SUPPLEMENTARY INFORMATION

Energy Conservation Technique improves dyspnoea when severe COPD patients climb stairs: a randomised crossover study

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METHODS

Study design

This randomised, cross-over, single received approval from the ethics committee Est-I, Dijon, France (N° 2018/24). All eligible participants were given information regarding the study and had to provide written consent for participation.

Participants

Participants were recruited from patients attending our department for pulmonary rehabilitation. The inclusion criteria were: diagnosis of COPD in accordance with the GOLD recommendations and with functional dyspnoea (modified medical research council scale ≥2). The exclusion criteria were: being clinically unstable (defined as (pH <7.35, body temperature >38°C), having cardiovascular contraindications to exercise, any sequela from neurological pathology, a musculoskeletal problem that prevented stair-climbing, a risk of falls (history of 2 falls in the previous 12 months), or being incapable of climbing 6 flights of stairs in less than 15 minutes (verified during the baseline assessment).

Baseline Assessment:

The baseline assessment was carried out at the start of the pulmonary rehabilitation program and included the patient's disease history, anthropometric characteristics, medication, blood gasses, quality of life (St George's Respiratory Questionnaire), anxiety/depression (Hospital Anxiety Depression scale), functional dyspnoea (modified Medical Research Council Scale), functional capacity (6-min walk test) and pulmonary function test in accordance with the international recommendations of the American Thoracic Society/European Respiratory

society.[1,2] The stair-climbing test (6 flights, 108 steps) was carried out during the initial evaluation to check that the individual was capable of participating in the study.

Intervention

The intervention was carried out between 48 hours and 7 days after the baseline assessment. We chose to use a 6-flight stair-climbing task in order to determine if the ECT could help patients to achieve a difficult task. A ramp was available and patients were told that they could use it as they liked, whilst climbing and/or during the rests in both conditions. No advice was given to the patients regarding their breathing pattern/control, either before or during the tests

Outcome measures

Primary outcome

The primary outcome was end-of-task dyspnoea measured using the modified Borg scale (scale from 0-10, 0=no dyspnoea, 10=maximal effort). Dyspnoea was evaluated at the start of the task (bottom of the stairs) and the end of the task (top of the stairs). We used the following instructions proposed by Asha Hareendran et al. (Int J Chron Obstruct Pulmon Dis. 2012) [3] to educate patients in the use of the modified Borg scale:

« The Borg scale is used to help us understand the intensity or severity of your breathlessness. We will ask you to use this scale to rate the intensity of your breathlessness before, during, and after your exercise. Please review the scale to see the various levels from which you can choose. The top of the scale, "0 or nothing at all," means no breathlessness at all.

The bottom of the scale, "10 or maximal," means the most severe breathlessness that you have ever experienced or could imagine experiencing. »

During the task, the following question was asked: "please rate the intensity of your breathlessness on the Borg scale".

Secondary outcomes

Leg discomfort was measured at the end of the exercise using the modified Borg scale.

SpO_2 and HR were continuously recorded during the test using a Spirodoc© device (Medical International Research, Italy) and respiratory rate (RR) was measured using a respiratory polygraph (Embletta Gold© (Embla, USA).

Oxygen saturation of the vastus lateralis muscle (StO2) was measured by Near-infrared spectroscopy (NIRS) and was continuously recorded during the task (one measurement/second) (Portamon© (Artinis Medical Systems, Netherlands) (more information is provided in [4]).

For SpO_2, StO_2 and HR, the mean value of the last 10 seconds of the task were used for the analysis.

Minute ventilation (Ve) and inspiratory capacity (IC) were measured using the Spirodoc© (Medical International Research, italy) and capillary lactate was measured using the Lactate Pro 2© (ARKRAY Europe, Pays-Bas). These variables were measured at the beginning and end of the exercise.

The time taken to climb the 6 flights and the number of rests (defined as ≥ 10 seconds) were measured using the accelerometer in the Spirodoc© (Medical International Research, Italy). We arbitrarily decided that a rest time of 10 seconds or more would not be considered as a standardised rest but as a recovery rest.

Each participant was asked two questions at the end of the study:

1) "Which condition did you prefer?"
2) "In which condition did you feel the least breathless?"

Sample size estimation

22 participants were required to reject the null hypothesis with a power of 90% and an alpha risk of ≤ 0.05. A mean difference in dyspnoea of 2 points on the modified Borg scale, with a standard deviation of 2 points was expected between the conditions to have a large effect size.

Statistical analysis

A treatment effect test (adjusted for period), a period effect test (adjusted for treatment), and a test for the interaction between treatment and period were successively used to assess respective effect of treatments, treatment sequence, and the first-order carryover risk.

Parameter changes across the cross-over study were calculated by subtracting the baseline value from the value at the end of each period [5]: V2 minus V1 (= y1) and V4 minus V3 (= y2).

Group AB (condition A first): dA = y1 – y2

Group BA (condition B first): dB = y2 – y1

- Treatment effect test: dA + dB
- Order effect test : dA - dB
- Interaction test : [y1 + y2 (for group A)] – [y1 + y2 (for group B)]

Condition A : ECT

Condition B : self-paced

These three effects were analysed using a Student t test or a Mann-Whitney test according to the distribution of data. Changes within each of the conditions were compared using a paired t-test or a Wilcoxon test, depending on normality.

Results:

All the patients included completed both conditions. Of the 29 patients excluded, only 8 were unable to climb the 6 flights in less than 15 minutes, due to severe respiratory disease and functional incapacity. The other 21 patients had a restrictive syndrome (2 patients), were undergoing pre-operative rehabilitation for non-small cell lung cancer (13 patients), had pulmonary fibrosis (4 patients) or had bronchiectasis (2 patients).

There was no loss of data for dyspnoea (primary outcome). Missing data were for heart rate (2 patients), SpO_2 (2 patients), respiratory rate (2 patients), inspiratory capacity (2 patients), minute ventilation (1 patient) and vastus lateralis oxygenation (6 patients). The main causes of missing data were either device dysfunction during the test or signal loss during the test.

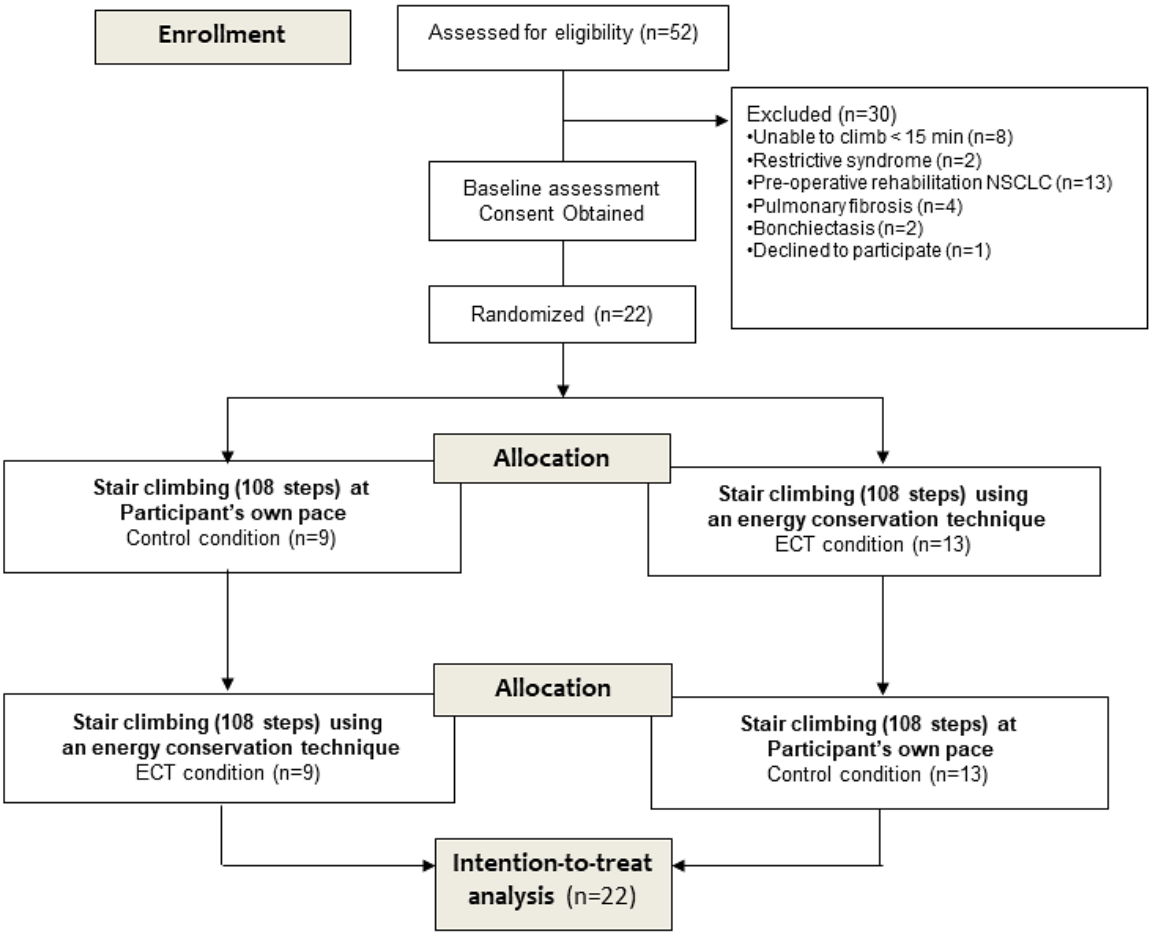
Additional comments on sample size estimation: the use of the difference in mean dyspnoea for the calculation of the sample size might have reduced the power of the non-parametric analysis. However, the non-parametric test carried out on the primary outcome produced a statistically significant result, thus suggesting there was no type-two error

TABLE

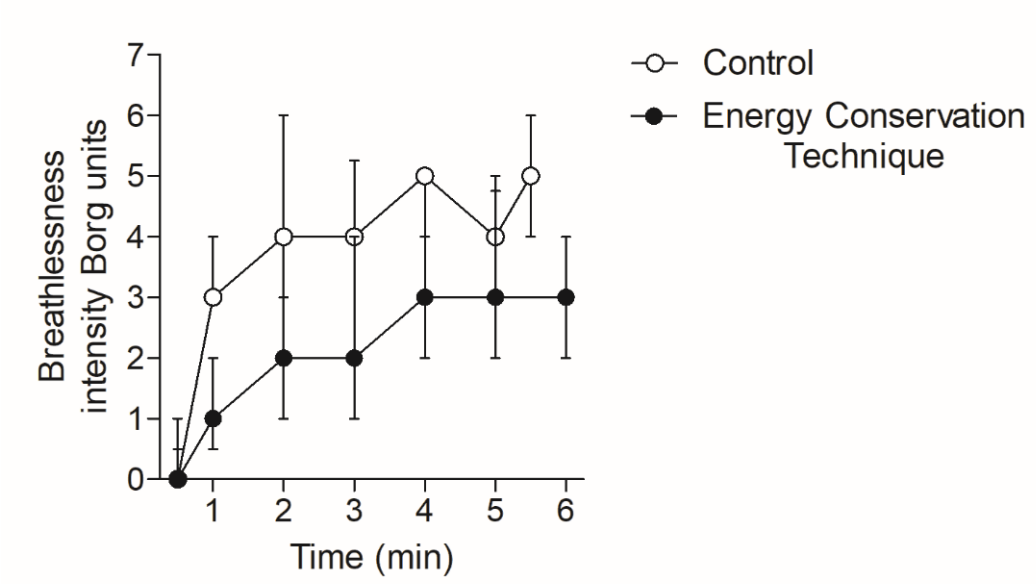
Supplementary table 1: p-values for carry-over effect (interaction between condition and order)

Variables	Carryover effect (interaction between condition and order), p-value
Breathlessness (mBorg)	0.63
Leg discomfort (mBorg)	0.97
SpO_2 (%)	0.72
StO_2 (%)	0.55
Heart Rate (bpm)	0.0480
Respiratory Rate (cpm)	0.38
Minute ventilation (L/min)	0.19
Inspiratory capacity (L)	0.65
Lactate (mmol/L)	0.45
Total task time (s)	0.0158
Total duration of breaks (s) (defined as break ≥ 10 s)	0.0533
Median Number of breaks	0.0410

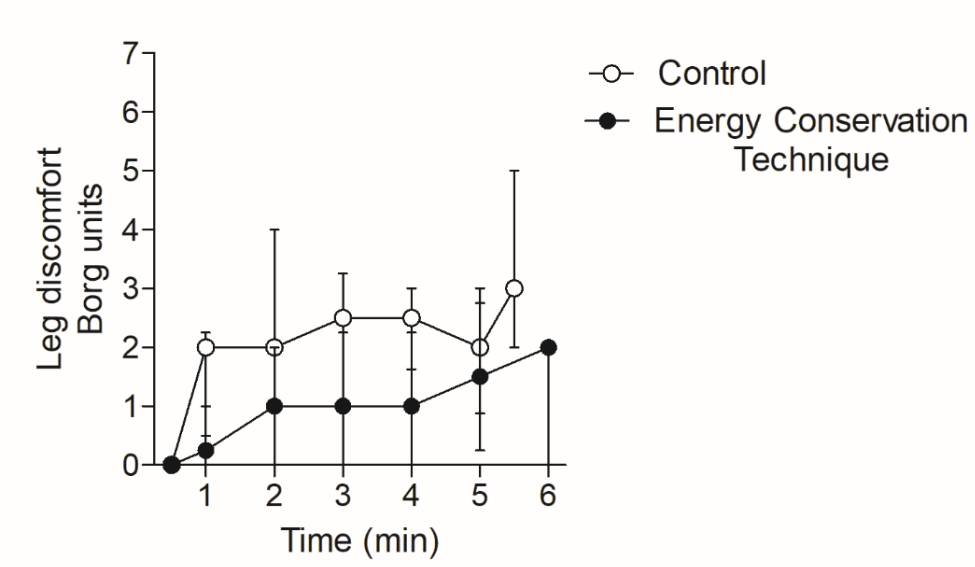
FIGURES



Supplementary Figure 1: CONSORT diagram of the study population.



Supplementary figure 2: Time course of breathlessness (each minute) in the energy conservation technique and control conditions during the ascension of 108 steps (6 flights). Data are presented as medians [25th;75th].



Supplementary figure 3: Time course of leg discomfort (each minute) in the energy conservation technique and control conditions during the ascension of 108 steps (6 flights). Data are presented as medians [25th;75th].

DATA SHARING

Question	Authors' Response
Will the data collected for your study be made available to others?	Yes
Would you like to offer context for your decision?	-
Which data?	Complete de-identified patient data set relevant for the purpose
Additional information about data	-
How or where can the data be obtained?	Email to gprieur.kine@gmail.com
When will data availability begin?	After publication
When will data availability end?	-
Will any supporting documents be available?	Yes
Which supporting documents?	French version of the patient information sheet, Informed Consent Form, blank CRFs
Additional information about supporting documents	-
How or where can supporting documents be obtained?	Email to gprieur.kine@gmail.com
When will supporting documents availability begin?	After publication
When will supporting documents availability end?	-
To whom will data be available?	Researchers whose proposed use of the data has been approved
For what type of analysis or purpose?	For any purpose
By what mechanism?	By a signed data access agreement
Any other restrictions?	-
Additional information	-

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