Breatheomics of mechanically ventilated intensive care patients.

Gepubliceerd: 11-02-2011 Laatst bijgewerkt: 18-08-2022

We hypothesize VOC signatures to discriminate between critically ill patients: 1. With and without sepsis; 2. With or without pneumonia; 3. With a gram positive or gram negative infection; 4. With and without organ failure, including: A. Acute...

Ethische beoordeling	Niet van toepassing
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON26899

Bron
Nationaal Trial Register

Verkorte titel
BREATHEOMICS

Aandoening

SIRS and sepsis and critical illness related organ failure

Ondersteuning

Primaire sponsor: Academic Medical Center, Amsterdam
Overige ondersteuning: Academic Medical Center, Amsterdam

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

1. Breathprints obtained by electronic nose (Cyranose and ContiNose);

2. Specific VOCs detected by GC-MS.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale:

Critically ill patients frequently develop secondary infections and/or failure of one or more vital organs during their stay in the intensive care unit (ICU). Secondary infections and multiple organ failure (MOF) are both associated with increased morbidity and mortality. Early recognition of secondary infections could allow for early initiation of antimicrobial therapy. Early recognition and adequate phenotyping of MOF could allow for early and targeted measures to prevent further injury to the organs.
Exhaled human breath contains thousands of volatile organic compounds (VOCs) in gas phase. Electronic noses (eNose) produce breathprints based on VOCs using an array of different sensors. Subsequently, these breathprints can be analyzed and used for diagnostic purposes.

Objective:

To determine whether exhaled air analysis can be a useful addition to the contemporary diagnostic tools in critically ill patients on the intensive care.

Hypothesis:

We hypothesize VOC signatures to discriminate between critically ill patients:

1. With and without sepsis;

2. With or without pneumonia;

3. With a gram positive or gram negative infection;

4. With and without organ failure, including:

A. Acute lung injury (ALI);

B. Acute kidney injury (AKI);

C. Acute liver failure;

D. Disseminated intravascular coagulation (DIC).

5. During organ failure vs. after organ failure;

6. With pulmonary edema based on ALI vs. – based on cardiac dysfunction.

We hypothesize VOC signatures to reflect:

1. Changes in systemic levels of biomarkers of systemic inflammation and organ failure;

2. Changes in local levels of biomarkers of pulmonary inflammation;

3. Changes in pulmonary microbiome;

4. Changes of specific VOCs in exhaled breath.

eNose measurements:

To perform measurements, the connector will be attached to the electronic nose (Cyranose 320, Smith Detections, Pasadena, Ca, USA), a handheld portable chemical vapor analyzer, containing a nanocomposite sensor array with 32 polymer sensors. Measurements will be taken for 60 seconds, in duplicate. The eNose will be purged and the control measurement will be made with ambient air in the patient's room. The raw data (changes in electrical resistance of each of the 32 sensors) will be stored in the onboard database, copied into an offline database to be used for further analysis with offline pattern-recognition software. Data from every first measurement will be disregarded in the analysis because of deviant raw data. This phenomenon is referred to as 'first sniff effect' by the manufacturer. In addition, continuous air sampling will be performed with a newly developed sensor array allowing real time monitoring (Comon Invent, Delft).

VOC detection:

Detection of individual VOCs will be done by gas-chromatography and mass-spectrometry (GC-MS) in subsets of patients. Specific VOCs in exhaled breath will be assessed by sampling two liter of gas from the connector onto adsorption tube filled with Tenax GR. Air flow will be limited to 100ml/min for 20 minutes using an air flow controller (EGE LD 550). These Tenax tubes will be shipped to Philips Research in Eindhoven, The Netherlands. There, the analytes are collected in a cryo-trap for re-focusing and subsequently injected into a gas chromatography column (HP 5890 series II) and identified by mass spectrometry (HP 5972

MSD), using a calibration mixture to check average sensitivity.

Timeline:

Breathprints will be obtained on day 0, 1 and 2, at the start and end of organ failure, every day during a sepsis/SIRS episode in patients included in the BASIC study (prospective observational study about the dynamics of biomarkers and pathogen growth) and before detubation.

VOCs are absorbed on tenax tubes for transport and subsequent GC-MS analysis on day 0, at the start of organ failure and sepsis and before detubation.

Analysis:

The analysis will follow the recommendations for establishing diagnostic accuracy and will be done according to the STARD Guidelines. Raw sensor data are presented as a relative resistance change (defined as ÄR/R) for each of the 32 sensors. Data will be analyzed with SPSS, version 15.0 (SPSS Inc., Chicago, IL, USA). A p-value < 0.05 will be considered to reflect significant differences.

Analysis consists of both Principal Component Analysis (PCA) and Canonical Discriminant Analysis (CDA). PCA reduces the initial data set to a set of principal components that capture the greatest variance of the original 32 sensors. Discriminating principal components are selected by means of One-way ANOVA. These principal components are subsequently used in a linear CDA, to minimize within-group variance and maximize between-group distance. This statistical analysis disregards the clinically defined research groups and creates a 'hypothesis-free' division of the acquired smell-prints. The Cross Validation Accuracy (CVA) will be calculated with the 'leave-one-out' method by creating a predictive algorithm on basis off all but one of the subjects. This algorithm is subsequently used to classify the excluded subjects in one of the categories created by CDA. This process is repeated until every subject has been excluded once from the classifying algorithm. The CVA is expressed as a percentage that is indicative of the amount of conformity between the clinically formed groups and the groups that are calculated on basis of CDA. Post-hoc testing of the selected principal components will provide a p-value, for the algorithm used for discrimination, which is indicative of its significance.
The subjects used for validation will be presented to the classifying algorithm. The percentage of correctly identified subjects will provide us with the sensitivity, specificity, negative and positive predictive value for this algorithm using ROC-analysis.

The data derived from GC-MS will be compared between groups by specific peak signal analysis as well as unselective broad spectrum analysis using PCA and CDA. Diagnostic accuracy will be assessed by strictly following the STARD-guidelines. This includes adequate

training and validation sets, and recommended statistical strategies to avoid falsely-positive results.

Doel van het onderzoek

We hypothesize VOC signatures to discriminate between critically ill patients:

1. With and without sepsis;

2. With or without pneumonia;

3. With a gram positive or gram negative infection;

4. With and without organ failure, including:

A. Acute lung injury (ALI);

B. Acute kidney injury (AKI);

C. Acute liver failure;

D. Disseminated intravascular coagulation (DIC).

5. During organ failure vs. after organ failure;

6. With pulmonary edema based on ALI vs. – based on cardiac dysfunction.

We hypothesize VOC signatures to reflect:

1. Changes in systemic levels of biomarkers of systemic inflammation and organ failure;

2. Changes in local levels of biomarkers of pulmonary inflammation;

3. Changes in pulmonary microbiome;

4. Changes of specific VOCs in exhaled breath.

Onderzoeksopzet

Breathprints will be obtained on day 0, 1 and 2, at the start and end of organ failure, every day during a sepsis/SIRS episode in patients included in the BASIC study (prospective observational study about the dynamics of biomarkers and pathogen growth) and before detubation.

VOCs are absorbed on tenax tubes for transport and subsequent GC-MS analysis on day 0, at the start of organ failure and sepsis and before detubation.

Onderzoeksproduct en/of interventie

N/A

Contactpersonen

Publiek

Academic Medical Center, Room G3-228
Meibergdreef 9
Lieuwe D.J. Bos
Amsterdam 1105 AZ
The Netherlands
+31 (0)20 5666345

Wetenschappelijk

Academic Medical Center, Room G3-228
Meibergdreef 9
Lieuwe D.J. Bos
Amsterdam 1105 AZ
The Netherlands
+31 (0)20 5666345

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Intubation and mechanically ventilation and an expected ICU-stay > 24 hours.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Age < 18 years;

2. Expected pregnancy.

The following patients will be measured but are excluded from primary analyses:

3. Known chronic pulmonary condition, detectable by electronic nose (asthma, pulmonary malignancy, tuberculosis, cystic fibrosis);

4. Admitted to another ICU in the last 7 days.

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm

Controle: N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-01-2011
Aantal proefpersonen:	1500
Type:	Verwachte startdatum

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL2622
NTR-old	NTR2750
Ander register	METC AMC : 10.17.0729
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A