Associations of circulating elastin degradation products (iso)desmosine with other blood biomarkers, CT-densitometry, arterial stiffness, lung function parameters, and copper in exhaled breath condensate

Published: 08-01-2019
Last updated: 11-04-2024

Evaluate whether CT lung densitometry and PWV associate with plasma DES concentrations. In addition, we want to determine whether certain other laboratory determinations in the blood and condensed exhalation vapor correlate with plasma DES.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON45757

Source
ToetsingOnline

Brief title
Correlation densitometry, pulse wave velocity and desmosine level

Condition

- Other condition
- Respiratory disorders NEC
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
COPD (chronic obstructive pulmonary disease), Emphysema

Health condition

Longparenchym: emfyseem

Research involving
Human

Sponsors and support

Primary sponsor: Canisius Wilhelmina Ziekenhuis
Source(s) of monetary or material Support: Chiesi Farmaceutici ,GlaxoSmithKline,R&D rekening Longartsen CWZ

Intervention

Keyword: Densitometry, Desmosine, Pulse wave velocity

Outcome measures

Primary outcome

Primary objective:

- Correlation of pDES level with CT-longdensitometrie

Secondary outcome

Secondary objectives:

- Correlation of pDES level with PWV

- Correlation of pDES level with lung function tests

- Correlation of pDES level with blood biomarkers

- Correlation of pDES level with copper concentration in exhalation vapor

condensate

- Correlation of pDES level with degree of vascular calcification at the site

of the carotid siphon artery

- Correlation of other biomarkers with each other, CT-lung densitometry, PWV,

lung function tests and degree of vascular calcification. the a. carotis siphon

Study description

Background summary

Chronic obstructive pulmonary disease (COPD) is a heterogeneous disease that is defined by the presence of a chronic airway obstruction. Multiple pathological mechanisms can be responsible for the development of COPD. Pulmonary emphysema is the COPD phenotype characterized by destruction of lung parenchyma caused by a protease / antiprotease imbalance resulting in accelerated degradation of elastin fibers.
The production of elastin fibers in the lungs takes place almost exclusively around birth [2022748]. The elastin precursor, tropoelastine, is first synthesized by different cell types and [1] tropoelastine monomers then fuse into polymers. The tropoelastine polymers are then cross-linked to mature elastin fibers [1] under the influence of the copper-dependent enzyme lysyl oxidase. During this crosslinking, desmosin and isodesmosin (jointly abbreviated as DES) are formed. In the process of elastin degradation, DES is released into the extracellular matrix, leaks into the bloodstream and is measurable in the plasma (pDES). The height of pDES reflects the activity of the elastin degradation process. In disorders characterized by accelerated elastin degradation, such as COPD, the pDES concentration is increased [2].
Currently, pulmonary lungfunction tests form the basics in diagnostics and follow up in COPD. Last past years, densitometry measurement using CT scan has become a reliable method to quantify the degree of destruction of the lung parenchyma, or the degree of emphysema [4]. The density of the lung tissue is calculated and compared with the density of healthy lung tissue. We expect that there is a correlation between the height of the pDES and the degree of lung destruction measured with densitometry and lung function tests.
Elastin is not only found in the lungs but in all dynamic tissues of the body and therefore also in the cardiovascular system. The degradation of elastin leads to damage to the blood vessels and therefore to an increased risk of cardiovascular morbidity and mortality [3]. Arterial stiffness is increased in COPD patients and is correlated with the severity of emphysema [5]. The vessel stiffness can be reflected by the Pulse Wave Velocity (PWV). This is a measurement method in which the pulse wave of the a.carotis and the pulse wave of the a.femoralis are measured. The time difference between the two waves gives information about the elasticity of the aorta. This is a good predictor for cardiovascular morbidity and mortality. Since elastin degradation leads to an increase in arterial stiffness, we expect that there is a correlation between the height of pDES and the PWV.
In addition to correlating pDES with the degree of loss of elasticity in the pulmonary and vascular compartment, we also want to try to identify biomarkers that influence the pDES content. The ultimate goal is to investigate whether it is possible to favorably influence these biomarkers in order to reduce the rate of elastin degradation. Decreasing the elastin degradation rate could have a

beneficial effect on disease progression in COPD. An earlier study by us showed that vitamin K is inversely correlated with pDES. It is possible that improving vitamin K status by vitamin K supplementation would also decrease pDES. In the present study, we also want to investigate the influence of substances other than vitamin K, such as phosphate, magnesium and copper, on pDES. We also want to investigate whether copper, as an essential factor of lysyl oxidase, is lowered in the lungs, as we suspect, and whether copper in exhalation vapor is correlated with pDES and CT lung densitometry.

Study objective

Evaluate whether CT lung densitometry and PWV associate with plasma DES concentrations. In addition, we want to determine whether certain other laboratory determinations in the blood and condensed exhalation vapor correlate with plasma DES.

Study design

Descriptive cross sectional study

Study burden and risks

Niet van toepassing.

Contacts

Public
Canisius Wilhelmina Ziekenhuis

Weg door Jonkerbos 100
Nijmegen 6532SZ
NL
Scientific
Canisius Wilhelmina Ziekenhuis

Weg door Jonkerbos 100
Nijmegen 6532SZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- COPD Gold I-IV with emphysema on CT thorax
- Willful patient
- Age 18-75 years
- COPD set according to the GOLD criteria; FEV1 / FVC ratio <0.7,
- history of nicotine abuses> 10 pack / years
- Radiologically determined emphysema
- Able to undergo a CT scan
- Able to undergo lung function examination
- Prepared to prick blood
- Able to undergo respiratory condensate collection

Exclusion criteria

- Unstable cardiac situation
- (active) malignancy
- Interstitial lung disease
- Status after lung surgery (lobectomy/pneumonectomy)
- Pregnancy
- Alpha-1 antitrypsin deficiency (MZ is allowed, but PI*ZZ, PI*Z/zero and PI*zero/zero is not allowed)

Study design

Design

Study type: Observational invasive
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-12-2019
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	08-01-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-05-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-09-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
CCMO	NL66498.091.18