A comparison between two diagnostic tools to identify dynamic hyperinflation in COPD-patients : 1. Metronome-Paced hyperventilation with inspiratory capacity manoeuvres. 2. CPET with inspiratory capacity manoeuvres.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders NEC
Study type	Observational non invasive

Summary

ID

NL-OMON41187

Source
ToetsingOnline

Brief title
comparison DH by CPET and MPH

Condition

- Respiratory disorders NEC

Synonym
Chronic Obstructive Pulmonary Disease

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Centrum Leeuwarden
Source(s) of monetary or material Support: Geen;behalve deels uit de kosten;die door het ziekenhuis worden gemaakt in de vorm van loon voor de werken en leren situatie van de onderzoeker. Het leeuwendeel van deze inspanning echter zal in haar vrije tijd plaatsvinden. Verder wordt er geen materiaal verbruikt. De benodigdheden zijn bijzonder gering en voorhanden op de longfunctie afdeling.

Intervention

Keyword: COPD-patients, CPET, Dynamic hyperinflation, Metronome-Paced hyperventlation

Outcome measures

Primary outcome

difference between mean ICMPH and ICrestMPH resulting from MPH.

difference between mean ICCPET and ICrestCPET resulting from CPET.

Secondary outcome

Not applicable

Study description

Background summary

Chronic obstructive pulmonary disease (COPD) is a progressive, treatable disease characterized by not fully reversible airflow limitation. The main feature is airway inflammation, induced by noxious particles like smoke or burning fumes. The airway inflammation leads to structural changes in the airway walls and loss of elasticity of the lung parenchyma.
The changes have important consequences for the expiratory airflow. During exercise, limitation of expiratory airflow may induce dynamic hyperinflation, an increase in end-expiratoy lung volume that is associated with exercise limitation in COPD.
Measurements of dynamic hyperinflation are commonly taken during cardiopulmonary exercise testing (CPET). CPET, however, is complex and laborious and only performed in a clinical setting. The development of dynamic

hyperinflation, especially in patients with mild and moderate COPD, therefore may go unnoticed until considerable exercise limitations occur. With an accurate simple screening tool to detect dynamic hyperinflation in patients with COPD early interventions, such as optimal bronchodilation or exercise training, can be offered to allow patients to continue their activities and prevent deconditioning. Such a simple surrogate to exercise testing might be metronome-paced hyperventilation (MPH). Gelb e.a. (2004) showed that dynamic hyperinflation induced by breathing for 20s at twice the resting breathing rate was similar to dynamic hyperinflation after maximal exercise testing in 16 patients with moderate-to-severe COPD. In subsequent studies, MPH was used to investigate lung volume responses to bronchodilator use (Gelb 2007, 2009) and the behaviour of dynamic hyperinflation during 2-year follow-up (Hannink, 2010).
More recently Lahaije et al (2013) found a good overall accuracy (sens 85%, spec 85%) to identify subjects with COPD susceptible to develop dynamic hyperinflation during CPET (the gold standard).
In our observational study at the MCL (Leeuwarden), we would like to investigate, whether we could find the same diagnostic accuracy for dynamic hyperinflation of MPH, thereby confirming the value of MPH as a diagnostic tool in clinical practice and improving our diagnostic process in COPD with less effort of the patients.

Study objective

The purpose of this study is to compare the Metronome-Paced Hyperventilationtest (MPH) with cardiopulmonary exercise testing (CPET) in patients with COPD for detecting dynamic hyperinflation, thereby establishing the diagnostic accuracy for dynamic hyperinflation in COPD patients of the MPH. With the CPET with inspiratory capacity manoeuvres as the gold standard for establishing dynamic hyperinflation, we would like to determine diagnostic equivalence of MPH in our laboratory and our COPD population.

hypothesis: Dynamic hyperinflation(DH) in patients with COPD in CPET is not different from DH in MPH. DH will be assessed by inspiratory capacity manoeuvres and represented by delta-IC (*IC).

Study design

Patients with COPD sent for a cardiopulmonary exercise test for any reason by the pulmonologist will be asked to voluntary participate in this study. participants will perform MPH and subsequently CPET (cardiopulmonary exercise testing), both with IC manoeuvres. Based on CPET, subjects will be classified as hyperinflators or non-hyperinflators. In this observational study the diagnostic accuracy of MPH for dynamic hyperinflation will be investigated. Because CPET can be very exhausting, MPH, that is much easier te perform, will precede CPET in the same visit to the pulmonary function laboratory.

Metronome-paced hyperventilation test (MPH)
Subjects are seated, breathing through a mouthpiece connected to the spirometer. After a quiet and stable breathing pattern is obtained, baseline IC (ICrestMPH) will be determined by taking the mean of three acceptable manoeuvres. Then, a metronome is set at twice the resting breathing rate and subjects will be asked to breathe at this pace for 20 s, immediately followed by a maximal inspiratory manoeuvre (ICMPH). To test reliability of ICMPH, the procedure will be repeated after subjects have returned to their resting breathing level. In line wit the criteria for baseline IC manoeuvres, mean ICMPH will be calculated from three acceptable manoeuvres, within 10% of each other. MPH-induced dynamic hyperinflation (* ICMPH) will be calculated as the difference between mean ICMPH and ICrestMPH).

Cardiopulmonary exercise test (CPET)
All subjects will perform a symptom-limited incremental exercise test using an electrically braked cycle ergometer (Lode B.V., Lode Excalibur Sport, Groningen, The Netherlands). Subjects wear a leak-age-free face mask with a turbine flow transducer and a gas sampling tube (ZAN, zan100, Accuramed, Belgium).
Measurements are performed according to the American Thoracic Society/European Respiratory Society guidelines for CPET (2003). Reference equations for the calculation of predicted values are those produced by Wasserman.
Dynamic hyperinflation will be estimated by measuring changes in IC. While the subjects sit upright and relaxed on the bike, baseline IC (ICrestCPET) will be determined by measuring three maximal inspiratory manoeuvres from a position of passive end-tidal expiration. At peak exercise, IC will be measured (ICCPET) and dynamic hyperinflation (*ICCPET) is calculated as the difference between ICCPET en ICrestCPET.

Pulmonary function tests
All measurements will be performed according to the American Thoracic Society/European Respiratory Society guidelines for lung function measurements (Miller e.a., 2005, Wanger e.a., 2005). Reference equations for the calculation of predicted values are those produced by the European Community for Steel and Coal (Quanjer,1993) and predicted values for inspiratory capacity (IC) are calculated as predicted total lung capacity (TLC) minus predicted functional residual capacity (FRC).

Statistics
This is an observational study. CPET will be used as the gold standard procedure for assessment of dynamic hyperinflation.

For the analysis we postulate diagnostic equivalence between both tests if the difference of delta-IC of both tests is not larger than 10%. one-sided paired t-test and the 95% confidence interval of the difference of delta-IC of both tests will be determined.
Bland-Altman plot will be used for agreement between both tests, illustrating

the difference in amount of delta-IC measured by both methods in the full range of results.
ROC-analysis (receiver operator curve) will be performed for diagnostic accuracy of MPH.
Sensitivity and specificity will be calculated using a cross table.

sample size calculation: Number of participants: 110.
A sample size of 110 pairs with a correlation of 0.200 (conservative estimation) the two tests achieves 80% power to detect equivalence when the margin of equivalence is from -0.250 to 0.250 and the actual mean difference is 0.000.
The significance level (alpha) is 0.050 using two one-sided Paired T-Tests.
These results are based on 5000 Monte Carlo samples from the null distribution: Normal(M0 S) - Normal(M1 S) and the alternative distribution: Normal(M0 S) - Normal(M0 S).
As stated for this analysis we postulate diagnostic equivalence between both tests if the difference of delta-IC of both tests is not larger than 10%. From the paper of Lahaije et al, the delta-IC in the COPD population of 2.6 liter (SD 0.7 liter) is used in this calculation.

Because of the conservative estimation of the used correlation coefficient of 0.20 an interim analysis will be performed after 60 patients to verify the assumptions of the sample size calculation.

Statistics will be analyzed by an independent epidemiologist. SPSS (SPSS Chicago, IL, USA) will be used.

Study burden and risks

not applicable

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

-Age: * 18 years.
-Diagnosis of COPD, based on a post-bronchodilator forced expiratory volume in one-second/forced vital capacity ratio (FEV1/VC) -Co-morbidity or medication is no exclusion criterium.
-All patients give their informed consent before entering the study.

Exclusion criteria

-Age: < 18 years.
-Not able to perform the IC-manoeuver well.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-09-2014
Enrollment:	110
Type:	Actual

Ethics review

Approved WMO

Date:	02-09-2014
Application type:	First submission
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
Other	aangemeld bij NTR 31-8-14
CCMO	NL50155.099.14