Platelet RNA as Biomarker for Delayed Cerebral Ischemia in Subarachnoid Hemorrhage

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

Summary

ID

NL-OMON55603

Source
ToetsingOnline

Brief title
Biomarkers in Subarachnoid Hemorrhage

Condition

- Central nervous system vascular disorders

Synonym
hemorrhage in the subarachnoid space, stroke

Research involving
Human

Sponsors and support

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

Intervention

Keyword: aneurysmal subarachnoid hemorrhage, biomarker, delayed cerebral ischemia, platelet RNA

Outcome measures

Primary outcome

The difference in blood platelet RNA-profile between the study population and

the control groups

Secondary outcome

the predictablity of functional outcome in mRS based on blood platelet

RNA-profiles

Study description

Background summary

Subarachnoid hemorrhage (SAH) is a relatively rare subtype of hemorrhagic stroke with a devastating outcome. The mortaity of 32-39% and a permanent disability rate of 50% among the survivors is mostly due to delayed cerebral ischemia (DCI), a common complication of the disease. DCI has a complex multifactorial pathophysiology, existing of cerebral vasospasm and several key pathophysiological pathways, such as cortical spreading depolarisation, endothelial dysfunction, microthrombosis, neuroinflammation and oxidative stress. As a result of this not fully understood complex pathofysiology no sufficiently effective diagnostic test nor treatment strategy has been developed yet.

Besides the abovementioned components of the multifactorial pathofysiology of DCI the pathogenesis also includes cell damage, inflammation, altered metabolism and vascular tone and microparticles. Blood platelets are key mediators in the generation of microthrombi, a hallmark of DCI pathogenesis, and are regarded as the immediate responders to local nd systemic inflammation in the human body, including in neuro-inflammatory diseases such as multiple sclerosis. Previous studies have shown that blood platelets are possibly associated with the development of DCI in SAH patients.

At the Neuro-Oncology Research Group (NRG) of Cancer Center Amsterdam, blood

platelets have been identified as a rich and stable biosource of (m)RNA, providing pan-cancer diagnostics in blood. SMARTer mRNA amplification and sequencing and SVM analysis of 100-500 pg of platelet RNA (equivalent to 1 drop of blood) resulted in the development of a pan-cancer diagnostic test that reached a 96% accuracy for detecting cancer in blood. Additionaly, the platelet RNA profiles contained repertoires associated to the primary tumor type. This research has been extended to encompass other forms of cancer, Alzheimer's disease, epilepsy and multiple sclerosis.

Subsequently, the question appeared whether this fast growing diagnostic and prognostic tool could contribute to improving DCI-identification and management in SAH patients. The development of a DCI-specifik blood platelet RNA-profile will lead to improved diagnostics and management of these patients and thereby improve functional outcome.

Study objective

The primary objective of this study is to evaluate whether SAH patients at risk of developing DCI show a distinguished platelet RNA profile compared to patients without DCI. Secundary objective; to evaluate whether platelet RNA analyses can predict clinical outcome in patients who develop DCI after SAH. Other objectives are: investigating the effect of tranexamic acid on platelet RNA profiles, to study whether SAH patients with DCI development show chronic changes in platelet RNA-profiles six months after SAH, to evaluate whether specific subtypes of SAH (aneurysmal/perimesencephalic/angio-negative) show a distinguished platelet RNA-profile, to evaluate whether other common complications of SAH (hydrocephalus, meningitis, delirium, rebleed and seizures) show a significantly different platelet RNA-profile and to provide biological observational insight into the role of platelets in the pathophysiology of DCI. Additionally, we will investigate by visco elastic testing ROTEM analyses whether alterations in coagulation are associated with DCI-development.

Study design

a monocenter, prospective observational study

Study burden and risks

In order to obtain a DCI-specific platelet RNA-profile of SAH-patients multiple blood sample collections are required. Blood samples will be collected at day 0, 4 and 10 post-SAH. The first blood collection will take place during routine blood collection at the Emergency Department of the AMC. The second blood collection, at day 4, will be part of routine blood collection at the Intensive Care or the Neurosurgery Department. Hence, for these blood samples no additional procedures are required. Blood collection at day 10 will only take

place when the patient is still admitted at the AMC. If the patient has already been discharged prior to the blood collection timepoint, blood samples will not be obtained. No extra visitations are required.

Blood collection on day 0 and day 4 post-SAH exists of: 2x2,7mL citrate tubes + 1x6mL EDTA tube
Blood collection on day 10 after the SAH exists of: 1x6mL EDTA tube

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Admission to Academic Medical Center, Amsterdam
Admission within <24h after symptom onset
CT confirmed SAH

Age 18 years and older

Exclusion criteria

Traumatic Subarachnoid Hemorrhage
Patients with first blood collection >24hours after SAH
Platelet isolation >12 hours of blood collection
Patients who do not speak either English or Dutch

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):	26-06-2018
Enrollment:	600
Type:	Actual

Ethics review

Approved WMO Date:	19-01-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-06-2018

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-08-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-09-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-10-2024
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

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	NL63308.018.17