COVID-19 patients with severe or fatal outcome have a pre-existing state of immune-aging; exploring determinants of disease

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To assess whether premature aging of both the innate and adaptive arms of theimmune system are associated with COVID-19 morbidity and mortality. Identify immune (andendocrine) parameters that might be of use in predicting disease progression and...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Endocrine and glandular disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON55094

Source
ToetsingOnline

Brief title
Pre-existing immune-aging in COVID-19

Condition

- Endocrine and glandular disorders NEC
- Immune disorders NEC
- Respiratory tract infections

Synonym
corona virus, COVID-19

Research involving
Human

Sponsors and support

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

Intervention

Keyword: ACE-2, COVID-19, Immune-aging

Outcome measures

Primary outcome

Cellular immune parameters

- Extensive immunophenotyping of T-lymphocyte maturation subsets, including recently thymic emigrants

- Extensive immunophenotyping of B-lymphocyte maturation subsets

- Extensive immunophenotyping of monocyte maturation subsets

- SARS-CoV-2 specific CD8+ T cell response using immunodominant peptides that are shared between SARS-CoV and SARS-CoV-2.

Molecular immune parameters

- Immune repertoire (T-cell receptor and B-cell receptor) sequencing, including replication history

- Gene expression profiles related to premature immunosenescence in monocytes

- HLA-typing

Serological immune parameters

- Cytokines, for instance:

CCL2/CCL3/CCL4/CCL7/CXCL10/FASL/G-CSF/Galectin-9/GM-CSF /IFN*/IFN*/

IL-1b/IL1Ra/IL-6/IL-7/IL-8/IL-10/Il-12/IL-18/sCD163/sCD206/sIL2R/sIL6R/TNF*

- Autoantibodies, for instance: ANA/ANCA/ anti-thyroid/anti-adrenal

Serological hormonal parameters

Hormonal axis; pituitary-growth hormone axis, pituitary-thyroid axis,

pituitary-adrenal axis, pituitary-thyroid axis and sex hormone axis

Insulin/glucose ratio

Lepthin-ghrelin-adipokines

Secondary outcome

Additional genetic analysis

Exome sequencing and gene expression profiles to analyze the involved pathways

obtained from cytokine analysis, (for example IL-6 pathway associated genes and

ACE-2 associated cytokine-receptors that are shed from the plasma membrane)

Study description

Background summary

A proper functioning immune system is crucial for clearance of acute viral infections. Ageing and obesity negatively affect immune functioning and aged or obese humans display an insufficiently strong/delayed immune response upon viral infection. We hypothesize, that patients that develop severe or fatal COVID-19 have a pre-existing state of immune-ageing that prevents the initiation and maintenance of a proper immune response against SARS-CoV2.

Study objective

To assess whether premature aging of both the innate and adaptive arms of the immune system are associated with COVID-19 morbidity and mortality. Identify immune (and

endocrine) parameters that might be of use in predicting disease progression and facilitate
optimal treatment choice.

More specific objectives
We want to determine:
(i) whether signs of pre-existing ageing of the peripheral blood T-cell and B-cell compartment
are related to COVID-19 morbidity and mortality
(ii) whether signs of pre-existing ageing of the peripheral blood monocyte compartment are
related to COVID-19 morbidity and mortality
(iii) whether certain serological cytokine/autoantibody/hormonal profiles are indicative of an
altered immune set-point and related to COVID-19 morbidity and mortality

Study design

A: comparative, non-randomized, observational, multi-center study
B: Observational cohort

Na-Heparin blood and serum will be obtained at the emergency department/intensive care unit and patient stratification will be applied (see below). From hospital admitted non-ICU and hospital admitted ICU patients longitudinal samples obtained once weekly will be collected. Heparin blood will be used for different types of cellular and molecular analysis, see below. Serum will be used for extensive cytokine, autoantibody and hormonal profiling.

Study burden and risks

Risks are negligible, burden is low

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

Suspected of COVID-19
Age * 18 years
Providing informed consent after reading patient information

Exclusion criteria

Insufficient knowledge of Dutch
No signed informed consent

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:	Recruiting
Start date (anticipated):	10-03-2021
Enrollment:	152
Type:	Actual

Ethics review

Approved WMO Date:	18-06-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-11-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL73846.078.20