Neuroinflammation in cognitive decline post-cardiac surgery: The FOCUS study

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Primary objective is to quantitatively assess differences in in vivo neuroinflammation in patients before and after coronary artery bypass grafting (CABG) surgery. Secondary objective is to study whether diffferences in in vivo neuroinflammation are...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Encephalopathies
Study type	Observational invasive

Summary

ID

NL-OMON42968

Source
ToetsingOnline

Brief title
The FOCUS study

Condition

- Encephalopathies
- Cardiac therapeutic procedures

Synonym
postoperative cerebral dysfunction, postoperative cognitive dysfunction (POCD)

Research involving
Human

Sponsors and support

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

Intervention

Keyword: coronary artery bypass grafting surgery (CABG), neuroinflammation, PET, TSPO

Outcome measures

Primary outcome

Differences in PET tracer uptake before and after CABG.

Secondary outcome

Neuropsychological outcomes.

Study description

Background summary

Following coronary artery bypass grafting (CABG) surgery, patients have a significantly increased risk for developing postoperative cognitive decline (POCD). To date, the etiology of POCD is not understood. Neuroinflammation plays an important role in the pathogenesis of neurodegenerative diseases. In animal models and post-mortem studies systemic inflammation, as occurs after cardiac surgery, can induce neuroinflammation. It is hypothesized that neuroinflammation after cardiac surgery is an important factor to the trajectory of postoperative cognitive decline after CABG.

Study objective

Primary objective is to quantitatively assess differences in in vivo neuroinflammation in patients before and after coronary artery bypass grafting (CABG) surgery.
Secondary objective is to study whether diffferences in in vivo neuroinflammation are related to long term cognitive outcomes.

Study design

Observational time series design.

Study burden and risks

Screening and informed consent on the pre-operative outpatient's clinic of the cardiothoracic surgery department and anesthesiology.

During hospital admission:
- questionnaires to assess pre-operative cognitive and functional state and frailty.
- neuropsychological examination before CABG surgery (approximately 1-1.5 hours)
- PET-CT scan and MRI scan of the brain before CABG (total scan duration 90 minutes, radiation dose is 2x4.8 mSv which is below safety limits and comparable to a normal abdominal CT-scan.
- Patients will undergo extra blood sampling three times, which will be performed from pre-existent arterial or venous cannulas.
- One week after CABG, just before hospital discharge, patients will undergo repeat PET-CT-scan and MRI and a neuropsychological exam.

After hospital admission:
- Follow-up at 6 weeks and 6 months after CABG surgery: neuropsychological examination.

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

Planned for coronary artery bypass grafting surgery (CABG)
Age > 50 years
High-affinity or mixed affinity binders based on rs6971 polymorphism for TSPO

Exclusion criteria

- Patients with cognitive disorders that have not recovered enough to be able to understand the study leaflets and information for participation.
- Pregnancy or wish to become pregnant within 2 weeks after PET-CT scan
- Contra-indication to undergo a PET/CT or MRI scan, including claustrophobia.
- Patients who undergo a combination of CABG surgery and additional valve surgery.
- Previous cardiac surgery.
- Low-affinity binder based on rs6971 polymorphism for TSPO, or unable to determine rs6971 polymorphism.
- Brain or spinal surgery within the last 6 months.
- Meningitis or brain infection within the last 6 months.
- Pre-existing dementia or neurodegenerative disease or cognitive impairment interfering with the ability to understand informational material about this research project.
- Presence of a CSF catheter or shunt.
- Patients with known brain tumors.
- Patients with brain injury (e.g. acute stroke, or subarachnoid hemorrhage) within the last 6 months.
- Severe brain trauma in previous medical history.
- Chronic (>2 weeks) use of immunosuppressive agents (see table 3.3.A).
- Concomitant diseases resulting in severe immunosuppression (e.g. HIV).
- Chronic use of neuroleptics, defined as pre-hospital use.
- Patients that do not speak Dutch or have disabilities that prevent accurate delirium diagnosis.
- Analphabetic patients.
- No written informed consent obtained.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-02-2019
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	N,N-diethyl-2-(2-(4-(2-fluoroethoxy)phenyl)-5,7-dimethylpyrazolo[1,5-&alfa;]pyrimidin-3-yl)acetamide
Generic name:	18F-DPA-714

Ethics review

Approved WMO Date:	19-09-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-03-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-12-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-02-2019

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-08-2020
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	ID
EudraCT	EUCTR2016-002016-40-NL
CCMO	NL57785.091.16