

COVID-19 and ischemic stroke - how to tame a dozing monster

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(1) Determine the prevalence of (asymptomatic) silent brain infarcts among patients with COVID-19 admitted to after discharge (at least

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Central nervous system vascular disorders
Study type	Observational invasive

Summary

ID

NL-OMON50979

Source

ToetsingOnline

Brief title

CORONIS

Condition

- Central nervous system vascular disorders
- Embolism and thrombosis

Synonym

brain infarct, Ischemia

Research involving

Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: COVID-19, Ischemic stroke, Observational study

Outcome measures

Primary outcome

- (1) The prevalence of (asymptomatic) silent brain infarcts among COVID-19 patients admitted to or discharged from the hospital (at least <3 months after positive PCR) and healthy (matched) controls without (previous) COVID-19 infection from the general population
- (2) Potential risk factors of brain infarcts, including presence of PFO, presence of cardiac arrhythmia, routine cardiovascular biomarkers, biomarkers of inflammation and coagulation, markers of cerebral small vessel disease and extra- and intracranial arterial wall enhancement on brain MRI,
- (3) Functional performance at 3 and 12 months after the day of admission in COVID-19 patients with and without brain infarcts, including the Hospital Anxiety and Depression Scale (HADS), Post-COVID-19 Functional Status (PCFS) and Modified Rankin scale (MRS)
- (4) Incidence of (new) silent brain infarcts after 3 months of follow-up in COVID-19 patients with and without brain infarcts.

Secondary outcome

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Study description

Background summary

Coronavirus disease 2019 (COVID-19) pneumonia is complicated by a high risk of thrombotic complications, occurring with an incidence of 41% in intensive care unit (ICU) patients and up to 9.2% at the general ward. These thrombotic complications are strongly associated with poor clinical outcome and death. In addition to pulmonary embolism, the most common complication, an increase in the number of ischemic strokes is reported. The magnitude, cause(s) and impact of this problem are currently unknown. We hypothesize that these ischemic strokes are either caused by intensive coagulation-induced (local) thrombosis and intracranial vessel wall inflammation, and/or are the result of a paradoxical embolism through a patent foramen ovale (PFO). Furthermore, in view of the intense procoagulant and proinflammatory COVID-19 response, we hypothesize that, in addition to symptomatic ischemic stroke, associated with a clear neurological deficit, COVID-19 patients are at risk of *clinically silent* ischemic brain lesions, which may reduce the chance of good recovery and return to functional independence.

Study objective

- (1) Determine the prevalence of (asymptomatic) silent brain infarcts among patients with COVID-19 admitted to or after discharge (at least <3 months after positive PCR test) from the hospital, compared with healthy controls.
- (2) Investigate risk factors of brain infarcts (symptomatic or asymptomatic)
- (3) Establish functional outcomes after 3 and 12 months in COVID-19 patients with and without brain infarcts (symptomatic or asymptomatic)
- (4) Establish incidence of (new) silent brain infarcts after 3 months in COVID-19 patients with and without brain infarcts (symptomatic or asymptomatic) at baseline examination

Study design

CORONIS is an observational multicentre study.

- (1) In a cross-sectional analysis, we will determine the prevalence of (asymptomatic) silent brain infarcts via brain MRI among COVID-19 patients admitted to or after discharge (at least <3 months after positive PCR) from the hospital and in healthy (matched) controls without (previous) COVID-19 infection from the general population.
- (2) In a case-control analysis we will investigate risk factors of brain ischemia. Cases represent COVID-19 patients with (symptomatic or asymptomatic) brain infarcts. Controls represent COVID-19 patients without any brain infarcts on MRI.
- (3) In a follow-up cohort study, we will determine the functional outcome at 3 and 12 months in COVID-19 patients with and without brain infarcts (symptomatic or asymptomatic).
- (4) In a follow-up cohort study, we will determine the incidence of new (asymptomatic) silent brain infarcts 3 months after baseline MRI in COVID-19

patients with and without brain infarcts (symptomatic or asymptomatic).

Study burden and risks

The healthy participants (controls) undergo a standardised MRI protocol.

The COVID-19 patients undergo a standardised MRI protocol, plus a contrast MRI to assess extra- and intracranial arterial wall enhancement, transthoracic bubble contrast echocardiography to identify PFO, venapuncture for blood sampling, a short cognitive screening and a questionnaire to examine lifestyle. In addition, patients will receive a Holter to monitor heart rhythm for a period of 72 hours. At month 3 and 12-24, through a telephone interview functional outcome will be measured.

All measurements are routinely applied in clinical practice. MRI is considered to be safe and without risks, as long all safety measures are adequately followed. For contrast-MRI a gadolinium-based contrast agent will be used. Side effects of injection of this contrast agent occur very incidentally and include mild effects such as nausea, headache and injection site reactions (sense of warm feeling). In case of adverse effects, patients will be treated reasonably and professionally. Similarly, transthoracic bubble contrast echocardiography is considered to be safe and harmless to subjects and is associated with only minor side effects, which occur very rarely. Collectively, we expect the physical or psychological burden to be low and classify the risk of study participation as negligible.

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

age $\geq$ 18 years

For the COVID-19 patients: admitted to discharged from the hospital because of COVID-19 from the start of the outbreak

Exclusion criteria

MRI contraindication and/or post COVID-19 disability interfering with MRI acquisition

Renal function eGFR $\leq$ 30 ml/min (for contrast-MRI)

Pregnancy at study entrance

Limited life-expectancy ($<$ 3 months)

Major disease interfering with study participation or follow-up

Not able to give 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:	Basic science

Recruitment

NL	
Recruitment status:	Recruiting
Start date (anticipated):	14-04-2021
Enrollment:	330
Type:	Actual

Ethics review

Approved WMO	
Date:	01-04-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	
Date:	15-07-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	
Date:	14-04-2022
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

CCMO

ID

NL75780.091.20