Explaining the underlying factors of moderate to severe fatigue in patients with chronic obstructive pulmonary disease (COPD)

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To identify physical, systemic, psychological, and behavioural factors that precipitate and/or perpetuate fatigue in patients with clinically stable COPD and to identify the impact of exacerbation-related hospitalizations on fatigue and its...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Observational invasive

Summary

ID

NL-OMON53067

Source
ToetsingOnline

Brief title
FAntasTIGUE

Condition

- Bronchial disorders (excl neoplasms)

Synonym
Lung disease, pulmonary disease

Research involving
Human

Sponsors and support

Primary sponsor: CIRO

Source(s) of monetary or material Support: Astra Zeneca,Boehringer Ingelheim,Longfonds

Intervention

Keyword: COPD, Fatigue, Underlying factors

Outcome measures

Primary outcome

The primary outcome, fatigue, will be measured by the subscale subjective fatigue of the Checklist Individual Strength (Cis-Fat) (8 items, 7-point Likert scale). Patients will be asked to fill out this questionnaire at baseline, and at months 4, 8, 12, 18 and 24, and during non-elective hospitalizations.

Secondary outcome

Nijmegen and Maastricht:

Day-to-day/diurnal fatigue (Ecological Momentary Assessment (EMA)) (Sub sample, n= 60).

Socio-demographic factors:

- Gender;
- Age;
- Social-economic status (SES);
- Marital status;
- Survival status.

Physiological factors:

- Body mass index (BMI);

- Activity-related dyspnoea (modified Medical Research Council dyspnoea grade (mMRC));
- Symptoms checklist (Visual Analogue Scale (VAS));
- Lower-limb muscle function (MicroFET2 hand-held dynamometer);
- History of COPD-related exacerbations and hospitalizations in the previous year;
- Current pulmonary and non-pulmonary medication;
- Self-reported comorbidities (Charlson Comorbidity Index (CCI);
- Waist circumference;
- Peripheral artery disease (Huntleigh D900 Doppler 8Mhz probe);
- Mobility (Short Physical Performance Battery (SPPB));
- Handgrip muscle strength (JAMAR);
- Functional exercise capacity (two times a 6 Minute Walking Test (6MWT), combined with continuous monitoring of a patients* SpO2 and heart rate by the use of a pulse oximeter);
- A Bioelectrical Impedance Analysis (BIA);
- A lung function.

Psychological factors:

- Disease specific and generic health-status (Nijmegen Clinical Screening Instrument (NCSI));
- COPD status (COPD Assessment Test (CAT));
- Generic health status (EQOL-5D-5L (EQ-5D-5L));
- Symptoms of anxiety and depression (Hospital Anxiety Depression Scale (HADS));

- Cognitive status (Montreal Cognitive Assessment (MOCA));

- Grief (Acceptance of Disease and Impairments Questionnaire (ADIQ));

- Qualitative experience of fatigue (KWAMOE);

- Fatigue-related self-efficacy (Self-Efficacy-5);

- Catastrophizing (Jacobsen Fatigue Catastrophizing Scale);

- Fear of progression (Fear Of Progression Questionnaire);

- Activity Cognitions Instrument (ACI);

- Patient Activation Measure (PAM).

Behavioural factors:

- Smoking status;

- Alcohol consumption;

- Caffeine consumption;

- Objectified physical activity (ActiGraph GT3X, 3-axis activity monitor,

3.8x3.7x1.8cm);

- Sleep quality (Pittsburgh Sleep Quality Index (PSQI) en accelerometer);

- Drowsiness (Epworth Sleepiness Scale (ESS));

- Attributions (Causal Attribution List (CAL));

- Social impairments (Sickness Impact Profile (SIP));

- Social support (Social Support List, Interactions and Discrepancies (SSL-I,

SSL-D)).

Systemic factors:

- Venous blood sampling (hs-CRP, IL-6, TNF-alfa, IL-1-alfa, IL-1-beta, IL-1-RN,

IL-10, fibrinogen, leukocytes, cortisol, haemoglobin, glucose, thyroid function (TSH), renal function (creatinine), sodium, Potassium, calcium, magnesium, vitamine B12, vitamine 25(OH)D3, liver function (ASAT and ALAT), NT-pro-BNP, blood sediment, ANA and DNA).

Additional tests for patients from the Maastricht region:

- A resting cardiac echocardiography;

- A resting electrocardiogram;

- Retinal imaging to assess retinal microcirculation.

Study description

Background summary

Fatigue is increased in patients with COPD compared to healthy elderly. Moderate to severe fatigue occurs frequently in clinically stable COPD (30-70%), and fatigue is next to dyspnoea the most dominant symptom in COPD. So, fatigue is a common, distressing symptom in patients with COPD but goes often undiagnosed and untreated. The pathobiology of fatigue is complex and it is thought to be caused by a cascade of events. Currently, the underlying causes of fatigue in COPD have been studied scarcely.

Study objective

To identify physical, systemic, psychological, and behavioural factors that precipitate and/or perpetuate fatigue in patients with clinically stable COPD and to identify the impact of exacerbation-related hospitalizations on fatigue and its perpetuating factors. Thirdly, to better understand the association between fatigue and 2-year all-cause hospitalization and mortality in patients with COPD.

Study design

A two-year longitudinal, observational study has been designed. 260 patients with clinically stable COPD (GOLD A to D, no exacerbation/hospitalization <4 weeks) will be recruited at the outpatient clinic of the Departments of

Respiratory Medicine in Maastricht and the Department of Pulmonary diseases in Nijmegen, and from the RNFM, ZIO and nHP. In addition, patients who participated in the Chance Study (recruitment period 2012-2015, METC MUMC+ 11-3-070, NTR 3416), were recruited from primary or secondary care, and had indicated on the Informed Consent that they may be approached for follow-up research were invited to take part in the FAntasTIGUE study. Primary, secondary and explanatory outcomes will be assessed at various time points.

The primary outcome, fatigue, will be measured by the subscale subjective fatigue of the Checklist Individual Strength (Cis-Fat) (8 items, 7-point Likert scale). Patients will be asked to fill out this questionnaire at baseline, and at months 4, 8, 12, 18 and 24, as well as during non-elective hospitalizations and two weeks after discharge.

The secondary outcome is the day-to-day/diurnal variations of fatigue as measured in a subsample (n=60) with Ecological Momentary Assessment (EMA). EMA will be registered at baseline, and month 4, 8 and 12.

Other, explanatory outcomes are physical-, systemic-, psychological and behavioural factors (the precipitating and perpetuating factors of fatigue) that will be measured at baseline and at month 12. Also, when patients are admitted to the hospital between baseline and 12 months due to an exacerbation of COPD, some tests will be repeated during hospitalization, and two weeks after discharge.

Finally, at month 18 and 24 (6 months and 1 year after completion of the study) fatigue, number of exacerbations, exacerbation-related hospitalizations, and survival will be assessed.

Study burden and risks

There are no serious risks associated with participation in this study. The only minor injury that can occur is a hematoma from the venous blood sampling, which will heal within a few days. Besides the hematoma, patients may experience muscle fatigue and shortness of breath while performing the six minute walk tests. We will compensate for this by giving the patient sufficient time to rest before and after the exercise. At last, participation requires time investment (approximately 7 hours in total for the whole study).

Contacts

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CIRO

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

In order to be eligible to participate in this study, a subject must be diagnosed with COPD according to the Global Strategy for the Diagnosis, Management, and Prevention of COPD (GOLD), may not use oral corticosteroids and/or antibiotics for an acute exacerbation/infection and/or has an exacerbation-related hospitalization less than 4 weeks before enrolment, and must provide written informed consent.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
1. Lack of sufficient understanding of the Dutch language;
2. Unable to complete questionnaires because of cognitive impairment;
3. Participating in other interventionstudies.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-04-2018
Enrollment:	260
Type:	Actual

Ethics review

Approved WMO Date:	22-12-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-07-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-12-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-10-2020
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-03-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 23962
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL60484.100.17
OMON	NL-OMON23962

Study results

Date completed:	17-07-2023
Actual enrolment:	260