Dutch ICH Surgery Trial; minimally invasive endoscopy-guided surgery for spontaneous intracerebral hemorrhage

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1. To study whether minimally invasive endoscopy-guided surgery, in addition to standard medical management, for the treatment of spontaneous supratentorial ICH performed within 8 hours of symptom onset, improves functional outcome in comparison...

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

Summary

ID

NL-OMON51777

Source
ToetsingOnline

Brief title
Dutch ICH Surgery Trial

Condition

- Central nervous system vascular disorders
- Nervous system, skull and spine therapeutic procedures

Synonym
Intracerebral hemorrhage; Intracerebral hematoma

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: ZonMw en Zorginstituut Nederland

(Subsidieregeling veelbelovende zorg),Penumbra, Inc.

Intervention

Keyword: Endoscopy, Intracerebral hemorrhage, Minimally invasive neurosurgery

Outcome measures

Primary outcome

The primary outcome parameter will be the modified Rankin scale (mRS) score at 180 days. This categorical scale measures functional outcome with scores ranging from 0 (no symptoms) to 6 (death). The treatment effect will be estimated with ordinal logistic regression analysis as common odds ratio, adjusted for prespecified prognostic factors. The adjusted common odds ratio will measure the likelihood that minimally invasive endoscopy-guided surgery will lead to lower mRS scores as compared to standard medical management alone.

Secondary outcome

Secondary outcomes will include: the score on the mRS at 90 and 365 days; favorable outcome (defined as a mRS 0-2 and 0-3) and all other possible dichotomizations of the mRS at 90, 180 and 365 days; NIHSS at day 6 (±1 day); death, Barthel Index, EuroQol-5D-5L, SS-QOL, health economic evaluations (medical consumption, productivity loss and burden for the caregiver), patient location and home time at 90, 180 and 365 days. Safety outcomes will be death within 24 hours, at 7 and at 30 days and procedure-related complications within 7 days. Technical effectiveness outcomes will be percentage volume reduction based on the baseline CT and CT at 24 hours (± 6 hours), percentage of participants with clot volume reduction >=70%, and >=80%, and with remaining clot volume <=10mL, and <=15mL, and conversion to craniotomy. In DIST-INFLAME,

outcomes will include perihematomal edema at 6 days (±1 day), functional outcome at 180 days and immune and metabolomic profiles at 3 (±12 hours) and 6 days (±1 day).

Study description

Background summary

Intracerebral hemorrhage (ICH) accounts for 16-19% of all strokes in Western Europe and contributes profoundly to mortality and disability. Thirty-day case fatality is 40% and of those surviving, only few gain independence. Except for stroke unit care and possibly early blood pressure lowering, there is currently no treatment of proven benefit. Surgical treatment, craniotomy, or minimally invasive surgery with the administration of alteplase, has so far not been proven effective. In the largest trials STICH I and II, and MISTIE III, the median time to treatment was more than 24 hours, which may be an important explanation for the lack of a treatment effect. A recent meta-analysis of randomized controlled trials showed that surgical treatment may be beneficial, in particular with minimally invasive procedures and when performed early. In the Dutch ICH Surgery pilot study, we showed that early minimally invasive endoscopy-guided surgical treatment performed within 8 hours of symptom onset in patients with supratentorial ICH is safe and technically effective. We hypothesize that early minimally invasive endoscopy-guided surgery improves the outcome in patients with supratentorial spontaneous ICH.

Study objective

1. To study whether minimally invasive endoscopy-guided surgery, in addition to standard medical management, for the treatment of spontaneous supratentorial ICH performed within 8 hours of symptom onset, improves functional outcome in comparison with standard medical management alone;
2. Determine whether patients treated with minimally invasive surgery develop less perihematomal edema on non-contrast CT at day 6 (±1 day) than controls, and whether the CT perfusion permeability surface-area product around the ICH at baseline modifies this effect (DIST-INFLAME);
3. Compare immune profiles over time in peripheral venous blood between surgically treated patients and controls (DIST-INFLAME);
4. To assess the cost-effectiveness and budget-impact of minimally invasive endoscopy-guided surgery for the treatment of spontaneous supratentorial ICH performed within 8 hours of symptom onset.

Study design

A multicenter, prospective, randomized, open, blinded endpoint (PROBE) clinical trial.

Intervention

Patients will be randomized (1:1) to minimally invasive endoscopy-guided surgery performed within 8 hours of symptom onset in addition to standard medical management or to standard medical management alone.

Study burden and risks

Minimally invasive endoscopy-guided surgery has been shown to carry limited risks and is of potential benefit to improve outcome, in particular when performed early. We therefore make use of deferred written informed consent. The main risks of surgery consist of persistent or recurrent intracranial hemorrhage, surgical site infection, intracranial infection and seizures. Besides the intervention for participants randomized to surgical treatment, the burden for all participants will consist of performing two additional non-contrast CT scans at 24 hours (± 6 hours) and 6 days (±1 day) after the baseline non-contrast CT, and a telephone interview for outcome assessment after 90, 180 and 365 days. Because patients with ICH may present with aphasia or decreased consciousness, we will include competent and non-competent patients (consent by proxy). In all participants in the surgical arm, a non-contrast CT immediately after surgery will be performed, to assess the achieved reduction in ICH volume. All participants will have blood samples drawn at baseline. In the participants in the DIST-INFLAME, a CT perfusion-scan will be performed at baseline and additional blood samples will be drawn on day 3 (±12 hours) and day 6 (±1 day).

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

1. Age 18 years or older;
2. NIHSS >= 2;
3. Supratentorial non-traumatic ICH confirmed by non-contrast CT, without a CTA confirmed causative vascular lesion (e.g. aneurysm, AVM, DAVF, CVST), or other known underlying lesion (e.g. tumor, cavernoma);
4. Minimal hematoma volume of 10 mL;
5. Intervention can be started within 8 hours of symptom onset;
6. Written informed consent (deferred).

Exclusion criteria

1. Considerable pre-stroke dependency in activities of daily living, defined as a pre-stroke mRS >=3;
2. ICH-GS score >=11;
3. Hemorrhage due to hemorrhagic transformation of an infarct;
4. Untreated coagulation abnormalities, including INR >1.3 (point of care measurement allowed), treatment with heparin and treatment with factor Xa inhibitors. Patients on vitamin K antagonist can be included after correction of the INR, and patients on dabigatran (direct thrombin inhibitor) can be included after reversal of dabigatran with idarucizumab;
5. Moribund (e.g. coning, bilateral dilated unresponsive pupils), or progressively deteriorating clinical course with imminent death;
6. Pregnancy;
7. DIST-INFLAME (sub-study): patients that use immunosuppressive or immune-modulating medication.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-11-2022
Enrollment:	600
Type:	Actual

Ethics review

Approved WMO Date:	05-08-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-10-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-01-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-02-2025

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	NL80112.078.22