the programs were three times a week with a mean of 1 hour duration for each session^(9,23,24,26). All protocols included the physical training and three included educational approach^(8,9,24) and just one included nutritional, psychiatric and social assistant follow-up and educational conferences⁽⁹⁾.

Table I - Clinical and socio-demographic characteristics from the patients of the analyzed studies (n=6).

Authors	Gender	Age	Diagnosis	Sample
Maury et al (2008) ⁽²³⁾	17 men 17 women	57 ± 4	COPD, Interstitial lung disease Bronchiectasis	Transplant candidates
Munro et al (2009) ⁽²⁴⁾	18 men 18 women	46 ± 14	Cystic fibrosis, COPD, Interstitial Disease, alpha-1 antitrypsin deficiency, Bronchiectasis, Pulmonary hypertension, Sarcoidosis	Lung transplant recipients
Vivodtzev et al (2011) ⁽²⁵⁾	10 men 02 women	22 ± 3	Cystic fibrosis, Histiocytosis, Emphysema, Pulmonary hypertension, COPD and Idiopathic pulmonary fibrosis	Lung transplant recipients
Florian et al (2013) ⁽⁹⁾	28 men 84 women	46 ± 14	Idiopathic pulmonary fibrosis, Emphysema, Lymphangiomyomatosis, Bronchiolitis Obliterans, Pneumoconiosis	Transplant candidates
Li et al (2013) ⁽²⁶⁾	191 men 154 women	51 ± 14	Pulmonary fibrosis, COPD, Cystic fibrosis, Pulmonary hypertension, Sarcoidosis, Bronchiectasis	Transplant candidates
Dierich et al (2013) ⁽⁸⁾	81 men 57 women	> 18 years	COPD, Interstitial lung disease, Cystic fibrosis, Pulmonary hypertension	Lung transplant recipients

COPD: Chronic Obstructive Pulmonary Disease

Table II - Methodological aspects of the analyzed studies (n= 6).

Authors	Type of study	Evaluation	Duration of the intervention	Sample (n)
Maury et al (2008) ⁽²³⁾	Observational cohort	6MWD; muscle force (isometric quadriceps and handgrip); lung function	3 months	36
Munro et al (2009) ⁽²⁴⁾	Prospective and longitudinal	6MWD; lung function; HRQoL (SF-36) Exercise capacity; Quadriceps force; HRQoL (CRQ)	3 months	36
Vivodtzev et al (2011) ⁽²⁵⁾	---	Lung function; body composition Skeletal muscle biopsy and muscle fibers; quadriceps twitch tension measurement; incremental exercise	3 months	12 lung transplant recipients and 7 age-matched healthy subjects 112
Florian et al (2013) ⁽⁹⁾	Prospective	Lung function; 6MWD; HRQoL (SF-36) Borg scale	3 months	(58 completed the PR and 54 didn't)
Li et al (2013) ⁽²⁶⁾	Retrospective cohort	6MWD; HRQoL (SF-36 and SGQ); EQ-5D Standard Gamble Visual Analog Scale	----	345
Dierich et al (2013) ⁽⁸⁾	Prospective observational cohort	6MWD; lung function; Cardiopulmonary exercise testing (cycle ergometry); ADL (Barthel's Index); HRQoL (SF-36); Hospital Anxiety and Depression Scale	3 weeks	138

6MWD: Six-Minute Walking Distance; HRQoL: Health-related quality of life; SF-36: Short-Form 36; SGRQ: Saint George Respiratory Questionnaire; ADL: Activity of daily life.

Table III - Characteristics of the Pulmonary Rehabilitation programs applied in the analyzed studies (n=6).

Authors	Kind of program	Frequency	Duration	General Protocol	Main Results
Maury et al (2008) ⁽²³⁾	Outpatient program	3 times/week	1.5 hour	Exercise training	- 6MWD (p<0.05) - Quadriceps force (p<0.05) - Handgrip force
Munro P.E. et al (2009) ⁽²⁴⁾	Outpatient program	3 times/week	1 hour	Supervised exercise training Education sessions (once a week)	- FEV ₁ and FVC (p<0.0001) - 6MWD from 451 to 543 (p<0.0001) - All domains of HRQoL (p<0.05)
Vivodtzev et al (2011) ⁽²⁵⁾	Home-based program	3 times/week	---	Exercise training	- VO _{2peak} was significantly improved in healthy subjects and a trend to improvement in LTR (p=0.059) - Endurance time improved in both groups (p=0.001) - Muscle strength was significantly improved in LTR and healthy subjects (p=0.047) - Trends to significant changes in the percentage of type I fiber (p=0.10) and the type II fiber diameter (p=0.10) in LTR - Statistically and clinically significant improvement in the dyspnea score in LTR (p=0.03). No significant changes were observed in other domains but a trend to improvement in the fatigue domain (p=0.07)
Florian et al (2013) ⁽⁹⁾	Outpatient program	3 times/week	90 minutes	Exercise training Physician consultation Follow-up with psychiatrist, nutritionist and social worker Educational sessions	- Improvement of a mean of 72m in the 6MWD - SF-36: Functional Capacity (p=0.001) Physical Aspects (p=0.045) Vitality (p<0.001) Social Aspects (p<0.001) Mental Health (p=0.001) - 6MWD 320±119m (at listing) 314±116m (at the final 6MWT) - All components of the SGRQ showed small but statistically significant declines - The mental health component of the SF-36 and the EQ-5D scores also decreased - No correlations were found between changes in 6MWD and changes in HRQoL outcomes
Li et al (2013) ⁽²⁶⁾	Outpatient program	3 times/week	1,5-2hours	Stretching Aerobic exercise Resistance training	- FEV ₁ , VO _{2peak} , 6MWD and HRQoL had significant improvement after PR (p<0.001)
Dierich et al (2013) ⁽⁸⁾	Inpatient center-based program	-----	-----	Interval exercise training Bicycle exercise training Upper and lower limb strength exercise training Respiratory physiotherapy Psychological support and educational program	

6MWD: Six-Minute Walking Distance; FEV₁: Forced expired volume in one second; FVC: Forced Vital Capacity; HRQoL: Health-related quality of life; VO_{2peak}: Peak Oxygen Consumption; LTR: Lung transplant recipients; SF-36: Short-Form 36; 6MWT: Six-minute Walking Test; SGRQ: Saint George Respiratory Questionnaire; PR: Pulmonary Rehabilitation

The principal results founded in the studies was the significant change in the distance walked in the 6MWT^(8,9,23,24), in the QoL evaluated by the Saint George Respiratory Questionnaire (SGRQ) which is an specific questionnaire and the SF-36^(8,9,24,25) and the quadriceps force^(9,23). Pulmonary function presented statistically significant results in those studies in which the values before and after transplant were compared^(8,24). The main results of the studies are described in table III.

In general, the protocols applied in the studies were based on exercise training (involving stretching, aerobic exercises and resistance training) and education sessions as shown in table III. The aerobic training were using a treadmill in two studies^(9,26) and the bicycle in other two^(8,25). Both aerobic training were used in the protocol of two other studies^(23,24). The quadriceps force training were identified in just two of the six studies^(23,26) and the stretching exercises in half of them^(9,24,26). Table IV describes the RP protocols in details.

Table IV - Details of the Pulmonary Rehabilitation protocols applied in the analyzed studies (n=6).

Authors	Protocol
Maury et al (2008) ⁽²³⁾	<ul style="list-style-type: none"> * Exercise training <ul style="list-style-type: none"> - bicycle - treadmill - stair-climbing exercise - quadriceps muscle resistance training (three series of eight repetitions)
Munro et al (2009) ⁽²⁴⁾	<ul style="list-style-type: none"> * Exercise training <ul style="list-style-type: none"> - 30' of endurance training (stationary cycling and treadmill walking) - upper and lower limb strength training (three sets of 10 to 15 repetitions with load progression) - stretches of major muscle groups (calf, hamstrings, quadriceps and biceps) - motion exercises of the neck, shoulder and trunk * Education sessions by the multidisciplinary team
Vivodtzev et al (2011) ⁽²⁵⁾	<ul style="list-style-type: none"> * Exercise training <ul style="list-style-type: none"> - Cycling (50% and progressively increasing up to 80% for 10' followed by 5' at 30% W_{peak} three times per sessions Supervision by a physiotherapist at home in the first sessions and via phone each subsequent week
Florian et al (2013) ⁽⁹⁾	<ul style="list-style-type: none"> * Exercise training <ul style="list-style-type: none"> - warm-up exercise - strengthening exercises for upper and lower limb - aerobic exercise (treadmill) - stretching exercises for the main muscle groups
Li et al (2013) ⁽²⁶⁾	<ul style="list-style-type: none"> * Exercise training <ul style="list-style-type: none"> - stretching exercises - aerobic exercises (arm ergometer, cycle ergometer and treadmill training with intensity of training determined by the physical therapist) - resistance training (strengthening exercises for biceps, triceps, quadriceps, hamstrings and hip muscles)
Dierich et al (2013) ⁽⁸⁾	<ul style="list-style-type: none"> * Exercise training <ul style="list-style-type: none"> - interval exercise - bicycle (six times a week for 25 min daily) - upper and lower limb strength exercise * Respiratory physiotherapy <ul style="list-style-type: none"> - breathing and relaxation techniques, reflective breathing therapy, rib cage mobilization, chest wall vibration, massage * Psychological support * Educational program (medical basics, self-management and behavioral strategies, return to work aspects and the eligible nutrition)

DISCUSSION

This literature review shows a scarcity of researches about PR in candidates to lung transplant and/or lung transplant recipients although all of them presented positive results. The different sizes of the samples of the studies can be explained by the kind of the study. A retrospective study⁽²⁶⁾, for example, allows a collected data bigger than a clinical trial⁽¹⁴⁾.

Even though there were a variability in the components of the PR programs applied in the analyzed studies, all of them had positive and statistically significant results, corroborating with the literature that does not present an specific protocol but essential aspects to the PR as the physical training and education in health^(10,27), the characteristics presented in most articles in this review. The majority of the programs applied, followed the standard guidelines of the British Thoracic Society and the American Thoracic Society of 4 to 12 weeks duration and the frequency of 2 to 5 times per week^(10,28). Just one study had 3 weeks duration and, although it was a short time intervention, it presented positive results⁽⁸⁾.

The PR protocols identified in this review didn't differ of what is done in patients with chronic lung diseases without a transplant indication. Nevertheless, candidates to lung transplant and lung transplant recipients need special attention and follow-up due the delicacy of the surgery process they will undergo^(29,30). The educational approach must be directed to the surgery, the professional team must prepare the patient to the intervention as well as his/her recovery that will need care and physical training follow-up in the PR⁽³¹⁾.

The evaluation protocols of the analyzed studies (lung function, QoL, exercise capacity and quadriceps force) were similar to other studies in different patients^(11,12,15,16). Recent study⁽³²⁾ showed that the delay in the recovery of the exercise capacity after lung transplant is not associated with the delay in the improvement of the function of the transplanted organ but it results to the slow recovery of the muscular force. Thus, the authors reinforce the necessity of clinical trials to a better comprehension about the influence of the physical activity in the improvement of the exercise capacity after lung transplant. The evaluation of the respiratory muscle⁽³³⁾ and the activities of daily living are also important aspects to be evaluated in candidates to lung transplant⁽³⁴⁾, although any study in this review had this aim.

The benefits of the PR programs described in this review reinforce its importance in the treatment of patients with chronic lung disease, highlighting, the election of lung transplant as the indication of this treatment⁽¹⁰⁾. Improvement in the QoL, exercise capacity and lung function certainly contributes to increase the years of life of the patients who

was in advanced disease stage and had the lung transplant as the last chance to change their life⁽⁷⁾. Nevertheless, it is important to emphasize that the results will be maintained according to the physical activity and care inherent of lung transplant recipients, fact that reflects the adherence or not to the treatment. In the same way, patients who do not do the transplant after the PR due the clinical improvements also need the maintenance of the physical activity to control the progression of the disease^(31,35).

CONCLUSION

This literature review showed its benefits in the QoL, exercise capacity and quadriceps muscle force contributing to the Health Promotion of the patients.

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