Breatheomics of mechanically ventilated intensive care patients.

No registrations found.

Ethical review	Not applicable
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON26899

Source
NTR

Brief title
BREATHEOMICS

Health condition

SIRS and sepsis and critical illness related organ failure

Sponsors and support

Primary sponsor: Academic Medical Center, Amsterdam
Source(s) of monetary or material Support: Academic Medical Center, Amsterdam

Intervention

Outcome measures

Primary outcome

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

2. Specific VOCs detected by GC-MS.

Secondary outcome

1. Sepsis and probability of infection;

2. Organ failure;

3. Systemic biomarkers of inflammation, coagulation, organ failure, etc;

4. Pulmonary biomarkers of inflammation, coagulation, etc;

5. Pulmonary microbiome.

Other:

General demographical, clinical and physiological data are collected for calculation of acute physiology, age and chronic health (APACHE) II and III scores, simplified acute physiology scores (SAPS) II, and sequential organ failure assessment (SOFA) scores. Daily laboratory include WBC & differentials, platelet counts, creatinine, ASAT, ALAT, glucose, PT, aPTT, and lactate. Infections on admission and during stay on the ICU are recorded. Outcome data include duration of mechanical ventilation, length of stay in ICU and hospital, and 30–day -, 90–day - and 1–year mortality.

Study description

Background summary

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.

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Study design

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Intervention

N/A

Contacts

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Eligibility criteria

Inclusion criteria

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

Exclusion criteria

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.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non controlled trial

Control: N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-01-2011
Enrollment:	1500
Type:	Anticipated

Ethics review

Not applicable
Application type: Not applicable

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
NTR-new	NL2622
NTR-old	NTR2750
Other	METC AMC : 10.17.0729
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A