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Stroke despite treatment with blood thinners: causes and outcomes

Submission date	Recruitment status	[_] Prospectively registered
06/06/2021	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
23/07/2021	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
11/04/2022	Circulatory System	

Plain English summary of protocol

Background and study aims

Atrial fibrillation is a heart condition that causes an irregular and often abnormally fast heart rate.

Anticoagulants are medicines that help prevent blood clots. They're given to people at a high risk of getting clots, to reduce their chances of developing serious conditions such as strokes and heart attacks.

Although oral anticoagulants reduce the risk of ischemic stroke in patients with atrial fibrillation (AF), they do not eliminate it. In fact, anticoagulated AF patients still have a substantial stroke risk of about 1.5% per year. There is only limited knowledge about the causes of stroke despite anticoagulation and the subsequent treatment strategies that are needed to prevent another future stroke.

Who can participate?

This is a retrospective observational study including data of adult patients (no upper age limit, both sexes) with (a) an imaging-proven ischemic stroke, (b) nonvalvular atrial fibrillation known before stroke onset and (c) treatment with oral anticoagulants at stroke onset.

What does the study involve?

This observational study will determine the most probable cause of stroke according to one of the following categories: (a) competing stroke etiology other than atrial fibrillation; (b) medication error or (c) treatment failure (neither (a) nor (b)). The study will examine the characteristics of patients stratified to these categories, as well as the subsequent prevention strategies (including but not limited to switching the type of anticoagulant and adding antiplatelets) and 3-month clinical outcomes using standard statistical methodology including multivariable regression analyses.

Where is the study run from?

The study is led by investigators from the University Hospitals of Bern, Basel and Heidelberg.

When is the study starting and how long is it expected to run for?

The study was conceived in June 2020 and data collection was completed in March 2021.

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
David J Seiffge, MD, David.Seiffge@insel.ch
Jan Purrucker, MD, Jan.Purrucker@med.uni-heidelberg.de
Alexandros A Polymeris, MD, Alexandros.Polymeris@usb.ch
Thomas R Meinel, MD, Thomas.Meinel@insel.ch

Contact information

Type(s)
Public

Contact name
Dr Alexandros Polymeris

ORCID ID
http://orcid.org/0000-0002-9475-2208

Contact details
Department of Neurology and Stroke Center, University Hospital Basel
Petersgraben 4
Basel
Switzerland
4031
+41 61 328 73 19
alexandros.polymeris@usb.ch

Type(s)
Scientific

Contact name
Dr David Seiffge

ORCID ID
http://orcid.org/0000-0003-3890-3849

Contact details
Department of Neurology and Stroke Center, Inselspital, University Hospital Bern
Freiburgstrasse 18
Bern
Switzerland
3010
+41 31 632 21 11
david.seiffge@insel.ch

Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
KEK Bern 2019-01010

Study information

Scientific Title
Ischemic stroke despite anticoagulant therapy in patients with atrial fibrillation - causes, subsequent treatment strategies and outcomes

Study objectives
1. The causes of ischemic stroke despite anticoagulation are heterogeneous.
2. Switching the type of anticoagulant or adding antiplatelets as subsequent prevention strategies do not reduce the risk of stroke recurrence.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/09/2019, KEK Bern (Murtenstrasse 31, 3010 Bern, Switzerland; +41 31 633 70 70; info.kek.kapa@gef.be.ch), ref: 2019-01010

Study design
Multicenter observational retrospective analysis of individual patient data

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Not applicable (retrospective study)

Health condition(s) or problem(s) studied
Ischemic stroke despite oral anticoagulation in patients with atrial fibrillation

Interventions

This retrospective observational study will determine the most probable cause of stroke according to one of the following categories:
(a) competing stroke etiology other than atrial fibrillation; (b) medication error or (c) treatment failure (neither (a) nor (b)).

The study will examine the characteristics of patients stratified to these categories, as well as the subsequent prevention strategies (including but not limited to switching the type of anticoagulant and adding antiplatelets) and 3-month clinical outcomes using standard statistical methodology including multivariable regression analyses.

Intervention Type
Other

Primary outcome measure
Measured using patient records:
1. Recurrent ischemic stroke at 3 months
2. Intracranial hemorrhage at 3 months
3. All-cause death at 3 months

Secondary outcome measures
There are no secondary outcome measures

Overall study start date
01/06/2020

Completion date
01/03/2021

Eligibility

Key inclusion criteria
Patients presenting with imaging proven ischemic stroke who had nonvalvular atrial fibrillation known before stroke onset and were on oral anticoagulant treatment at stroke onset

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
2,000 - 3,000

Total final enrolment
2946

Key exclusion criteria

Patients with mechanical heart valves and those without information on anticoagulant treatment at stroke onset

Date of first enrolment
01/01/2012

Date of final enrolment
31/12/2020

Locations

Countries of recruitment
Germany

Switzerland

United States of America

Study participating centre
University Hospital Bern
Freiburgstrasse
Bern
Switzerland
3010

Study participating centre
University Hospital Basel
Petersgraben 4
Basel
Switzerland
4031

Study participating centre
University Hospital Charité Berlin
Lindenberger Weg 80
Berlin
Germany
13125

Study participating centre

EOC Neurocenter Lugano
Lugano
Switzerland
6900

Study participating centre
University Hospital Heidelberg
Heidelberg
Germany
69120

Study participating centre
University Hospital Erlangen
Erlangen
Germany
91054

Study participating centre
George Washington University Hospital
Washington, DC
United States of America
20052

Study participating centre
University Hospital Mainz
Mainz
Germany
55131

Study participating centre
University Hospital Zurich
Zurich
Switzerland
8006

Study participating centre

University Hospital Lausanne
Lausanne
Switzerland
1011

Study participating centre
Warren Alpert Medical School of Brown University
Providence
United States of America
RI 02903

Sponsor information

Organisation
University Hospital of Bern

Sponsor details
Freiburgstrasse 18
3010 Bern
Switzerland
Bern
Switzerland
3010
+41 31 632 21 11
david.seiffge@insel.ch

Sponsor type
Hospital/treatment centre

Website
http://www.insel.ch/en/

ROR
https://ror.org/01q9sj412

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
01/03/2022

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request (Alexandros.Polymeris@usb.ch)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		08/04/2022	11/04/2022	Yes	No