

**Relationship between the Severity of
Bronchiectasis and Exercise Capacity after a
Pilot Program for Home Respiratory
Rehabilitation at the Virgen Macarena University
Hospital**

**C.P. SCHNR15 - C.I. 1550-N-17
May 07, 2018**

Relationship between the Severity of Bronchiectasis and Exercise Capacity after a Pilot Program for Home Respiratory Rehabilitation at the Virgen Macarena University Hospital

BACKGROUND AND CURRENT STATE OF THE SUBJECT

Bronchiectasis not associated with cystic fibrosis (non CF bronchiectasis) is bronchial dilatations characterized by inadequate mucociliary clearance, whose main clinical expression is cough with purulent expectoration and dyspnea, leading to exercise limitation. In order to try to quantify the severity of the disease and its prognosis, in recent years different scales have been developed that take into account clinical, radiological and functional parameters (FACED and BSI).

The objective of the treatment of the disease lies in the prevention of exacerbations, reduction of symptoms, improvement in quality of life and stabilization of lung function (Polverino et al. 2017). Based on these objectives, we have tried to develop tools, until now not available in all media, such as the development of specific respiratory rehabilitation programs (PRR). Although the long-term benefits of PPRR have not been objectified or demonstrated, there is a common consensus on the need to include this type of intervention in the management of patients with bronchiectasis (strong level of recommendation) (Polverino et al. 2017), since they could stabilize lung function and exercise capacity, as well as influence exacerbations, although more studies are still needed in this regard. On the other hand, it is also not very clear where and when to carry out this type of program, and there is a need to implement and optimize respiratory rehabilitation programs in non-traditional settings, at home or in an exacerbation (Rochester et al. 2015) (Wedzicha et al. 2017)(Pasteur et al. 2010).

Most of the studies carried out in relation to RR and non-CF bronchiectasis have focused on outcomes on quality of life and lung function with disparate results (Annemarie L Lee et al. 2014), however there are fewer data in relation home base rehabilitation program . To date, there are several clinical trials that analyze exercise capacity and tolerance in patients with bronchiectasis undergoing RP, with a clear improvement in these parameters after completion (Murray, Pentland, and Hill 2009)(Zanini et al. 2015)(Singh et al. 2014)(J. Bradley, Moran, and Greenstone 2002).

The most recent meta-analysis (Annemarie L. Lee et al. 2017) includes four clinical trials with the aim of evaluating the effect of respiratory rehabilitation (RR) in terms of exercise capacity and tolerance, exacerbations, symptoms, quality of life and mortality.

BIBLIOGRAPHY

- Bradley, J, F Moran, and M Greenstone. 2002. "Physical training for bronchiectasis (Cochrane review) [with consumer summary]." *Cochrane Database of Systematic Reviews 2002 Issue 2* .
- Bradley, Judy M et al. 2015. "Sedentary behavior and physical activity in bronchiectasis: a cross-sectional study." *BMC pulmonary medicine* 15: 61. <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4456779&tool=pmcentrez&rendertype=abstract>.
- Lee, AL et al. 2014. "Minimal important difference in field walking tests in non-cystic fibrosis bronchiectasis following exercise training." *Respiratory Medicine* 108(9): 1303-9.
- Lee, Annemarie L et al. 2014. "The short and long term effects of exercise training in non-cystic fibrosis bronchiectasis--a randomized controlled trial." *Respiratory research* 15(1): 44. <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3996132&tool=pmcentrez&rendertype=abstract>.
- Lee, Annemarie L., Catherine J. Hill, Christine F. McDonald, and Anne E. Holland. 2017. "Pulmonary Rehabilitation in Individuals With Non-Cystic Fibrosis Bronchiectasis: A Systematic Review." *Archives of Physical Medicine and Rehabilitation* 98(4): 774-782.e1. <http://dx.doi.org/10.1016/j.apmr.2016.05.017>.
- Mandal, P. et al. 2012. "A pilot study of pulmonary rehabilitation and chest physiotherapy versus chest physiotherapy alone in bronchiectasis." *Respiratory Medicine* 106(12): 1647-54.
- Murray, MP et al. 2009. "Validation of the Leicester Cough Questionnaire in non-cystic fibrosis bronchiectasis." *European Respiratory Journal* 34(1): 125-31.
- Murray, MP, JL Pentland, and AT Hill. 2009. "A randomized crossover trial of chest physiotherapy in non-cystic fibrosis bronchiectasis." *European Respiratory Journal* 34(5): 1086-92.
- NJ., Greening et al. 2014. "An early rehabilitation intervention to enhance recovery during hospital admission for an exacerbation of chronic respiratory disease: randomized controlled trial." *BMJ (Clinical research ed.)* 349(PG-g4315): g4315.
- Olveira, C, F Espíldora, a Padilla, and JL De la Cruz Rios. 2010. "Evaluation and treatment of the patient with non-CF bronchiectasis." *Manual of diagnosis and therapy in Pulmonology* · 2nd Edition. : 495-509.
- Olveira, Casilda, João Cordeiro da Costa, and Miguel Ángel Martínez-García. 2016. "How to Assess the Severity and Prognosis of Bronchiectasis." *Monographs from Archivos de Bronconeumología* 3(1): 10-18.
- Pacheco, V Almadana. 2016. «Changes in physical activity after a respiratory rehabilitation program in COPD». 28(4): 214-21.

- Pasteur, MC, D Bilton, AT Hill, and British Thoracic Society Bronchiectasis non-CF Guideline Group. 2010. "British Thoracic Society guideline for non-CF bronchiectasis." *Thorax* 65 Suppl 1: i1-58. <http://www.ncbi.nlm.nih.gov/pubmed/20627931>.
- Polverino, Eva et al. 2017. «European Respiratory Society guidelines for the management of adult bronchiectasis». *European Respiratory Journal* 50(3): 1700629. <http://erj.ersjournals.com/lookup/doi/10.1183/13993003.00629-2017>.
- Rochester, Carolyn L. et al. 2015. "An official American Thoracic Society/European Respiratory Society policy statement: Enhancing implementation, use, and delivery of pulmonary rehabilitation." *American Journal of Respiratory and Critical Care Medicine* 192(11): 1373-86.
- Singh, Sally J. et al. 2014. «An official systematic review of the European Respiratory Society/American Thoracic Society: Measurement properties of field walking tests in chronic respiratory disease». *European Respiratory Journal* 44(6): 1447-78.
- Soto Campos, Jose. 2009. «Quality of life applied to Pulmonology». *Diagnostic and Therapeutic Manual in Pulmonology* : 105-14.
- Wedzicha, Jadwiga A. et al. 2017. «Management of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline». *European Respiratory Journal* 49(3): 1600791. <http://erj.ersjournals.com/lookup/doi/10.1183/13993003.00791-2016>.
- Zanini, Andrea et al. 2015. "Effects of Pulmonary Rehabilitation in Patients with Non-Cystic Fibrosis Bronchiectasis: A Retrospective Analysis of Clinical and Functional Predictors of Efficacy." *breathing; international review of thoracic diseases* 89(6): 525-33. <http://www.ncbi.nlm.nih.gov/pubmed/25924686>.

WORK HYPOTHESIS

Exercise tolerance and capacity can be modified after completing a respiratory rehabilitation program with a decrease in the perception of symptoms, exacerbations and quality of life.

SPECIFIC OBJECTIVES

Primary

To determine the capacity and tolerance to exercise by means of a cardiopulmonary test and to assess the effects and changes after a PRR in patients with BE without CF.

Secondary

Assess the degree of baseline physical activity of patients with BE without CF and its changes after PR.

Know the severity through the prognostic scale E-FACED

Determine the impact of PR on health-related quality of life and anxious/depressive state, symptoms, exacerbations

METHOD

- **Population (inclusion and exclusion criteria).**

The study population will be the patients of the monographic consultation of Bronchiectasis of the Virgen Macarena University Hospital.

Inclusion criteria

- Established radiological diagnosis of bronchiectasis (HRCT of the chest).
- Non-CF bronchiectasis older than 18 years.
- Non-CF bronchiectasis in a stable situation, who have not required antibiotic therapy in the last 6 weeks.
- Dyspnea greater than 1 according to the modified scale of the Medical Research Council (mMRC).

Exclusion criteria

- Smokers or former smokers of less than 6 months or with a history of consumption of 15 packs/year.
- Cystic fibrosis.
- Active infections (bronchopulmonary aspergillosis, pulmonary tuberculosis).
- Active tuberculosis.
- poorly controlled asthma

- Chronic obstructive pulmonary disease.
- Diseases that prevent adequate performance of exercise (neuromuscular pathology or residual injuries)
- Medical diseases that put the individual at risk of a decompensation due to the performance of any physical activity or cardiopulmonary stress test (unstable ischemic heart disease, acute myocardial infarction less than 1 month).
- Pregnancy.
- Mental disorder that prevents the adequate interpretation of the indications or performance of the tests.

• Study design.

Prospective and randomized study with consecutive inclusion of patients from the Non-CF bronchiectasis BE monographic clinic of the Virgen Macarena Hospital (Seville). Patients who meet the inclusion criteria will be randomized into two groups: control and intervention, patients will be assigned to each group using a numerical sequence generated by computer until the sample size is obtained.

The control group will receive basic recommendations on physical activity and the intervention group will be included in a mixed respiratory rehabilitation program (combining home and hospital sessions).

Visit 1: inclusion of patients with BE who comply with inclusion. Signature of inform consent and randomization of patients.

Visit 2: All patients will undergo an initial assessment of the degree of physical activity by means of accelerometers (@Sensewear arm band) for 3 days including weekends, as well as pulmonary function and exercise tolerance tests, stratification of severity according to the E-FACED scales.

* Control group: written recommendations on performing some physical activity for at least 30 minutes of moderate intensity according to the recommendations of the Spanish Society of Pulmonology and the Andalusian Society of Pulmonology and Thoracic Surgery. (Casilda Oliveira, Costa, and Martínez-García 2016) , (C Oliveira et al. 2010). A phone call every 15 days to assess the physical activity carried out without talking about exercise or physical activity.

* Intervention group: Patients will be included in an 8-week outpatient program with recall sessions led by our physiotherapist once every 2 weeks in the hospital's Respiratory Rehabilitation gym. In the first session, patients will be instructed on how to perform home exercises as well as how to use the Borg scale. A phone calls weekly to provide support and general advice about exercise or physical activity.

The program will combine isotonic strength and resistance exercises. Resistance training will consist of bicycle or walking exercises (depending on the availability of each patient), with a progressive increase in distance or time of completion depending on symptom control.

The strength training program will include upper and lower limb exercises that will begin with no load and to which weights will be progressively added depending on the control of symptoms, in 2 sets of 6-8 repetitions:

- Hanger (to work the latissimus dorsi muscle).
- Butterfly (pectoralis major muscle work).
- Neck press (brachial triceps and deltoid work).
- Flexion of legs (work of biceps femoris and gastrocnemius).
- Extension of legs (work of quadriceps femoris): place a weight or ballast. Stretch the leg and raise the thigh
- Exercises with elastic bands: upper and lower limbs. Separate both ends of the tape as much as possible.
- Walking: increase the walking time progressively.
- Bicycle or treadmill: submaximal exercise. Constant pedaling at about 60 rpm with moderate intensity.

Patients will be encouraged to maintain the exercises after the study.

Visits 3, 4 and 5: at 8 weeks (time of completion of the rehabilitation programs), 6 months and 12 months, respectively. At the end-of-program and follow-up visits, all the measurements made at the baseline visit will be repeated, as well as the record of exacerbations.

All patients will receive an educational program about their disease as well as an individualized respiratory physiotherapy program including relaxation techniques, secretion management and assessment of nutritional status.

Measurement methods and variables

- **Assessment of exercise capacity with cycle ergometry.** Cycle-ergometry will be performed in progressive steps of one minute up to its maximum. We will use a state-of-the-art Vyntus CPX ergospirometer from the firm Jaeger-CareFusion. Maximum oxygen consumption, aerobic-anaerobic thresholds, respiratory compensation point, ventilatory limitation study, calorimetry, forced spirometry F/V, slow spirometry + MVV, maximum voluntary ventilation, cardiac output and physiological dead space will be assessed. The subsequent evaluation of the data will be carried out through the Sentry program platform
- **6-minute walk test (6MWT):** it is carried out in an absolutely flat corridor with a length equal to or greater than 30m, placing cones to mark the ends of the route. The distance traveled in a period of 6 minutes will be

calculated according to the recommendations of the American Thoracic Society (ATS)

- **Physical activity level** using the Multisensor ArmBand accelerometer. (SenseWear mini armband; BodyMedia,) as referenced in the study by Almadana et al (Pacheco 2016). It is placed on the right triceps and provides information on calorie consumption and physical activity levels, which are subsequently, analyzed using specific software (INNERVIEW professional version 8, BodyMedia, Pittsburgh, PA). → Quality of life in Saint George respiratory questionnaire (Soto Campos 2009). 50 items divided into three scales: symptoms, activity and impact. Symptom scale items refer to frequency and severity of respiratory symptoms
- **Cough Severity Questionnaire with LCQ** (Murray et al. 2009)(Annemarie L. Lee et al. 2017). The LCQ measures the physical, psychological, and social impact of chronic cough. It consists of 19 items. Validated in BQ not CF.
- **Severity and prognosis by E-FACED:** number of exacerbations in the previous year; F: percentage of predicted FEV1; A: age; C: chronic colonization by *Pseudomonas aeruginosa*; E: Extension [number of lung lobes affected by bronchiectasis]; D: dyspnea) have been proposed to stratify BE patients according to their main dimensions (symptoms, lung function, imaging, and microbiology). 0-3 points: mild bronchiectasis. 4-6 points: moderate bronchiectasis. 7-9 points: severe bronchiectasis
- **Pulmonary function test:** measurements through a Jaeger Viasys Mastercope spirometer. Forced expiratory volume in 1 s (FEV1), Forced vital capacity (FVC).
- **Other variables:** demographic (sex, age, weight, height, body mass index), comorbidities (hypertension, diabetes, dyslipidemia), smoking (packs/year): Modified dyspnea scale. Medical Research Council (MRC).
- Other variables: demographic (Sex, age, weight, height, body mass index), comorbidities (HBP, Diabetes, Dyslipidemia), Smoking (packs/year): Modified dyspnea scale. Medical Research Council (MRC).

Statistical analysis

For the calculation of the sample size, a power of 95% is used, a hypothetical loss rate during the study of 15%, a total of 30 patients per group would be included, enough to demonstrate our hypothesis and find statistically significant differences in the capacity of exercise and the change in physical activity in the two populations.

Statistical analysis was performed using the statistical analysis software IBM SPSS Statistics (SPSS v23, Chicago, IL, USA). For quantitative variables, the values are expressed as mean \pm standard deviation, while in the case of qualitative variables; their values are included as frequency and percentage. The comparison between groups was carried out using the T test for independent samples in the event that the data behaved according to a normal distribution. Otherwise, the Mann-Whitney U test was used for independent samples. The comparison of the effects of respiratory rehabilitation was performed with the Student's t test for related samples when the data follow a normal distribution and the Wilcoxon signed rank test for related samples. In all cases, the minimum level of significance was considered to be $p < 0.05$. If statistically significant differences are identified between the different groups studied, "a posteriori" comparison tests will be carried out, such as the Mann-Whitney U test according to application criteria, with the level of significance corrected.

Ethical aspects

All participants will sign the informed consent, the version of which is being evaluated by the ethics committee of our hospital. The rights of the subjects will be at all times protected by the Declaration of Helsinki. The data will be treated with absolute confidentiality and will be subject to the Data Protection Law 15/1999 of December 13. The nature of the study, the voluntary nature of participation and the proposed objectives will be reported. They may leave the study at any time, if they wish.

Potential Job Limitations

Due to the natural history of the disease, we cannot foresee decompensations, so there may be losses in the development of the study, having to increase the sample size from the outset.

In this study, since it is a home program, this may be greater due to the lack of stimulation generated by the groups to carry out physical activity.

Work calendar

Once the 3-month recruitment period has ended and the initial assessment tests have been completed, an 8-week rehabilitation program will begin with a subsequent 12-month follow-up from the start of the PRR. After this, the analysis, exploitation of the data and subsequent dissemination of the results will be carried out.

- **Data exploitation period:** once the recruitment period has ended, the collected data will be analyzed and exploited, with the aim of subsequently disseminating the results.

Experience of the research team on the subject

Clinical experience having a monographic consultation of Bronchiectasis, in addition to the experience of more than almost a decade in carrying out respiratory rehabilitation programs (Dr. Almadana) with publications in the area of respiratory rehabilitation

-Pacheco VA. Changes in physical activity after a respiratory rehabilitation program in COPD. 2016;28(4):214-21.

-Almadana Pacheco V, Pavón Masa M, Gómez-Bastero Fernández AP, Muñíz Rodríguez AM, Tallón Moreno R, Montemayor Rubio T. Profile of patients who drop out of a respiratory rehabilitation program. Arch Bronconeumol. 2017;53(5):257-62.

Potential practical applicability of the results

The applicability of this project stems from the possibility of knowing the possible factors that may predispose to poor exercise tolerance and being able to take measures to improve this situation. In addition, determining if there is a relationship between effort tolerance and the severity of bronchiectasis according to the measurement scales could help us decide at what time to start a rehabilitation program. physical activity program, without this entailing additional economic costs. In addition, the development of the RR Program would provide an increase in exercise capacity and consequently an improvement in health-related quality of life, which would translate into a reduction in direct expenses such as hospitalizations or emergency visits (due to better control of exacerbations) or indirect, derived from social costs (due to the dependence and limitations of these patients in decompensation).

For all these reasons, the interest of the work extends to the entire health system to promote a sustainable method and improve exercise tolerance and fundamentally the quality of life of patients and survival.

Facilities and techniques already available for the project

We have a Pulmonary Function Laboratory of the Pneumology UGC of the HUV Macarena where cycle ergometry and pulmonary function tests will be carried out, in addition to the space set aside for carrying out the 6-minute walk test.

The recruitment of Non-CF Bronchiectasis patients will be carried out in the specialized bronchiectasis clinic of the Virgen Macarena Hospital. We also have research support staff; aimed at the initial assessment of patients, signing the consent, help with questions about the questionnaires and diagnostic tests.