Systemic manifestation and co-morbidity in COPD are associated with circulating markers of aging

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Part I of the study: I) to determine if one or a batch of aging marker(s) is/are associated with the presence of objectively diagnosed COPD related co-morbidity (muscle wasting, osteoporosis, cardiovascular risk, glucose intolerance, renal failure,...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lower respiratory tract disorders (excl obstruction and infection)
Study type	Observational invasive

Summary

ID

NL-OMON39160

Source
ToetsingOnline

Brief title
COPD as a syndrome of accelerated aging

Condition

- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
COPD

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Nederland astma fonds

Intervention

Keyword: Aging, chronic obstructive, co-morbidity, inflammation, oxidative stress, pulmonary disease

Outcome measures

Primary outcome

Part I of the study: Markers of accelerated aging in blood, and objective outcomes of co-morbidity; Part II of the study: circulating hepatokines; Part III of the study: respiratory microbiome analysis.

Secondary outcome

Markers of systemic COPD phenotypes (markers of systemic inflammation and oxidative stress). The respiratory microbiome related to clinical characteristics.

Study description

Background summary

Chronic obstructive pulmonary disease (COPD) is currently generally recognized as a systemic disease with various extra-pulmonary features. There is currently considerable scientific interest in exploring the role and utility of biomarkers in insights in the outcome of COPD. Indeed, there is a need for biomarkers in COPD to better diagnose and assess the severity of the disease. Based on the parallelism between the manifestation of COPD and the process of aging, the aim of the present study is to investigate if COPD can be described as a syndrome of accelerated aging. Moreover, the underlying case for the elevated presence of co-morbidity (cardiovascular co-morbidity, diabetes, osteoporosis, muscle wasting, renal failure, metabolic syndrome and depressive symptoms) is not known yet. It is likely that the systemic consequences of the disease -systemic inflammation and oxidative stress- play a role in the pathogenesis. In addition, the contribution of the liver induced adipokines (hepatokines) to the extra-pulmonary manifestation of COPD will be investigated. With increasing age, respiratory infections become more frequent and severe. Colonization with respiratory pathogens, such as S. pneumoniae and H. influenzae seem to play an important role in this. More recently, it was

found the both COPD patients, as healthy subjects, have a rich respiratory microbiome, without symptoms of an infection, which is possibly related to disease progression and exacerbations in COPD patients. Part III of the study will focus on the respiratory microbiome of COPD patients, in comparison with that of control subjects.

Study objective

Part I of the study: I) to determine if one or a batch of aging marker(s) is/are associated with the presence of objectively diagnosed COPD related co-morbidity (muscle wasting, osteoporosis, cardiovascular risk, glucose intolerance, renal failure, metabolic syndrome and depressive symptoms) or systemic COPD phenotypes (systemic inflammation and oxidative stress) at baseline in a COPD population admitted for pulmonary rehabilitation; II) to determine if one or a batch of aging marker(s) can predict the presence of objectively diagnosed COPD related co-morbidity (muscle wasting, osteoporosis, cardiovascular risk, glucose intolerance, renal failure, metabolic syndrome and depressive symptoms) at baseline in a COPD population admitted for pulmonary rehabilitation; III) to determine if the change in aging markers over 2 years if different in patients with COPD compared to healthy subjects. Part II of the study: I) to determine if the hepatokines are associated with the extra-pulmonary manifestation of COPD (co-morbidity and systemic COPD phenotypes). Part III of the study: I) to define the respiratory microbiome of stable COPD patients and compare this with the respiratory microbiome of elderly smokers and non-smokers; II) to assess the microbial diversity of the respiratory microbiome of stable COPD patients and compare this with that of elderly smokers and non-smokers; III) to assess if there is a relationship between the respiratory microbiome and clinical characteristics of COPD patients (e.g. frequent exacerbations).

Study design

observational cross-sectional study with a longitudinal follow-up of two years.

Part I of the study: Participation includes two test days: Test day 1 at the Center of expertise for chronic organ failure (Ciro) Horn: in the fasted state, venous blood will be collected for the assessment of cardiovascular risk markers, glucose intolerance, markers of systemic inflammation and oxidative stress and the markers of accelerated aging. In total, about 50 ml venous blood will be collected, an amount which is not of clinical relevance. Also in the fasted state, urine will be collected, the electrocardiography and the pulse wave velocity will also be measured and the dual x-ray absorptiometry scan will be performed after emptying the bladder. After breakfast, a lung function measurement and measuring the waist circumference will take place, and the HADs questionnaire will be filled in. On the second day, all subjects will be invited to the MUMC+ for a high resolution computed tomography (HRCT) scan of

the thorax. As the measurement of the lung function and body composition are included in the assessment of the COPD patients, these tests do not have to repeated during participation of the test. The test days will be planned before the start of the rehabilitation for the COPD patients. Part II of the study: A subgroup of 50 patients with COPD and 50 healthy subjects, hepatokines will be analyzed during a second blood sampling during the second test day. Part III of the study: a subgroup of 70 COPD patients and 70 healthy subjects, throat swab and (induced) sputum will be collected at T1.

Study burden and risks

The performance of these tests are virtually without any risks. Blood sampling will occur by venapunction and a bleu spot may occur. However, subjects who are really frightened of blood sampling will be advised not to participate in the study. During the assessment of the cardiovascular risk, blood flow of the arm will be minimized for 5 minutes. This procedure can result in a tingling feeling of the arm that disappears after the occlusion. The radiation dose of the different scans (DEXA, HRCT) is very low and virtually without any risk. The risks associated with collecting spontaneous sputum is negligible. The risks associated with collecting induced sputum are dyspnoea, fear and cough. However, induced sputum is performed according to internationally accepted protocols, including frequent assessment of lung function in order to minimize risks.The control subjects will receive a health check including lung function measurements, body composition and cardiovascular risk assessment by participating the study. Although this is not direct benefit of the study, it may be interesting for the subjects to receive this information.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

For the COPD patients: diagnosis of COPD according to the American Thoracic Society (ATS) GOLD guidelines (FEV1 < 80% predicted and FEV1/FVC < 70% [18]; both male and female, age-range from 45 to 75 y; no respiratory tract infection or exacerbation of the disease for < 4 weeks before the study; capable of providing informed consent.
For the healthy subjects: subjects without the objectively diagnosed diseases assessed in the present study: COPD, untreated diabetes mellitus type II, severe and untreated osteoporosis, severe renal failure or heart failure. Both male and female, age-range from 45 to 75 y will be included in the study.

Exclusion criteria

For the COPD patients and controls: any kind of carcinogenic pathology <5 y before study participation; chronic use of oral corticosteroids > 10mg/day; participation in any other studies involving investigational or marketed products concomitantly or < 4 weeks prior to entry into the study, investigator's uncertainty about the willingness or ability of the subject to comply with the protocol requirements.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-12-2010
Enrollment:	800
Type:	Actual

Ethics review

Approved WMO Date:	20-10-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	01-12-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-12-2010
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	24-01-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	13-04-2011

Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-06-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-06-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	22-07-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-04-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	12-05-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
ISRCTN	ISRCTN86049077
CCMO	NL30806.068.10