EFFECT OF NON-INVASIVE MECHANICAL VENTILATION ON NEURORESPIRATORY COUPLING DURING EXERCISE IN PATIENTS WITH SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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BACKGROUND AND CURRENT STATUS OF THE ISSUE

In patients with chronic obstructive pulmonary disease (COPD), during exercise, limitation of expiratory flow and increased respiratory rate can decrease expiratory time, resulting in increased residual volume, a condition known as dynamic hyperinflation (O'Donnell, Revill et al. 2001). The inevitable consequence of this condition is an increase in intrinsic telexpiratory positive pressure (PEEPi) and increased work of breathing. Finally, the result is severe dyspnea during physical exertion that reduces exercise tolerance (Babb, Viggiano et al. 1991, Marin, Carrizo et al. 2001, Soffler, Hayes et al. 2017, Marrara, Di Lorenzo et al. 2018).

Recently, great interest has developed in the use of non-invasive mechanical ventilation (NIV) to increase physical capacity during exercise (Hill and Holland 2014, Ambrosino and Xie 2017, Furlanetto and Pitta 2017, Marrara, Di Lorenzo et al. 2018), because of evidence that assisted ventilation reduces muscle load, which would allow the patient to train with higher intensity exercises.

During physical exercise of COPD patients, who have increased respiratory work, there may be a redistribution of blood flow from the extremities to the respiratory muscles, which would induce early muscle fatigue in the extremities, a recognized cause of exercise disruption. This redistribution could, at least in part, be reduced if ventilation is assisted during exercise (Ambrosino and Cigni 2015), and prevention of exercise-induced diaphragmatic exhaustion through NIV has already been demonstrated in some studies (Babcock, Pegelow et al. 2002, Borghi-Silva, Oliveira et al. 2008).

As PEEPi and exhaustion of inspiratory muscles in COPD patients contribute to the development of dyspnoea, it is possible that NIV provides at least symptomatic benefit through muscle unloading and decreased work of breathing. By unloading the respiratory muscles, they may need less blood flow and thus avoid redistribution from the extremities that limits the patient's physical capacity (Ambrosino and Cigni 2015).

The message from these physiological studies is clear: NIV during exercise may reduce respiratory work and dyspnea, increasing exercise tolerance, but the available evidence is controversial. Some studies have found no benefit of NIV during exercise using a hybrid ventilatory mode of positive pressure proportional to patient effort and not a fixed support pressure (Bianchi, Foglio et al. 2002), while others have found an increase in exercise intensity in patients with NIV even with the same ventilatory mode (Hawkins, Johnson et al. 2002), compared to patients with spontaneous ventilation. However, two meta-analyses on the subject conclude that, given the small number of studies available and the small sample size, randomized clinical studies are necessary to determine the real effects of NIV in COPD and validate its widespread recommendation in rehabilitation programs (Menadue, Piper et al. 2014, Ricci, Terzoni et al. 2014). Since most patients with moderate and severe COPD are candidates for rehabilitation programs, and rehabilitation is an important component in the management of dyspnea (Ambrosino and Cigni 2015), the use of NIV during exercise is a major issue.

A recent study (Marrara, Di Lorenzo et al. 2018) demonstrated the effect of performing treadmill rehabilitation with the aid of NIV. Although inspiratory pressures were discrete (mean IPAP 12cmH2O), an improvement in peak expiratory pressure, improved oxygen consumption and exercise capacity was demonstrated, compared with the spontaneous ventilation rehabilitation program.

Although it is widely accepted that awareness of increased muscular respiratory work by central breathing centers is important for the sensation of dyspnea, the identification of a reliable physiological measurement of the respiratory neural drive (RND) represents a significant challenge. In addition, we know that dyspnoea increases disproportionately when the ventilatory response is limited by mechanical alterations in the lungs (Scano, Innocenti-

Bruni et al. 2010), such as in COPD, a phenomenon known as neuroventilatory uncoupling (DNR)(Jolley, Luo et al. 2015).

Ventilation-related measurements do not adequately reflect the DNR in COPD patients, because their alterations in respiratory mechanics modify the relationship between the DNR and inspiratory flow. Nor can it be related to variables relating to respiratory system pressures, because these vary according to the contractile capacity of the respiratory muscles and their tension, properties that are independent of the DNR, especially in the presence of pulmonary hyperinflation (Cherniack and Snidal 1956).

But recently the measurement of diaphragmatic contraction using an oesophageal probe with electrodes, diaphragmatic electromyography (EMGdi) (Sinderby, Spahija et al. 2001, Spahija, de Marchie et al. 2010, Reilly, Ward et al. 2011) Thishas allowed the precise quantification of DNR, since a measure is obtained that is, from a neurophysiological point of view, closer to the generation of the respiratory impulse than changes in pleural pressure (Luo, He et al. 2014). The measurement of DNR by EMGdi has demonstrated a close relationship between the increase in dyspnea, measured by the Borg scale, and DNR. The measurement of the respiratory minute volume is poorly related to dyspnea because under physical effort, and once the decoupling point is exceeded, despite the compensatory increase in respiratory rate and muscle effort and respiratory drive, the minute volume reaches a plateau. Despite the parallel increase in dyspnoea and neural drive, no increase in minute volume is obtained (Jolley, Luo et al. 2015).

The study of DNR behaviour, as described above, has been conducted in patients with severe COPD at rest and during physical exercise (Jolley, Luo et al. 2015),but has not been studied in patients with WV. It is possible that WV, by increasing alveolar ventilation and tidal volume, may modify the respiratory mechanical characteristics responsible for VN, and we have therefore set out to investigate the behavior of VN in patients with COPD and WV at baseline and during exercise.

The measurement of the neural drive from diaphragmatic electromyography is considered the "gold standard" method but has a number of associated problems. Perhaps the most relevant is the invasiveness of the method: it

requires the use of an esophageal probe with multiple electrodes, whose insertion may be uncomfortable for the patient.

Recently, the use of parasternal electromyography has been proposed as a surrogate marker of diaphragmatic muscle electrical activity with a good correlation to diaphragmatic electromyography through an esophageal catheter (Lin, Guan et al. 2019). Its use, in patients at rest, seems promising to obtain a signal with clinical relevance, having been proposed as a marker of increased respiratory muscle effort in stable and acute COPD (Murphy, Kumar et al. 2011), in pediatric population with cystic fibrosis (Reilly, Ward et al. 2011) and in other respiratory patients. Its use during exercise is controversial, since the muscle activation of the shoulder girdle that occurs when grasping the handlebars of the bicycle conditions an interference in the registration of the sternal muscles(Ramsook, Mitchell et al. 2017). The use of recumbent bicycles is proposed to keep the arms at rest and limit this interference.

Finally, in recent years a new method of ventilatory support has burst onto the scene, the high flow nasal goggle (HNFG), whose usefulness in the field of acute respiratory failure, especially hypoxemic, has led to its widespread use in acute units. There is little experience with the use of this technique in a stable COPD situation and even less during rehabilitation. However, it has been shown to improve dyspnea, exercise capacity and oxygenation during effort. (Cirio, Piran et al. 2016). It seems that, given that it is capable of generating a certain PEEP(Okuda, Tanaka et al. 2017) effect, it may be useful to compensate for the dynamic hyperinflation generated in COPD patients, and therefore, neurorepiratory coupling.

HYPOTHESIS

Theoretical hypothesis: non-invasive mechanical ventilation can correct the neurorespiratory decoupling that develops in patients with severe COPD during physical exercise.

Operational hypothesis: non-invasive mechanical ventilation reduces the difference that develops during exercise between the respiratory neural drive and the respiratory minute volume, which causes neurorepiratory decoupling.

Statistical hypothesis:

H0: no difference in the development of neurorespiratory decoupling in COPD patients under physical exercise with spontaneous or mechanically assisted ventilation. (NVUvm =NVUesp)

H1: neurorespiratory decoupling is less in COPD patients under physical exercise with non-invasive mechanical ventilation than in the same patients with spontaneous ventilation. (NVUvm> NVUesp)

Objectives

Main objective:

- Demonstrate that non-invasive mechanical ventilation during incremental exercise decreases neurorespiratory decoupling in patients with very severe COPD.

Secondary objectives:

- To study the behaviour of dyspnoea with the use of non-invasive mechanical ventilation during exercise in patients with severe COPD
- To study the behaviour of residual volume, air entrapment and exercise-induced hypercapnia in patients with severe COPD on non-invasive mechanical ventilation

METHODS

Population

Inclusion criteria:

- Patients with severe COPD or Cystic Fibrosis (with obstructive pattern and air entrapment) on the waiting list for lung transplant, assessed by the Pulmonary Transplant Unit of the Hospital Universitario 12 de Octubre In these patients, the exhaustive study they have undergone for the assessment of the indication for transplant, allows us to rule out interference in the results of this study due to comorbidities.

- Meet GOLD diagnostic criteria for COPD, and evidence of air entrapment plethysmography (residual volume greater than 120% of theoretical)
- Evidence of developing dynamic air entrapment by analyzing flow/volume curves during physical exercise.
- Patients already adapted to non-invasive mechanical ventilation at home (NMV) as a bridge to transplantation To avoid an extra intervention, those patients previously adapted to MDM, who have their own ventilation equipment, are acclimatized to its use and comply with this treatment, and have not suffered side effects that have contraindicated its use, will be included.

Exclusion criteria:

- Presence of uncontrollable comorbidities that limit the patient's capacity for physical effort (uncontrolled ischemic heart disease, severe pulmonary hypertension, neuromuscular pathology).
- Refusal of treatment with non-invasive mechanical ventilation, or inclusion in the study.

- Inability to perform the proposed exercise under basal conditions and with ventilation.

Ethical aspects

The study protocol has been approved by the Research Ethics Committee of the CEIC of the Hospital 12 de Octubre (resolution 18/025). Attached is informed consent. Participation in this study is completely voluntary, and does not affect the assessment of the patient on the transplant waiting list. From the point of view of confidentiality, compliance with the provisions of the LOPD 1.5/1999 will be ensured. Specifically, a database will be generated with a consecutive number as the only data identifying the patient. The correlation between the number of inclusion in the study and the number of the clinical history (as a unique identifier) will be stored in a database located in the folder of the Pneumology service in the "Y" server, with access protected by a password, only authorized to the two investigators of the work (Sayas and Hernández-Voth).

The intervention on the patients does not pose any risk (derived from the determination of surface electromyography) and only consists of the measurement of muscle activity during basal effort, with NIV and with high-flow nasal glasses, in a similar way to how rehabilitation of these patients is currently carried out, and within the usual rehabilitation program.

Studio design

Experimental, longitudinal, prospective and controlled study, with a branch and comparison before/after the same individuals.

Variables and measurements

First visit, baseline situation (coinciding with scheduled review in ventilation or transplant consultation or rehabilitation):

Medical history: smoking history (packet)

Anthropometric variables: age, weight, height, BMI.

Functional variables: BODE, BODEx, FEV1 (%) FVC (%), VR, TLC, DLCO, DLCO/VA Basal arterial blood gas and basal mean tcpCO2.

Clinical variables: measurement of dyspnea using Borg and MRC scales.

Checking inclusion/exclusion criteria and signing IC

The usual pre-transplant respiratory rehabilitation program includes 24 sessions, with a frequency of 2 sessions per week, in which it is performed:

- Warm-up exercises, elongations of spine, thorax and shoulder girdle.
- Respiratory physiotherapy exercises.
- Upper limb strengthening with progressive weight dumbbells (80% of 1RP 3 sets of 15 repetitions for biceps, triceps and deltoid)
- 30 minutes of training in recumbent cycloergometer. Exercise at constant load with ascent ramp 5 W/min until the plateau phase in load of 60% to 80% of the maximum load achieved in the Incremental stress test and cooling phase until the exercise is stopped.
- Cooling and relaxation exercises to recover from basal rest.

Second visit, fixed-duration intervallic exercise with spontaneous ventilation

- INCREMENTAL STRESS TEST ON CYCLOERGOMETER
- With this test, the exercise to be performed by the patient will be individually prescribed. It is part of the usual care activity in the respiratory rehabilitation unit, and it allows to determine the level of exercise that the patient tolerates.
- The test will be started by explaining to the patient what it will consist of, showing him/her the Borg's fatigue and dyspnea measurement scale modified to make him/her familiar with it. With the patient monitored (Oximetry, EKG, blood pressure, watt load) the test is started, supervised at all times by the Rehabilitation Doctor in the Lung Rehabilitation room. We will ask at the beginning of the test and every minute as well as at the end of the perception of dyspnea and fatigue.
    - 3 minutes rest on the cycloergometer with the patient seated
    - 3 minutes of free pedaling without load
    - Exercise with an increase in the ramp load of 10 watts every 3 minutes, until the test is stopped due to the patient's symptom limitation or objective data on their monitoring that force us to stop it:
        - MMII muscle fatigue limit
        - Severe dyspnea preventing you from continuing (modified Borg dyspnea scale of 0-10)

- Heart arrhythmia maintained.
- Tachycardia exceeding 80% of the calculated FCmax (220-age)
- Dizziness, instability, chest tightness.
- Desaturation (<85% during exercise despite correct oxygen intake or <90% in patients with PTH)

- *Third visit, exercise at constant load, of fixed duration with spontaneous ventilation:*
  - 10 minutes of constant exercise will be performed, at 75% of the maximum tolerated load as determined in the second visit, by the rehabilitation physician.
  - We will insist on maintaining a constant pedaling cadence, between 35 and 40 cycles per minute.
  - It's registered:
- Neuro-respiratory coupling: NVU: EMGDimax%/Vt. To determine the neurorepiratory coupling (NVU variable) the peak value (above the baseline) of the maximum muscular activity (averaged by square root of the EMG value in mV) both diaphragmatic (EMGDimax) and parasternal (EMGparamax) in the maneuvers of maximum voluntary ventilation and maximum inspiratory pressure (MIP) will be taken. On that value, taken as 100%, the average value of EMGpara and standardized EMGdi (RMS) in each ventilatory situation (spontaneous or low NIV ventilation) will be calculated. At each point of effort (in each minute of the exercise protocol) the ratio between the standardized EMG value (parasternal and diaphragmatic) and the tidal volume (obtained by integration of the flow signal by means of a pneumotachograph connected to the MV-in NIV circuit or an oronasal airtight mask-in Vesp) shall be measured. To facilitate the interpretation of the exhaled VC, a non-leak mask with the intentional leak connected to the circuit shall be used before the pneumotachograph.
- The degree of dyspnea will be determined with a Borg and Analog-Visual scale at 60" of effort
- The entire effort protocol will be monitored by TcpCO2

- Total pedaling time and number of stops will be collected.

- At the end of this second visit, after about 20 minutes of rest, an exercise of about 10 minutes at constant load will be started to adjust the NIV parameters.
    - Based on the previously titrated home parameters, the inspiratory trigger is adjusted and EPAP is progressively increased until ineffective efforts are eliminated and trigger delay is minimized, and support (IPAP) is increased until a subjective decrease of at least 20% in the mean RMS value is achieved or until patient tolerance limits it.

Third visit, exercise with non-invasive mechanical ventilation:

- Effort protocol: it will be done in a similar way to the one done in spontaneous ventilation with similar calculations and measurements.
- In this third visit, exercise will be performed under non-invasive ventilation
- Ventilator programming: the parameters set in visit 2 will be used, recording the changes made with respect to the previous home programming.
- It will be performed at the same load in W as the test in spontaneous ventilation, maintaining a constant pedaling frequency between 35 and 40 cpm.
- They will be collected as other variables:
    - Rate of asynchronies during effort and % of ineffective effort
    - Neuro-respiratory coupling: NVU: EMGDimax%/Vt
    - Borg in times of 60" effort
    - TcpCO2 final

- ETCO2 final effort
- Number of stops and total pedalling time.

Fourth visit, exercise with high flow oxygen therapy:

Within the rehabilitation program, and as with mechanical ventilation, the patient will be offered exercise under high flow oxygen therapy, at constant flows of 50lpm and with FiO2 adjusted according to SPO2, to obtain a constant saturation between 92 and 94%. The same load and pedaling frequency will be maintained, with similar variables collected.

In summary, the included subject is scheduled for 4 study related visits: baseline, exercise level determination, spontaneous exercise, NIV exercise and high flow exercise. These visits fall within the normal care process of the pre-transplant rehabilitation program, not requiring additional patient visits for the study. The only difference with the care process is that neurorespiratory coupling (EMG for and exhaled flow) will be measured during exercise. The exercise program is the same that would have to be performed during conventional rehabilitation. Currently, the use of NIV or high flow during rehabilitation is routine, but the objective is to measure the physiological effect of rehabilitation, in a non-invasive way.

Statistical analysis

The statistical program SPSS 22.0 will be used for the analysis of the variables studied, to estimate the measures of centralization and dispersion of the results of the tests carried out and for multivariate analysis and correlations between the variables.

The NVU variable will be compared by means of a single-factor ANOVA with repeated measurements between the spontaneous and non-invasive ventilation determinations.

A difference of more than 20% is expected to be found in this value. It will be considered significant if $p<0.05$.

The remaining secondary variables will be compared by t for repeated samples once their normal distribution has been confirmed.

Sample size calculation:

According to previously published work (Jolley, Luo et al. 2015), all COPD patients expressed neuro-respiratory decoupling. Assuming a 10% decrease in NVU as clinically significant, with a 95% confidence level (alpha 5% error) and a power of 80% (1-beta), assuming 5% losses, a required number of 18 patients is calculated. The sample size calculator for ANOVA provided by http://powerandsamplesize.com/ has been used.

Potential limitations

- Measurement of neurorespiratory decoupling: in general, there are works that have questioned the reliability of EMG measurement for subrogation of EMGdi in conventional cyclo-ergometers, given the activation that the handlebar attachment induces in the parasternal musculature (Ramsook, Mitchell et al. 2017). Therefore, in order to minimize this effect, the use of a recumbent bicycle (there are 2 available in the rehabilitation room) is proposed, without arm support, which would be relaxed along the thorax.
- The use of an oronasal mask without leakage, placing the leak in the circuit, can eventually facilitate re-inhalation. This effect is expected to be minimal at the pressures expected to be used, and this variable will be continuously monitored by TcpCO2. However, in spontaneous ventilation, given the severity of the obstruction to flow presented by patients, the addition of a pneumotachograph may generate greater inspiratory resistance and worsen tolerance.
- Need to have personnel trained in performing electromyography of respiratory muscles.
- Recruitment: this is usually a handicap in this type of study, but access to a population of severe COPD on a lung transplant waiting list makes recruitment much easier. They are patients already followed up in the ventilation and transplant clinic.

- NIV adaptation and tolerance, since the study population will already be adapted to a respirator, adaptation and synchronization are not expected to be a problem in this case.

Work Plan

- February-March 2018: final study protocol, drafting of the IC, approval by CEIC.
- March-April 2017: identification of candidates, assignment of test dates
- April 2018- September 2018: stress tests
- September 2018 - December 2018: analysis of results.
- January 2019 - March 2019: drafting of originals for publication

ESTIMATED BUDGET

Description	Amount
• Database design and maintenance	2.000€
• Final statistical analysis	2.000€
• Presentation of results at conferences and publication expenses	3.000€
• Data analysis of respiratory physiological variables: Powerlab 16 channels	12.000€
• Pulmonary Function Equipment: Respiratory and Exercise Physiology: Exhaled Volume per Minute ($\dot{V}E$) Oxygen Consumption ($\dot{V}O_2$) Carbon Dioxide Production ($\dot{V}CO_2$) Respiratory Exchange Rate (RER)	8.000€
• Transcutaneous capnography equipment	8.000€
• Indirect expenses foundation (10 %)	3.500€
Total	**38.500€**

INFORMATION SHEET FOR PARTICIPATION IN THE RESEARCH PROJECT: "EFFECT OF NON-INVASIVE MECHANICAL VENTILATION ON NEURORESPIRATORY COUPLING DURING EXERCISE IN PATIENTS WITH SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Project: EFFECT OF NON-INVASIVE MECHANICAL VENTILATION ON NEURORESPIRATORY COUPLING DURING EXERCISE IN PATIENTS WITH SERIOUS OBSTRUCTIVE PULMONARY DISEASE

Principal Investigator: Dr Javier Sayas Catalán. Pneumology Service . 12 de Octubre Hospital

INTRODUCTION

We are contacting you to inform you about a research study in which you are invited to participate. The study has been approved by the Research Ethics Committee of Hospital Doce de Octubre, in accordance with current legislation, and is being carried out in accordance with the principles set out in the Declaration of Helsinki and the standards of good clinical practice.

Our intention is that you receive correct and sufficient information so that you can evaluate and judge whether or not you want to participate in this study. To do this, please read this information sheet carefully and we will answer any questions you may have after the explanation. In addition, you can consult with the people you consider appropriate.

VOLUNTARY PARTICIPATION

You should know that your participation in this study is voluntary and that you can decide not to participate or change your decision and withdraw consent at any time, without altering your relationship with your doctor. If you decide to revoke your consent, no new data will be collected, but this revocation will not affect the research conducted so far.

GENERAL DESCRIPTION OF THE STUDY:

We are conducting a study to evaluate whether the use of non-invasive mechanical ventilation during exercise/rehabilitation contributes to decreasing your dyspnea, increasing your ability to exert yourself and improving muscle capacity.

You already use, as part of the treatment of your illness, a mechanical ventilation device at home, through a mask, mainly at night, although occasionally we have indicated that you do so during training and rehabilitation sessions.

The objective of the present work is to determine if using this device (ventilator) as the one you already use, during the exercise, you are able to perform it with less choking and with better use of your respiratory muscles. Additionally we will ask you to perform this exercise with a system similar to the nasal oxygen glasses you use, with more flow than usual, as a more comfortable way to give support during the exercise.

The study consists of exercising on the bicycle, in the same room where you have already completed your pre-transplant rehabilitation program, but this time measuring the activity of your respiratory muscles by means of surface electrodes placed on your chest. These are similar to those used to perform electrocardiograms.

We will perform these measurements when you breathe spontaneously, with your respirator, and additionally with a high-flow nasal goggle system.

Since he is already on non-invasive ventilation, no adverse effects other than those already present in his usual treatment are expected.

With the results of the measurements we will compare whether doing the exercise with your respirator allows you to relieve the choking more significantly.

We will not ask you to go to the hospital more times than you are already scheduled to go in your rehabilitation program. The only thing that will change with respect to your usual rehabilitation program is that you will exercise with your respirator (as you usually do) and with 3 electrodes on your chest, similar to those of an electrocardiogram. Additionally, a small tube will be placed in the circuit of the ventilator to collect a flow and pressure signal.

benefits and risks arising from your participation in the study

The main benefit you can expect is a better understanding of how your respiratory muscles work under exercise and the most appropriate way to relieve the overexertion they make with the ventilator. This will allow you to demonstrate with concrete measurements the beneficial effect of relieving the dyspnea you already notice when you exercise with your ventilator. And

therefore, it will allow you to extend this practice and allow other patients like you to benefit from training on the ventilator.

Participation in this study is strictly voluntary. You have the right to access, correct or delete your data at any time. The information collected will be kept confidential and will not be used for any purpose other than this research. The data we collect will be entered into an electronic database in an anonymous form.

CONFIDENTIALITY

The promoter/researcher is committed to complying with the Organic Law 1511999 of 13 December on the protection of personal data and the Royal Decree that develops it (RD 172012007). The data collected for the study will be identified by a code, so that it does not include information that could identify you, and only your study doctor/collaborators will be able to relate this data to you and your medical history. Therefore, your identity will not be disclosed to anyone except in the case of a medical emergency or legal requirement.

The processing, communication and transfer of personal data of all participants will be in accordance with the provisions of this law. Access to your personally identifiable information will be restricted to the study physician/collaborators, health authorities and the Research Ethics Committee and authorized personnel, when necessary to verify the data and procedures of the study, but always maintaining the confidentiality of the same in accordance with current legislation. The data will be collected in a centre research file and will be treated solely and exclusively within the framework of their participation in this study. In accordance with data protection legislation, you may exercise your rights to access, modify, oppose and cancel the data, for which you must contact your study doctor. If you decide to withdraw your consent to participate in this study, no new data will be added to the database, but those already collected will be used.

If you have any questions about this project, you can ask them at any time during your participation in it. You may also withdraw from the study at any time without prejudice in any way. If any of the questions during the interview seem uncomfortable to you, you have the right to let the researcher know or not to answer them.

We thank you for your participation.

RESEARCH PROJECT CONSENT: **EFFECT OF NON-INVASIVE MECHANICAL VENTILATION ON NEURORESPIRATORY COUPLING DURING EXERCISE IN PATIENTS WITH SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE**

Principal Investigator: Dr J Sayas Catalán, Sº de Neumología, Hospital 12 de Octubre.

I

I've read the information sheet I was given.

I've been able to ask questions about the study.

I've spoken to:

I understand that my participation is voluntary. I understand that I can withdraw from the study:

1 Whenever you want
2 Without having to give explanations
3 Without affecting my medical care

Signature of the Principal Investigator Patient's signature

Madrid, on ___ of _____201_

Version 2.0, Madrid 27/11/2017

Data collection notebook:

*Subject No. _____

*Ethiology: COPD☐ CF☐

*Date of Birth _____

*Functional situation:

** FEV1: l(%) FVC: l(%) FEV1/FVC: %

** DLCO-SB: (%) DLCO/VA: %

**VR L(%) **CPT L (%) **VR/CPT: %

**Gasometry: Basal/FiO2____ ph: pCO2 mmHg pO2: mmHg

*Prognostic scales:

**BODE:

**BODEx:

*Basal RMS: RMS EMG for PIM: mV EMG for VentVolMax mV

**Basal exercise:

Date:___/____/_____

Conditions: O2 per gn at lpm

Exercise protocol:

Total load: W

Maximum peak load; W

tcpCO2 initial

tcpCO2 media

tcpCO2 maximum

Initial SpO2

SpO2 average

Minimum SpO2

	1	5	10	15	20	25	30	35	40
BORG Dyspnea									
EVA Dyspnea									
NVU									
Vte									
RMS max									

End of visit 1, 10 minutes with constant load 10W:

Initial IPAP:_____ cmH2O Final IPAP:_____ cmH2O

Initial EPAP:_____ cmH2O Final EPAP:_____ CMH2O

Initial Trigger Ins: Final_____ Trigger Ins_____

Other changes:_____

**NV exercise 1:

Date:___/____/_____

Conditions: Respirator:_____ IPAP:_____ EPAP:_____

Tsub:____

O2 added:_____ lpm

Exercise protocol:

Total load: W

Maximum peak load; W.

tcpCO2 initial

tcpCO2 media

tcpCO2 maximum

Initial SpO2

SpO2 average

Minimum SpO2

	1	5	10	15	20	25	30	35	40
BORG Dyspnea									
EVA Dyspnea									
NVU									
Vte									
RMS max									

**High flow exercise:

Date:___/____/_____

Conditions: High nasal flow:_____ FiO2 flow_____

Exercise protocol:

Total load: W

Maximum peak load; W

tcpCO2 initial

tcpCO2 media

tcpCO2 maximum

Initial SpO2

SpO2 average

Minimum SpO2

	1	5	10	15	20	25	30	35	40
BORG Dyspnea									
EVA Dyspnea									
NVU									
Vte									
RMS max									