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Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery

Submission date 08/09/2005	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 27/04/2006	**Overall study status** Completed	
Last Edited 25/11/2010	**Condition category** Surgery	

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.strokecenter.org/trials/TrialDetail.aspx?tid=590

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title

Acronym
DESTINY

Study objectives
To demonstrate the efficacy of decompressive surgery in addition to conservative treatment to reduce mortality and to improve functional outcome after malignant hemispheric ischemic cerebral infarction with space-occupying edema with conservative treatment alone.

Please note that as of 09/01/09 the secondary outcomes of this trial have been updated. Please see the relevant field for details.

Please note that as of 09/02/10 the secondary outcomes of this trial have been updated. Please see the relevant field for details.

Please note that as of 25/11/10 the secondary outcomes have been updated. Patients will now be followed for 5 years.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The study protocol was approved by the ethics committees of all participating centres.

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Malignant middle cerebral artery infarction

Interventions

Decompressive surgery (the following protocol is a consensus protocol that was worked out by Prof Unterberg (Department of Neurosurgery, University of Heidelberg) as a written paper and as a video and has been approved by all participating neurosurgeons): Decompressive surgery will consist of a large hemicraniectomy and a duraplasty. In summary, a large (reversed) question mark-shaped skin incision based at the ear will be made. A bone flap with a diameter of at least 12 cm (including the frontal, parietal, temporal and parts of the occipital squama) will be removed. Additional temporal bone will be removed so that the floor of the middle cerebral fossa can be explored. The dura will be opened and an augmented dural patch, consisting of either homologous periost and/or temporal fascia, or lyophylised cadaver dura, will be inserted. The dura will be fixed at the margin of the craniotomy to prevent epidural bleeding. The temporal muscle and the skin flap will then be re-approximated and secured. Infarcted brain tissue will not be resected. A sensor for registration of intracranial pressure may be inserted. In surviving patients, cranioplasty will be performed after at least 6 weeks, using the stored bone flap or an artificial bone flap. After surgery, patients will be transferred to the intensive care unit (ICU). The complete procedure is documented on video for post protocol analysis.

Conservative treatment: So far no mode of treatment of raised intracranial pressure has been proven to be superior to another. So treatment options listed here may vary from one institution to another. However, as much consistency of treatment between the centres as possible should be given. Therefore the following treatment modalities are given (the following protocol has been worked out by Dr Münch [Department of Anesthesiology and Intensive Care Medicine Mannheim, University of Heidelberg] and Dr Jüttler [Department of Neurology, University of Heidelberg] including the latest recommendations in neurological intensive care, stroke therapy and anesthesiological intensive care medicine and has been approved by all participating anesthesiological and neurological intensive care physicians):

1. Osmotherapy: osmotherapy should be started immediately after randomisation. The use of mannitol (i.e. Osmofundin 100 ml 15% solution 4 times per day) or glycerol (i.e. Glycerosteril 250 ml 10% solution, 4 times per day) is recommended. Dosage depends on serum osmolality and should reach 315 to 320 mOsm.
2. Intubation and mechanical ventilation: Patients will be intubated at a Glasgow Coma Score (GCS) lower than 8, or if there are any signs of respiratory insufficiency (pO_2 <60 mmHg, pCO_2 >48 mmHg), or if the airway is compromised. However, earlier intubation is left at the discretion of the treating physician. The same goes for ventilation mode. The following parameters should be reached: pO_2 >75 mmHg, pCO_2 36-44 mmHg. In case of raised intracranial pressure the ventilation mode is changed to a frequency of 35 and pO_2 >100 mmHg.
3. Hyperventilation: The use of hyperventilation is discouraged in the early phase of treatment. In the case of further neurological deterioration and/or uncontrolled increase in intracranial pressure, hyperventilation may be started as ultima ratio. If hyperventilation is started, it is advised to monitor venous oxygenation with jugular bulb oxymetry and to maintain saturation higher than 50%. If venous oxygen saturation is not monitored, the pCO_2 may be reduced to 28-32 mmHg.
4. Intracranial pressure (ICP) monitoring: The mode of invasive monitoring of the intracranial pressure is left at the discretion of the treating physician. If used, measurement should be performed in the ipsilateral side.
5. Sedation: The mode of sedation is left at the discretion of the treating physician. If sedation is required because of mechanical ventilation, further neurological deterioration, or uncontrolled increase of intracranial pressure, patients should be sedated with propofol. The use of barbiturates is discouraged because they may reduce cerebral perfusion pressure and often do not lead to sustained control of intracranial pressure. The use of muscle relaxants is left at the

discretion of the treating physician.
6. Blood pressure control: blood pressure is controlled according to the latest recommendations of the treatment of acute ischemic stroke (Hacke et al. 2000). Recommended blood pressure in formerly hypertensive patients is 180/100-105 mmHg and in formerly normotensive patients 160-180/90-100 mmHg. The use of catecholamines or antihypertensive drugs is left at the discretion of the treating physician. An exception is made in patients receiving decompressive surgery. In these cases blood pressure during the postoperative phase of the first 8 hours after surgery is kept at 140-160 mmHg to avoid severe bleedings.
7. Positioning: elevation of the head 30 degrees
8. Body core temperature: normothermia should be reached. Therefore elevated body temperature is treated as soon as it exceeds 37.5 °C (Hacke et al. 2000). The use of antipyretics, external cooling or intravasal cooling is left at the discretion of the treating physician.
9. Blood glucose level: according to the latest recommendations of the treatment of acute ischemic stroke (Hacke et al. 2000) and recommendations of intensive care medicine (van den Berghe et al. 2001) blood glucose level should not exceed 140 mg/dl, 8 mmol/l, respectively. The parameter that should be reached is 80-110 mg/dl. Insulin should be used for control of blood glucose level. Hypoglycemia is treated with 10% or 20% glucose.
10. Hemoglobin concentration should be >10 g/dl (Hb >10 g/dl)
11. Prophylaxis of deep venous thrombosis is done with low-molecular-weight heparin (i.e. Fragmin once a day)

All treatment on the ICU is documented for post protocol analysis.

Intervention Type
Procedure/Surgery

Phase
Not Applicable

Primary outcome measure
Functional outcome after six months measured by the modified Rankin Scale

Secondary outcome measures
Amended 25/11/10:
1. Mortality after 30 days, 1, 2, 3, 4 and 5 years
2. Functional outcome after 1, 2, 3, 4 and 5 years
3. Retrospective agreement to the procedure by the patients and caregivers after 1, 2, 3, 4 and 5 years
All other outcomes remain unchanged.

Current information as of 09/02/10:
1. Mortality after 30 days, 1, 2, 3 and 4 years
2. Functional outcome after 1, 2, 3, and 4 years, measured by the following:
2.1. Modified Rankin Scale
2.2. National Institutes of Health Stroke Scale (NIHSS)
2.3. Barthel Index
2.4. Stroke Impact Scale (SIS)
2.5. SF-36® Health Survey
2.6. Aachen Aphasia Inventory
3. Retrospective agreement to the procedure by the patients and caregivers after 1, 2, 3, and 4 years

4. Complications related to surgery
5. Infarct size after days 2-3 and 4-8, measured by computerised tomography

Current information as of 09/01/2009:
1. Mortality after 30 days, 12 and 36 months
2. Functional outcome after 12 and 36 months, measured by the following:
2.1. Modified Rankin Scale
2.2. National Institutes of Health Stroke Scale (NIHSS)
2.3. Barthel Index
2.4. Stroke Impact Scale (SIS)
2.5. SF-36® Health Survey
3. Retrospective agreement to the procedure by the patients and caregivers
4. Complications related to surgery
5. Infarct size after days 2-3 and 4-8, measured by computerised tomography

Initial information at time of registration:
1. Mortality after 30 days
2. Mortality after 12 months
3. Functional outcome after 12 months measured by the following:
3.1. Modified Rankin Scale
3.2. National Institutes of Health Stroke Scale (NIHSS)
3.3. Barthel Index
3.4. SF-36® Health Survey
4. Complications related to surgery
5. Infarct size after days 2-3 and 4-8, measured by computerised tomography

Overall study start date
28/02/2004

Completion date
31/12/2007

Eligibility

Key inclusion criteria
1. Age 18 up to and including 60 years
2. Clinical signs of an ischemic infarction of the middle cerebral artery with a score on the National Institutes of Health Stroke Scale (NIHSS) >18 for lesions of the non-dominant hemisphere and >20 for lesions of the dominant hemisphere
3. Neuroradiological signs of an unilateral infarction of the middle cerebral artery including at least two-thirds or more of the territory of the middle cerebral artery and including at least partly the basal ganglia, with or without an additional infarction of the anterior or posterior cerebral artery on the same side
4. Onset of symptoms before more than 12 and less than 36 hours prior to a possible surgical intervention
5. Possibility to start treatment or surgery within 6 hours after randomisation

Participant type(s)
Patient

Age group

Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
68

Key exclusion criteria
1. Pre-stroke score on the modified Rankin Scale >2 or on the Barthel Index <95 (Rankin et al. 1957, Mahoney et al. 1965)
2. Glasgow Coma Scale <6 at the time of randomisation
3. Coincidental other brain lesion (i.e. trauma)
4. Two fixed dilated pupils
5. Secondary bleeding in the area of infarction
6. Known systemic bleeding disorder
7. Life expectancy <3 years
8. Other serious illness that may confound treatment assessment

Date of first enrolment
28/02/2004

Date of final enrolment
31/12/2007

Locations

Countries of recruitment
Germany

Study participating centre
Im Neuenheimer Feld 400
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Sponsor information

Organisation
University of Heidelberg (Germany)

Sponsor details

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Sponsor type
University/education

Website
http://www.klinikum.uni-heidelberg.de/index.php?id=600

ROR
https://ror.org/038t36y30

Funder(s)

Funder type
University/education

Funder Name
University of Heidelberg (Germany) - Department of Neurology

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/09/2007		Yes	No