

Protocol Summary

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Does decompressive craniotomy improve outcome after traumatic brain injury?

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BACKGROUND AND INTRODUCTION: The optimal management of TBI with refractory intracranial hypertension remains vexing. Decompressive craniotomy has been utilized primarily as a salvage procedure when medical therapy has failed, yielding mixed results. Several case series of early decompressive craniotomy have demonstrated superior outcomes but with a high incidence of procedure-related complications. The magnitude of effect, appropriate patient population and optimal timing of decompressive craniotomy remains unclear.

Decompressive craniotomy (DC) has been employed for refractory intracranial hypertension (ICH) for more than 50 years and has regained therapeutic interest during the past decade. However, treatment guidelines for traumatic brain injury (TBI) from German, European (European Brain Injury Consortium)¹ North-American (Brain Trauma Foundation)² and international (pediatric neurosurgery)³ medical societies consider DC only as last resort treatment strategy after failure of conservative therapy. Not surprisingly, DC was viewed as a maneuver with little therapeutic benefit since it had traditionally been applied after failure of days of medical therapy when the degree of secondary brain injury had already reached an irreversible point.

More recently, DC has been incorporated into intracranial pressure treatment algorithms at an earlier time point in centers with aggressive neurocritical care units with some encouraging results.⁴⁻¹⁰ Unfortunately, the majority of these trials are case series and lack appropriate controls for comparison. Furthermore, the time frame over which DC is employed in these trials ranges from less than 24 hours after injury to several days, again making it difficult to draw conclusions regarding the efficacy of DC.

Clearly, a randomized clinical trial to assess the effectiveness of DC is warranted, but the fact that there are significant complications associated with

DC makes enrollment difficult, particularly if it is to be employed as an early prophylactic modality. Additionally, a randomized controlled trial of a surgical intervention to medical therapy requires that the surgical intervention be paid for and not charged to the patient. This makes such a study prohibitively expensive and unlikely to ever be performed with sufficient numbers to address outcomes adequately. In the absence of a well designed, randomized trial other methods need to be used to determine if DC has a role in the management of TBI. Propensity score analysis employs a novel statistical methodology which creates two balanced groups of patients and compares their outcome according to whether or not they received a specific treatment similar to a randomized control trial. It is this type of analysis which will therefore be used in the current study.

OBJECTIVES: To characterize the use of decompressive craniotomy in trauma centers across the US and determine the effect of decompressive craniotomy on mortality and neurologic outcome in patients with TBI.

PARTICIPANT SELECTION CRITERIA: We will perform a retrospective chart review for every patient who has the characteristics of traumatic brain injury (TBI). Patients admitted with a Glasgow Coma Score of 13 or less with evidence of TBI on their admission head CT will be included. The age range is 0-99 years with any patient over the age of 89 years listed in a group classified as > 89 years of age. Patients excluded will be those older than 99 years of age and those who do not have the characteristics of TBI. Patients for this study will be identified using the [Your Institution] Trauma Registry/chart data from 2005-2009.

DESIGN: Multi-center retrospective review of trauma registry/chart data from 2005-2009.

STATISTICAL METHODS, DATA ANALYSIS AND INTERPRETATION: The outcomes to be assessed are in-patient mortality, complications, ICU length of stay, ventilator days, hospital length of stay, disposition, charges, and GCS at discharge. Inclusion criteria are all blunt injured trauma patients of any age who have an admission GCS of 13 or less with evidence of traumatic brain injury on their admission head CT. It is important to include the spectrum of head injury cases from moderate to severe as the injury and physiology factors of moderate head injury that obviate the need for DC are important for model building. That is, those patients with moderate TBI that don't undergo DC will have important characteristics that are distinct from more severe TBI patients that do undergo DC. It is these factors that are important to measure and include in the propensity score model. Through the large sample size it is anticipated that a sufficient number of severe TBI patients will be included in order to create a model of high predictability for the use of DC.

Our site will be provided with access to a secure on-line data entry program, created by the American Association for the Surgery of Trauma Multicenter Institutional Trials Committee, into which study data will be entered.

Information will be entered in a de-identified manner such that only our approved research personnel can identify patient data to allow for adequate data collection. Therefore, only de-identified data will be submitted to the primary research data analysis site (University of Utah). A de-identified copy of the admission head CT scan will be mailed to the primary site with a unique identifier code that links the scan to the de-identified data entered onto the secure server. At the conclusion of the study a copy of the de-identified data will be maintained on a CD which will be kept in a locked storage cabinet in anticipation for a long term follow up study to be undertaken approximately 2 years after the completion of the current study. In the event that this subsequent study is not undertaken the disc and its data will be destroyed. All other research data will be destroyed both in paper format and electronically deleted at the conclusion of the currently proposed study.

A propensity score for the likelihood of DC will be calculated using logistic regression techniques and assigned to each patient in the dataset. Variables incorporated into the propensity score calculation will be exhaustive in order to create a robust model that maximizes the accuracy of the score in predicting the likelihood of undergoing DC. This will include a radiologic grading of the admission head CT to be performed by the coordinating team using a well accepted strategy which correlates well with subsequent neurologic outcome.¹¹ In addition, to measure the clinical variability in practice, a survey measurement of frequency of adherence to Brain Trauma Foundation guidelines will be included for each participating center.

Patients will then be grouped into quintiles, based upon their propensity score of receiving a DC. Patients within each quintile will therefore represent a balanced group in terms of the likelihood of receiving the intervention (DC) similar to that of a randomization process. The outcomes will then be assessed using regression techniques comparing those that actually underwent early DC to those who underwent late DC or to those who received medical therapy alone for a given quintile. Additionally, timing of DC will also be measured to determine if it is related to outcome.

Sample Size Estimate: The mortality rate of patients with moderate to severe TBI ranges from 20% to 50% with standard medical therapy.¹²⁻¹⁴ Assuming a reduction in mortality of 15% with early DC and average mortality rate of 35% in the medical treatment group, one would need 198 patients in the treatment and control arms respectively to adequately power a study with alpha set at 0.05 and beta set at 0.9 assuming equal variances. Since DC is not routinely performed at most centers a conservative estimate is that approximately 5% of patients in this group would undergo DC. Therefore, to ensure that the number of patients undergoing DC is adequately represented in the dataset enrollment of 3960 TBI patients will be required.

After 2000 TBI patients are enrolled, the data will be examined for the rate of DC to determine if further enrollment is required and to estimate how many additional patients will likely need to be enrolled or if the data collection process can be closed.

It is expected that our site will contribute approximately 400 patients to the

primary site from the 5 year period.

Study Resources: A secure website will be created by the American Association for the Surgery of Trauma Multi-Institutional Trials IT personnel for patient data entry. Only the individual site co-investigators and their authorized research personnel will have access to their own data entry website. The principal investigator (Dr. Nirula), and authorized research personnel at the University of Utah will have access to the de-identified data and images entered from all of the participating sites. All data entry and viewing will be password protected. Once all data is received it will be removed from web access and saved to a CD for analysis. Information will be entered in a de-identified manner but will be done by the participating sites such that only they can identify patient data to allow for adequate data collection to enter the necessary data). Only de-identified data will be submitted to the primary research data analysis site. We will keep a code that will allow access to the identifiers and that code will be kept in a locked filing cabinet. At the conclusion of the study a copy of the de-identified data will be maintained on a CD which will be kept in a locked storage cabinet in anticipation for a long term follow up study to be undertaken approximately 2 years after the completion of the current study. In the event that this subsequent study is not undertaken the disc and its data will be destroyed. All other research data will be destroyed both in paper format and electronically deleted at the conclusion of the currently proposed study.

Study Duration:

IRB approval (through expedited process for retrospective data collection with no intended research-related interventions): by 1/1/10

Data collection: completion of all data collection and submission of data forms and CT scans to the coordinating center at the University of Utah by 12/31/10

Data analysis: by 6/1/11

Paper write-up and distribution for comments: by 9/1/11

Submission of abstract to AAST meeting: February 28th, 2012

REFERENCES AND APPENDICES:

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Decompressive Craniotomy Data Sheet

Center Information: To be completed only once for each institution

Institution Name:

Trauma Center Designation: Yes No

If yes: ACS State Both

Level: I II

Population: Adult Trauma Pediatric Trauma Both

of Trauma admits/year: <1000 1000-2000 2000-3000 3000-4000 >4000

In-house neurosurgery residents: Yes No

In-house trauma attending: Yes No

Do you have an ICP management protocol in your ICU? Yes No

Do you have a ventilator weaning protocol in your ICU? Yes No

Do you have a closed ICU? Yes No

Case Information:

Admit Date (mm/dd/yyyy)

Admit Time

Admission Unit: NeuroICU TraumaICU Med/SurgICU Other

Age

Gender

Admit weight (kg)

Admit height (cm)

Comorbidities:

Previous MI

Previous stroke

CHF

COPD

Smoker

Dialysis

Liver Disease

Diabetes (insulin dependent)

Diabetes (non-insulin dependent)

Malignancy

HIV/AIDS

On Coumadin

On Beta Blockers

On Statins

Insurance on admission:

Self Pay

Medicare

Medicaid

Commercial

Time from Injury to arrival at your institution: <15min, 15m-1hr, 1hr-3hr, 3hr-6hr,

>6hr
Admission Physiology:
HR
SBP
Temp (Celcius)
Base Deficit (within 24 hours of admission)
Lactate (within 24 hours of admission)
Hct
INR (within 24 hours of admission)
GCS:
 Eye
 Verbal
 Motor
Chemically paralyzed at the time of GCS (Yes/No)
Intubated in field (Yes/No)
Intubated in ED (Yes/No)
Injury Data
Mechanism:
 Blunt: MVC, Auto vs. Peds, Fall, Assault, MCC, Machinery, Other
 Penetrating: GSW, Shot gun, Stab, Other
Head AIS
Chest AIS
Abd AIS
Spine AIS
Lower Ext AIS
Upper Ext AIS
ISS
Abdominal Compartment Syndrome
Amount of pRBCs given in first 24 hours
Number of FFP units in first 24 hrs
Factor VII in first 24 hrs
First Head CT shows cerebral trauma (Yes/No)
Procedures performed in first 24 hours (yes/no):
Laparotomy
Thoracotomy/Sternotomy
Arterial Embolization
Lower extremity fracture fixation
Upper extremity fracture fixation
PA Catheter Placement
ICP monitor/Ventriculostomy placement
Evaluation in 24 hours
Highest GCS recorded in first 24 hours
 Eye
 Verbal
 Motor

First ICP measurement recorded mmHg? cmH2O? (circle units)
Highest ICP recorded Day 1=
Corresponding MAP at this time point(within30 minutes)=
Highest ICP recorded Day 2=
Corresponding MAP at this time point(within30 minutes)=
Highest ICP recorded Day 3=
Corresponding MAP at this time point(within30 minutes)=
Highest Hct Day 1=
Highest Hct Day 2=
Highest Hct Day 3=
Highest Hct Day 4=
Highest Hct Day 5=

Decompressive Craniotomy/Craniectomy (yes/no)

Reason:

Primary (for cerebral edema)

Secondary (to another neurosurgical procedure, eg.– A patient has a subdural hemorrhage evacuated and the surgeon decides to leave the bone flap off because of swelling or anticipated swelling)

Time from Injury to Decompression <24 hours, 24-48hrs, 48-72 hrs, 72-96 hrs, >96hrs

Was the DC performed for medically refractory ICH?

If no, was it performed prophylactically?

Outcomes

In-hospital Death (yes/no)

Death Date (mm/dd/yyyy)

ICU length of stay

Hospital length of stay

Discharge Dispo – Home, Rehab, SNF, nursing home/long term care

GCS at Discharge

Ventilator Associated Pneumonia (Date of Diagnosis)

ARDS (Date of Diagnosis)

DVT (Date of Diagnosis)

CRBSI (Date of Diagnosis)

Intracranial abscess (Date of Diagnosis)

Meningitis (Date of Diagnosis)

Other DC related complication (Specify complication and date)