Mechanism of Death after Decompressive Craniectomy in Non-Traumatic Brain Injury

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ABSTRACT: Decompressive craniectomy (DC) after devastating brain injury (DBI) may influence the manner in which patients die, having implications for end-of-life care and organ donation. We performed a retrospective review of deaths following a non-traumatic DBI between 2008 and 2012. 160 patients were reviewed; 26 were treated with DC and 134 received standard care. There was no relationship between DC and mechanism of death, (OR 1.18, 95% CI 0.44-3.17). Prospective studies are required to confirm these preliminary finding. DC studies should report the mechanism of death.

RÉSUMÉ: Mécanismes du décès et craniectomie de décompression à la suite d'une lésion cérébrale non-traumatique. À la suite de lésions cérébrales sévères, la craniectomie de décompression (CD) peut influencer la façon dont les patients décèdent, en plus d'avoir une incidence sur les soins de fin de vie et le don d'organes. Nous avons ainsi mené une analyse rétrospective des décès survenus entre 2008 et 2012 à la suite de lésions cérébrales sévères non-traumatiques. Pour ce faire, nous avons passé en revue 160 dossiers de patients : 26 d'entre eux avaient été traités au moyen de la CD alors que 134 avaient bénéficié de soins standards. Aucun lien n'a été trouvé entre la CD et des mécanismes du décès (ratio d'incidence rapproché ou RIR = 1,18 ; IC95% = 0,44-3,17). Des études prospectives sont donc nécessaires pour confirmer ces conclusions préliminaires. De plus, les études menées au sujet de la CD devraient veiller à signaler le mécanisme du décès en cause.

Keywords: Brain death, decompressive craniectomy, organ donation, death, devastating brain injury, non-traumatic brain injury, donation after circulatory death

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Introduction

The growing supply-demand imbalance of transplantable organs is a complex problem with global implications. Deceased organ donors must be determined dead based on neurological criteria (NDD, also known as brain death) or circulatory criteria (DCD, donation after circulatory death). For NDD, the irreversible cessation of all brain functions[1] occurs after devastating brain injury (DBI), most frequently after traumatic brain injury, a cerebrovascular accident, or hypoxic-ischemic damage after resuscitated cardiac arrest.[2]

Decompressive craniectomy (DC), whereby a portion of the skull is removed, in combination with duraplasty, is a surgical procedure that allows the brain to swell without hindrance. This procedure has the potential to interrupt the typical progression of refractory intracranial hypertension (ICH) resulting in herniation and the arrest of brain blood flow, leading to the irreversible cessation of brain function. Under these assumptions, patients who have suffered a DBI and are treated with DC would be more likely to have a better functional outcome than those treated with standard care. In patients who do not survive the DBI, DC may complicate death determination. These patients may die either with brain or circulatory determinations of death. The worldwide practice of DCD is limited in comparison to donation after NDD, and the number of organs transplanted per donor is significantly lower with 1.51 less transplants per donor.[3] Thus, the consequences of DC include the potential to improve functional outcome after DBI but also to influence organ donation potential in non-survivors.

To further investigate the influence of DC on the mechanism of death in patients who die after a DBI, we performed a systematic review of the DC literature with the purpose of determining whether DC decreases the likelihood of NDD in patients with a DBI (see Supplemental Material for study process and complete search strategy). We included original studies that reported on the practice of DC in patients (adult or pediatric) with a DBI and that recorded the mechanism of death of patients who died. DBI was defined as an injury to the brain caused by traumatic brain injury, brain contusions, cerebrovascular accident, craniocerebral trauma, hypoxia-ischemia, cerebral infarction, intracranial hemorrhage, brain edema, or ICH resulting in a patient Glasgow Coma Score of

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8 or less. Study design was limited to randomized control trials (RCTs). The study language was limited to English and French. Only one study of DC for DBI in pediatric patients reported the mechanism of death.[4] Given the paucity in the published literature on the influence of DC on the mechanism of death, and the possible impact that DC could have on organ donation potential, we felt further study was warranted. We conducted a chart review with the purpose of determining whether there is a higher ratio of death determined by circulatory criteria versus NDD among patients who died after DC compared to standard care.

Material And Methods

Patient Selection/Study Population

We conducted a retrospective chart review of patients who died following a non-traumatic DBI at the Montreal Neurological Institute between January 2008 and December 2012. The Montreal Neurological Institute is not a trauma center. For the purposes of this study, non-traumatic DBI was defined as brain injury caused by cerebrovascular accident, anoxia, intracranial hemorrhage, subarachnoid hemorrhage, intraventricular hemorrhage, subdural hematoma, vasospasm, or venous thrombosis. Exclusion criteria were: (1) patients who did not die as a direct result of their brain injury, but rather from complications (eg. respiratory, hemodynamic or infectious); and (2) patients who were treated, died at a different location, and were subsequently brought to this center for the sole purpose of organ donation.

Data Collection

We collected the following data: sex; age; type of non-traumatic DBI; date and time of injury; date and time of admission to the intensive care unit (ICU); Glasgow Coma Score (GCS) at ICU admission and at the time of decision for DC or no further surgical intervention; initial imaging report; mechanism, date, and time of death; and ICP management (DC, subdural ICP monitor, ventricular drainage, hyperosmolar therapy, barbiturate coma). Criteria for DC eligibility were per the *DECIMAL, DESTINY and HAMLET trials.*[5-7] The timing of DC, type of DC, and highest ICP and cerebral perfusion pressure (CPP) values within 24 hours before and after DC were also collected.

If GCS data was missing for a given subject, the description of their level of consciousness was recorded and subsequently converted into a GCS score by a neurologist review (JT). The variable "mechanism of death" was defined as death determined by neurological criteria (NDD) or by circulatory criteria (DCD, e.g. death following cardiac arrest; including after withdrawal of life-sustaining treatment).

Statistical Analysis

Statistical analysis was done using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp. Armonk, NY). Continuous variables are presented as mean or median values with ranges, and compared by the t-test. Discrete variables are presented as frequencies with percentages. Categorical variables were compared by the χ^2 test. The point estimate, odds ratio, and 95% confidence interval and p-value was calculated for the incident death by circulatory criteria between the DC and non-DC groups.

Results

160 patients who died following a non-traumatic DBI at the Montreal Neurological Institute between January 2008 and December 2012 were included in this retrospective study. 26 patients were treated with DC and 134 patients received standard of care. Descriptive data of the overall sample and of the groups is found in Table 1. The DC group was significantly younger ($p = 0.001$). There was no difference in GCSs at admission ($p = 0.184$) or at decision for DC versus no further surgical intervention ($p = 0.172$). There was no relationship between DC status and gender (χ^2 $(1) = 0.606$, $p = 0.436$), or mechanism of injury (χ^2 $(5) = 4.576$, $p = 0.470$). There was a relationship between DC status and ICP monitoring (χ^2 $(1) = 12.362$, $p < 0.001$), hyperosmolar therapy (χ^2 $(1) = 8.712$, $p = 0.003$), and barbiturate use (χ^2 $(1) = 5.7102.p = 0.017$), indicating that the DC group had significantly higher levels of pressure monitoring and management prior to decompression, and more barbiturate use compared to the standard treatment group.

The average time from injury to DC was 33.65 hours, with a median time of 9.83 hours (3-227 hours). The most frequent type of DC was fronto-temporo-parietal (57.7%), followed by fronto-temporal (11.5%), suboccipital (11.5%), fronto-parietal (7.7%), temporal (3.8%), occipital (3.8%), and complete hemicraniectomy (3.8%). For patients receiving DC, death was determined using circulatory criteria in 20 (76.9%) and neurologic criteria in 6 (23.1%). For patients receiving standard care, death was determined using circulatory criteria in 99 (73.9%) and neurologic criteria in 35 (26.1%). There was no relationship between DC status and mechanism of death (OR 1.18, 95% CI 0.44-3.17).

Discussion And Conclusion

In this retrospective chart review of 160 patients who died after non-traumatic DBI, we did not find a significant difference in the mechanism of death between patients who received DC and those who did not. The findings of this study may be influenced by limitations of the study design, including its retrospective nature and the small, unequal, and unmatched sample sizes in the DC versus standard care group. These findings are in contradiction to a matched retrospective cohort study, by our group, of patients who died after traumatic DBI, which showed that DC increases the incidence of death by circulatory criteria.[9] Although our findings are preliminary, and further prospective studies are required, it may be that the influence of DC on the mechanism of death and resulting potential for organ donation depends on the etiology of the DBI. Age and comorbid cerebrovascular disease as well as differing approaches regarding WLST decisions may also be factors. It is possible that the group in whom DC was not offered simply did not have a large component of intracranial hypertension and that their morbidity was due to the large amount of ischemic damage. They would then not be an equivalent group, and it would not be surprising that they did not die from herniation and brain death.

In this cohort, criteria for DC eligibility were per the *DECIMAL, DESTINY and HAMLET trials,*[5-7] but the final decision to intervene with DC was at the discretion of the attending neurosurgeon and not protocolized. Although there was no difference in the GCS scores, the results suggest that the DC group were in the age group known to benefit most from DC and that had indicators of more severe intracranial hypertension, with higher

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Table 1: Patient demographics

	Total Sample (n = 160)	Decompressive Craniectomy (n = 26)	Standard Care (n = 134)	*P value*
Age, mean (range) years	65(23-93)	56(23-78)	66(28-93)	0.001
Gender, Male (%)	75(42)	14(54)	61(46)	0.436
GCS, mean (range)				
At admission	6.9(3-15)*	7.4(3-15)	6.8(3-14)*	0.184
At decision for DC/no further surgical intervention	6.0(3-15)*	6.5(3-15)	5.9(3-15)*	0.172
Mechanism of Injury				0.470
CVA	19(11.9%)	2(7.7%)	17(12.7%)	
ICH alone	71(44.4%)	12(46.2%)	59(44%)	
ICH with added pathology (SAH, IVH, Subdural Hematoma, Anoxic Brain Injury)	18(11.3%)	4(15.4%)	14(10.4%)	
SAH alone and SAH with added pathology (Anoxic Brain Injury, Vasospasm, Subdural Hematoma, IVH)	42(26.3%)	5(19.2%)	37(27.6%)	
Venous thrombosis	2(1.3%)	0(0%)	2(1.5%)	
Subdural Hematoma	8(5%)	3(11.5%)	5(3.7%)	
ICP Monitoring				$<0.001^{\dagger}$
Ventricular Drainage	84(52.5%)	21(80.8%)	63(47%)	
Subdural ICP Monitor	1(0.6%)	1(3.8%)	0(0%)	
None	75(46.9%)	4(15.4%)	71(53%)	
Hyperosmolar Therapy				$0.003^{\dagger}$
Hypertonic Saline	8(5%)	2(7.7%)	6(4.5%)	
Mannitol	42(26.3%)	9(34.6%)	33(24.6%)	
Hypertonic Saline & Mannitol	66(41.3%)	14(53.8%)	52(38.8%)	
None	44(27.5%)	1(3.8%)	43(32.1%)	
Barbiturates				$0.017^{\dagger}$
Low dosage	2(1.3%)	1(3.8%)	1(0.7%)	
Higher dosage - Barbiturate Coma	1(0.6%)	1(3.8%)	0(0%)	
None	157(98.1%)	24(92.3%)	133(99.3%)	

GCS = Glasgow Coma Scale; DC = Decompressive Craniectomy; CVA = cerebrovascular accident; ICH = intracranial hemorrhage; SAH = subarachnoid hemorrhage; IVH = intraventricular hemorrhage; ICP = intracranial pressure.

*GCS at admission: n = 126 for Standard Care Group, n = 152 for total sample; GCS at decision for no further surgical intervention in the Standard Care Group: n = 132 and n = 158 for the total sample.

†p values for Chi-Square testing were for the following comparisons: ventricular drainage or subdural ICP monitor vs no monitoring; hypertonic saline or mannitol or hypertonic saline and mannitol vs no hyperosmolar therapy; low dose barbiturate or high dose barbiturate (barbiturate coma) vs no barbiturates.

use of intracranial pressure monitors, hyperosmolar therapies, and barbiturates.

In preparation for this study we also conducted a systematic review of RCTs that reported outcomes after DC in all forms of DBI. The RCT by Taylor et al.[4] was the only study selected for full text review that met our inclusion criteria of reporting the mechanism of death. No clear conclusions could be made. One other recent retrospective study investigated the impact of DC on the evolution to brain death, with 206/698 patients with various brain injuries receiving DC.[8] Their findings are similar to ours in that they did not detect a significant difference in mechanism of death after DC. The vast majority of previous studies do not distinguish mechanism of death in DC. We would advocate that any outcome study in DBI include the manner in which death is determined, as organ donation potential is a societally relevant outcome to follow.

Supplementary Material

To view supplementary material for this article, please visit https://doi.org/10.1017/cjn.2016.320

Disclosures

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Statement of Authorship

KT, LH, JT, and SDS participated in the conception, design, data analysis, interpretation, drafting and the critical revising for

important intellectual content of this manuscript, and approved the final version. KT, LH, and JT participated in the data collection.

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