Researching the Effects of Sepsis on Quality Of life, Vitality, Epigenome and gene expression during RecoverY from sepsis (REQOVERY)

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To study the long-term changes in DNA methylation and gene expression in sepsis survivors and their association with long-term morbidity and mortality after sepsis.

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

Summary

ID

NL-OMON50782

Source
ToetsingOnline

Brief title
REQOVERY

Condition

- Other condition
- Infections - pathogen unspecified

Synonym
sepsis

Health condition

sepsis

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: epigenetic, post-sepsis syndrome, recovery, transcriptome

Outcome measures

Primary outcome

The primary objective of the current project is to measure changes in DNA methylation (i.e. epigenetics) and gene expression (i.e. transcriptomics) of blood leukocytes between sepsis survivors at ED admission and three months after hospital discharge.

Secondary outcome

The secondary objectives are to correlate these changes with DNA methylation and gene expression with clinical data of sepsis survivors including post-sepsis syndrome symptoms (e.g. cognition, neuropsychiatric symptoms, quality of life), cytometric and biochemical parameters that assess organ function, rehospitalization frequency, and mortality, as well as the soluble proteome and metabolome in blood to explore regulatory mechanisms. Lastly, we will compare the DNA methylation and gene expression profile with the age and sex-matched control group.

Study description

Background summary

Sepsis is a life-threatening dysregulated immune response to infection associated with multi-organ failure and a high mortality rate.While researchers have focused mainly on acute sepsis, post-sepsis care of survivors has long been neglected despite the observation that many sepsis survivors suffer from debilitating post-sepsis syndrome.This syndrome is characterized by frequent hospital readmissions and increased mortality due to persistent immune dysfunction, cardiovascular disease, and cognitive impairment, causing poor quality of life and a substantial burden on the healthcare system. Disconcertingly, the number of sepsis survivors at risk for hospital readmission continues to rise. Of the post-sepsis symptoms, post-sepsis immunosuppression is perhaps the most clinically important. While sepsis presents as an initial phase of hyperinflammation (a *cytokine storm*), it is followed by an immunosuppressive phase that is now understood to last weeks to months and predisposes survivors to lethal secondary infections and sepsis recurrence. A third of deaths eight years post-sepsis are caused by recurrent sepsis. We hypothesize that changes in the transcriptome and DNA methylome in immune cells of survivors might be the underlying driver for prolonged immunosuppression, and may also be correlated with long-term morbidity and mortality post-sepsis, as well as other symptoms of post-sepsis syndrome including PTSD and cardiovascular disease.

Study objective

To study the long-term changes in DNA methylation and gene expression in sepsis survivors and their association with long-term morbidity and mortality after sepsis.

Study design

Observational longitudinal study with three-month follow up.

Study burden and risks

Participants already donated blood through a (minimally invasive) venipuncture during their stay in the hospital for the Acutelines study. They will be asked to donate blood as well after three months of hospital discharge. Control subjects do not have to give blood after three months, as only the blood from hospitalization will be used. To collect blood during follow-up, the study participant will travel to the hospital where they will receive additional clinical follow-up and treatment of possible comorbidities, which can be seen as a minor benefit of joining this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Inclusion criteria sepsis group:
- Adult patients, aged between 18 and 85 years
- Able to provide informed consent themselves or informed consent can be obtained via next of kin or legal guardian
- Included in Acutelines, where blood sample were was drawn within 24 hours upon of ED admission according to Acutelines protocol
- Satisfy the Sepsis-3 criteria for sepsis (Figure 2), combined with clinical suspicion of infection and/or fever (body temperature > 38.5°C)
- Survive at 3 months post discharge

Inclusion criteria control group: adult patients, aged between 18 and 85 years
- Able to provide informed consent themselves or informed consent can be

obtained via next of kin or legal guardian
- Included in Acutelines, where blood sample was drawn upon ED admission
- Non-infectious reason of admission, specifically syncope, electrolyte disturbance, intoxication, gastro-intestinal bleeding, undifferentiated complaints

Exclusion criteria

- Transfer from another hospital
- Emergency room visit in connection with accidental exposure of bodily material to patient ("needle stick injury")
- Visit an emergency room in connection with organ transplantation
- Discharged home without hospital admittance after ED visit
- Unable to give blood
- Immunosuppressive therapies such as corticosteroids (>10mg) or small molecule immune suppressants within the last three months, or biologicals administered within the last year
- Radiotherapy or systemic chemotherapy within the last three months
- Known pregnancy; the presence of pregnancy will be verified by asking the potential participant
- A hospitalization of more than 21 days

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	08-10-2021
Enrollment:	120

Type:	Actual

Ethics review

Approved WMO Date:	23-06-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL76827.042.21