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Investigating the optimal time for surgical repair of the skull by cranioplasty following a traumatic brain injury or stroke.

Submission date
14/01/2019

Recruitment status
No longer recruiting

Registration date
22/03/2019

Overall study status
Completed

Last Edited
22/03/2019

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
In the first few days after a serious traumatic brain injury (TBI) or a large stroke, patients can develop swelling in the brain which, in turn, can lead to brain damage or even death. Craniectomy is a surgical procedure in which part of the skull is removed to relieve brain swelling. A number of high-quality studies, including one from the UK published in 2016, have shown that a craniectomy can be helpful in the management of patients with dangerous levels of swelling. Patients who survive undergo an operation, known as cranioplasty, in order to have their skull reconstructed a few months later. Traditionally, cranioplasties were undertaken around 10-12 months after the craniectomy, as it was thought that early cranioplasty can increase the risk of infection. However, recent systematic reviews have challenged this view. In addition, a number of small studies have suggested that early cranioplasty may enhance recovery.

Who can participate?
All adult (>16) patients, who are stable after undergoing a craniectomy following a traumatic brain injury or stroke will be considered for the research project.

What does the study involve?
Following consent, patients will be randomly placed into one of the two groups of the study: one group will have the cranioplasty within 3 months, while the other group will have it more than 6 months after the craniectomy. All patients will otherwise be managed as per usual local practice.

Patients will be followed up for up to 18 months after the craniectomy, with the focus on activities of daily living, behavioural and psychological symptoms, quality of life, and complications.

What are the possible benefits and risks of participating?
There is no guarantee that patients will benefit from taking part in this study. They will have assessments which may identify improvements in function and cognition. Information collected as part participation in this study may benefit future patients requiring a cranioplasty operation.

In the past there has been small studies suggesting that there is a slight increase risk of skull plate infection, if put in early, but this has been challenged. There is also a small increased risk of seizures and build-up of fluid around the brain. Late surgery could lead to worse cognition, syndrome of the trephined (sinking skin flap leads shows worse cognitive function) and also seizures. We have no guarantee if patients will benefit from a particular time-point of the operation. All other care is unchanged and there are no other specific risks resulting from being in this study.

Where is the study run from?
The study is a single site study being run from the neurosurgical department at Cambridge University Hospital.

When is the study starting and how long is it expected to run for?
The study is starting to recruit at the beginning of March 2019. We aim to recruit patients for 1 year and follow them up for 18 months in total. Therefore, the anticipated study duration is 2.5 years.

Who is funding the study?
The study is jointly funded by the University of Cambridge and Cambridge University Hospitals NHS Foundation Trust.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Integrated Research Application System (IRAS)
252606

Protocol serial number
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Study information

Scientific Title
Comparing the functional outcome of adult patients who have undergone a supratentorial craniectomy due to traumatic brain injury or a large ischaemic stroke after early vs late cranioplasty: a pilot randomised controlled trial.

Acronym
REEL Cranioplasty Trial

Study objectives
Early cranioplasty (within 3 months) enhances the cognitive and functional recovery of patients following craniectomy for traumatic brain injury or middle cerebral artery infarcts.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Wales REC, 22/01/2019, ref. 18/WA/0425.

Primary study design
Interventional

Study design
A pilot, prospective, parallel group randomised controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Traumatic brain injury or middle cerebral infarct.

Interventions
The REEL trial is a pilot, prospective, parallel group randomised trial with 1:1 allocation ratio to early v late cranioplasty. The aim is to understand better whether a strategy of early cranioplasty (within 3 months following craniectomy) improve the functional and cognitive outcome of adults who have had a craniectomy due to a TBI or MCA infarct compared to a strategy of late cranioplasty (more than 6 months after craniectomy)? This is a pragmatic trial, comparing two treatment periods in which a cranioplasty can take place, either early or late.

Standard care pathways are being adhered to as closely as possible in both arms, with only the timing of the cranioplasty being defined. Currently there is no standard time in which a cranioplasty should be done. Traditionally, patients have waited between 6 and 12 months and sometimes longer but now earlier cranioplasties are being performed, however there is still limited evidence for the optimal timing of a cranioplasty.

Our hypothesis is that an early cranioplasty will increase the rate of recovery both cognitively and functionally, rather than increase the overall outcome of the patient. We are predicting to be able to capture an early divergence of functional and cognitive improvement within the early group, which we predict will narrow at the 12 month and 18-month period. This will hopefully

enable clinicians to be able to make better, evidence based, informed decisions on the optimal time for a cranioplasty.

Randomisation will occur once the patient is medically stable. Allocation will be stratified by pathology, either TBI or MCA infarct. The system will provide an immediate allocation along with the patient identifier number for the trial. A confirmatory email will be sent to the email addresses of the members of the study team randomising the patient. Blocked randomisation will be used, with a block size of 4 or 6 and allocation ratio of 1:1, and subjects are allocated randomly within each block.

Intervention Type
Other

Primary outcome(s)
Patient status will be measured using the extended Glasgow Outcome Scale at 6 months.

Key secondary outcome(s)
To be measured at baseline and 2 months after craniectomy, with additional follow up at 6, 12 and 18 months:
1. Long-term clinical effectiveness of early vs late cranioplasty will be measured at the 18 months follow-up period.
2. Quality of life will be measured using the EQ-5D-5L and QOLIBRI.
3. Behavioural and psychological symptoms will be measured using the NPI-Q.
4. Surgical complications will be measured using patient reporting and medical notes.
5. Adverse events will be measured using patient reporting and medical notes.
6. Health economics evaluation will be measured using the EQ-5D-5L at 18 months.

Completion date
31/08/2021

Eligibility

Key inclusion criteria
1. Aged 16 or over
2. Require a cranioplasty after a supratentorial decompressive craniectomy for TBI or MCA infarct.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria

1. Cranioplasty cannot be undertaken within 3 months from the craniectomy date.
2. Craniectomy is undertaken for a condition other than TBI or ischaemic stroke.
3. If consent cannot be gained by either patient or next of kin or family member.

Date of first enrolment
04/03/2019

Date of final enrolment
04/03/2020

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Hills Road
Cambridge
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Sponsor information

Organisation
University of Cambridge and Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
University of Cambridge and Cambridge University Hospitals NHS Foundation Trust

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No