Hemicraniectomy for Supratentorial Primary Intracerebral Hemorrhage: A Retrospective, Propensity Score Matched Study

Kasey L. Gildersleeve, MD,* Mohammad I. Hirzallah, MD,*
Yoshua Esquenazi, MD,† Charles J. Moomaw, PhD,‡ Padmini Sekar, MS,‡
Chunyan Cai, PhD,§ Nitin Tandon, MD,† Daniel Woo, MD,‡ and
Nicole R. Gonzales, MD*

Background and Purpose: Spontaneous supratentorial intracerebral hemorrhage (ICH) contributes disproportionately to stroke mortality, and randomized trials of surgical treatments for ICH have not shown benefit. Decompressive hemicraniectomy (DHC) improves functional outcome in patients with malignant middle cerebral artery ischemic stroke, but data in ICH patients is limited. We hypothesized that DHC would reduce in-hospital mortality and poor functional status (defined as modified Rankin scale ≥5) among survivors at 3 months, without increased complications. *Methods:* We performed a retrospective, case-control, propensity score matched study to determine whether hemicraniectomy affected outcome in patients with spontaneous supratentorial ICH. The propensity score consisted of variables associated with outcome or predictors of hemicraniectomy. Forty-three surgical patients were matched to 43 medically managed patients on ICH location, sex, and nearest neighbor matching. Three-month functional outcomes, in-hospital mortality, and in-hospital complications were measured. *Results:* In the medical management group, 72.1% of patients had poor outcome at 3 months compared with 37.2% who underwent hemicraniectomy (odds ratio 4.8, confidence interval 1.6-14). In-hospital mortality was 51.2% for medically managed patients and 16.3% for hemicraniectomy patients (odds ratio 8.5, confidence interval 2.0-36.8). There were no statistically significant differences in the occurrence of in-hospital complications. *Conclusions:* In our retrospective study of selected patients with spontaneous supratentorial ICH, DHC resulted in lower rate of in-hospital mortality and better 3-month functional status compared with medically managed patients. A randomized trial is necessary to evaluate DHC as a treatment for certain patients with spontaneous supratentorial ICH.
Key Words: Intracerebral hemorrhage—hemicraniectomy—mortality—functional outcomes
© 2019 Elsevier Inc. All rights reserved.

Introduction

Despite advances in stroke care, spontaneous intracerebral hemorrhage (ICH) remains fatal in up to 50% of patients within 30 days of ictus.[1] Though prognostic factors such as age, hematoma location, and neurologic deficit on presentation are fixed, potentially modifiable factors such as hematoma size and expansion have become the targets of interventions in randomized control trials in hope of improving patient outcomes.[2,3]

Given the absence of clear benefit of medical interventions in ICH patients, attention has shifted toward the potential benefit of surgical management via reduction of the direct mass effects of the hematoma. The International Surgical Trial in Intracerebral Hemorrhage (STICH I) study compared early surgery with initial conservative management for spontaneous supratentorial ICH, and it found no difference in neurologic outcome at 6 months; however, a subgroup of patients with hemorrhage within 10 mm of cortical surface appeared to benefit from early surgery.[4] Consequently, STICH II compared early surgery with initial conservative management in this particular patient population, but it also found no significant difference in neurologic outcome.[5] The authors of STICH II added their data to an existing meta-analysis of published data that compared surgery versus conservative management for ICH. They found that surgery reduced the odds of unfavorable outcome (defined as severe disability, vegetative state, or death on Extended Glasgow Outcome Scale), yet the meta-analysis had significant heterogeneity in patient populations and surgical treatments.[5,6] Of note, craniotomy with clot evacuation was the procedure performed in 75% of STICH I patients and 99% of STICH II patients; very few underwent minimally invasive surgery, which was evaluated in the Minimally Invasive Surgery Plus Rt-PA for ICH Evacuation (MISTIE) phase 3 trial[4,5,7] and still being evaluated in the Early Minimally invasive Removal of Intracerebral Hemorrhage (ENRICH) trial. In current practice, surgical intervention is offered to select patients at clinicians' discretion.[8]

The natural history of malignant middle cerebral artery (MCA) ischemic stroke leads to death in nearly 80% of patients despite medical treatment, in large part due to significant mass effect and edema that progressively causes herniation. The pooled study of DESTINY (decompressive surgery for the treatment of malignant infarction of the MCA), DECIMAL (decompressive craniectomy in malignant MCA infarcts), and HAMLET (hemicraniectomy after MCA infarction with life-threatening edema) demonstrated that decompressive hemicraniectomy (DHC) for malignant MCA ischemic stroke resulted in a 50% absolute risk reduction in both mortality and unfavorable neurologic outcome (defined as modified Rankin scale (mRS) ≥5) at 1 year. In essence, 2 patients are needed to undergo surgery to achieve 1 fewer fatality or unfavorable neurologic outcome.[9] Given that similar space-occupying effects are seen in some patients with ICH, it makes intuitive sense that DHC might offer benefit for selected ICH patients as well.

We performed a retrospective case-control study of DHC for supratentorial spontaneous ICH, with the hypothesis that DHC would reduce both in-hospital mortality and poor functional outcome at 3 months, without increased in-hospital complications.

Materials and Methods

In 2010, we developed a protocol for surgical management of patients with ICH at McGovern Medical School at The University of Texas-Houston. Inclusion criteria for consideration of DHC were admission Glasgow Coma Scale (GCS) score 12-15 with deterioration, age ≤60, and ICH volume 20-70 cc with mass effect. For this project's surgical cohort, we screened patients in our prospectively collected stroke registry[10] and hospital administrative data, and identified patients who were discharged between January 2011 and August 2014 with the diagnosis of ICH. Patients were subsequently included if they received a DHC with or without hematoma evacuation during their hospitalization; patients were excluded if they had infratentorial (brainstem or cerebellar) ICH, secondary cause of ICH (e. g., trauma, vascular malformation, mass), or care directed toward comfort measures within 48 hours of admission. The local institutional review board approved the study and waived the need for patient consent.

For our control cohort, we retrospectively screened cases enrolled in the prospective multicenter Ethnic/ Racial Variations of Intracerebral Hemorrhage (ERICH)[11] study and identified participants enrolled between January 2011 and August 2014, contemporaneous with our surgical cohort. ERICH did not enroll cases with secondary causes of ICH. For the present analysis, in addition to infratentorial ICH and patients with care directed toward comfort measures, we also excluded patients who received a surgical intervention for management of their ICH, namely hemicraniectomy, craniotomy, or minimally invasive surgery. We did not exclude patients whose only intervention was extraventricular drain or intracranial pressure monitor placement.

Matched controls were identified based on location of ICH (deep or lobar), sex, and nearest neighbor matching within specified propensity score calipers. The propensity score model consisted of patient factors deemed to be associated with clinician's decision to pursue DHC or to affect outcome. The variables incorporated into the original model were age, presence of intraventricular hemorrhage, ICH volume, anticoagulant use, right hemisphere lesion, GCS) on presentation, and insurance status (categorized as either self-pay or insured). Following a stepwise approach of incorporating the most influential variables into the model, age, volume, and GCS remained. Anticoagulant use and right hemisphere were not found to be predictive, but they were forced into the propensity score model based upon the assumed weight

these variables carry in physicians' determination of risk of complications from surgery and postprocedure functional outcome. Matched pairs in which the difference in propensity score between the case and control was ≤.1 were used for analysis. Hematoma volumes were measured on CT scans in an automated fashion using the Analyze 12.0 software, and the ICH volumes used for the model were the largest preoperative volume for DHC cases and the largest ICH volume within 24 hours of admission for controls.

The primary outcome was poor neurologic function at 3 months, defined as mRS of 5 (severe disability; bedridden, incontinent and requiring constant nursing care and attention) or 6 (deceased). Secondary outcomes included in-hospital mortality, hospital complications (e.g., recurrent ICH, seizure, sepsis, venous thromboembolism, and cardiac arrest), and discharge disposition to inpatient rehabilitation. The mRS for the surgical cohort was extrapolated from available clinical information in the medical record, and for the control cohort mRS was routinely collected at specific time points as part of the ERICH study.

Statistical analysis: To assess for differences in demographic and clinical characteristics between cases and controls, we performed a 2-sampled t test for continuous data, Wilcoxon rank-sum test for ordinal data, and chi-square/Fisher's exact test for categorical data. We performed conditional logistic regression to assess for differences in poor outcome between cases and controls.

Results

A total of 43 patients met eligibility criteria for the surgical cohort; they were matched to 43 contemporaneous controls from the ERICH database. Baseline demographic information is outlined in Table 1. The mean age was 49 years in patients who underwent DHC compared with 52 years in the control group, but this difference was not statistically significant. Higher proportions of patients in the control group were Hispanic, had a history of alcohol use, and were on antiplatelet medication at time of presentation. There were no significant differences in baseline clinical or radiographic characteristics (Table 2). The geometric mean ICH volumes were 55 mL for HC and 61 mL for controls, and median GCS and presence of IVH were similar between groups. There was nearly equal representation of lobar and deep ICH within cases and controls. The median time to surgical intervention in the HC group was 5 hours, and most of the patients in the HC cohort also underwent hematoma evacuation.

The primary outcome of poor neurological status at 3 months was significantly higher for the control cohort (Table 3), 72.1% versus 37.2% (odds ratio 4.8, 95% confidence interval 1.6, 14.0, $P = .005$). A total of 14% of patients in the control group had mRS score of 0-3 compared with 11% of patients in the DHC group. A mRS score of 4 occurred in 14% and 37% of patients in the control and DHC groups, respectively. A score of 5 on the mRS scale was more common in the DHC group; however, death occurred much less frequently in the DHC group (Fig 1). For the secondary outcomes, patients who were medically managed had significantly higher in-hospital mortality compared with patients who underwent DHC (51.2% versus 16.3%; odds ratio 8.5, 95% confidence interval 2.0, 36.8, $P = .004$). There were no significant differences in rates of complications between groups; however, 5 ischemic strokes occurred in the DHC group versus none in the medically managed group. A higher percentage of patients who underwent DHC were discharged to inpatient rehab, but this did not reach significance.

Table 1. *Baseline demographic characteristics of cases and controls matched on propensity score*

	Hemicraniectomy (n = 43)	No hemicraniectomy (n = 43)	*P* value
Age, mean (SD)	49.2 (12.3)	52.1 (16.0)	.3408
Sex, male (%)	26 (60.5)	26 (60.5)	Matched
Race			
White, n (%)	14 (32.6)	10 (23.3)	
Black	11 (25.6)	12 (27.9)	.0358
Hispanic	11 (25.6)	21 (48.8)	
Other	7 (16.3)	0 (0)	
Comorbidities			
Stroke, n (%)	1 (2.3)	3 (7.0)	.6160
CAD/MI, n (%)	4 (9.3)	3 (7.0)	1.000
Dementia, n (%)	0 (0)	4 (9.3)	.1162
Alcohol use, n (%)	9 (20.9)	29 (67.4)	<.0001
Illicit drug use, n (%)	6 (14.0)	12 (27.9)	.1117
Medications			
Antiplatelet, n (%)	4 (9.3)	15 (34.9)	.0042
Anticoagulant, n (%)	2 (4.7)	4 (9.3)	.6761
Insurance status			
Self-pay, n (%)	5 (11.6)	9 (20.9)	.2427

Abbreviations: CAD/MI, coronary artery disease/myocardial infarction.

Table 2. *Clinical and radiographic characteristics of cases and controls matched on propensity score*

	Hemicraniectomy (n = 43)	No hemicraniectomy (n = 43)	*P* value
GCS, median (IQR)	8 (3, 11)	6 (3, 11)	.9581
ICH volume (cc), geometric mean (95% CI)	55.3 (48.3, 63.2)	61.1 (52.1, 71.6)	.3357
Side			
Right, n (%)	24 (55.8)	18 (41.9)	.1955
Location			
Deep, n (%)	21 (48.8)	21 (48.8)	Matched
Lobar, n (%)	22 (51.2)	22 (51.2)	
Presence of IVH, n (%)	28 (65.1)	31 (72.1)	.4858
Coagulopathy, n (%)	10 (23.3)	14 (37.8)	.1559
Time to surgery (min), median (IQR)	309 (118,804)	-	
Hematoma evacuation, n (%)	33 (76.7)	0 (0)	-

Abbreviations: IQR, interquartile range; CI, confidence interval; GCS, Glasgow coma scale; ICH: intracerebral hemorrhage; IVH, intraventricular hemorrhage.

Table 3. *Clinical outcomes of cases and controls matched on propensity score*

	Hemicraniectomy (n = 43)	No hemicraniectomy (n = 43)	Odds ratio (95% CI)	*P* value
Primary outcome				
mRS ≥ 5 at 3 months, n (%)	16 (37.2)	31 (72.1)	4.8 (1.6, 14.0)	.0046
Secondary outcomes				
In-hospital mortality, n (%)	7 (16.3)	22 (51.2)	8.5 (2.0, 36.8)	.0042
Discharge to inpatient rehabilitation, n (%)	14 (32.6)	6 (14.0)	2.3 (0.8, 7.4)	.1153
Complications (%)				
Recurrent ICH	3 (7.0)	0 (0)		.2412
Seizure	7 (16.3)	6 (14.0)		.7634
Ischemic stroke	5 (11.6)	0 (0)		.0553
Cardiac arrest	3 (7.0)	2 (4.7)		1.000
MI	1 (2.3)	0 (0)		1.000
Sepsis	5 (11.6)	3 (7.0)		.7130
DVT/PE	1 (2.3)	0 (0)		1.000

Abbreviations: DVT/PE, deep venous thrombosis/pulmonary embolism; ICH, intracerebral hemorrhage; MI, myocardial infarction; mRS, modified Rankin scale score.
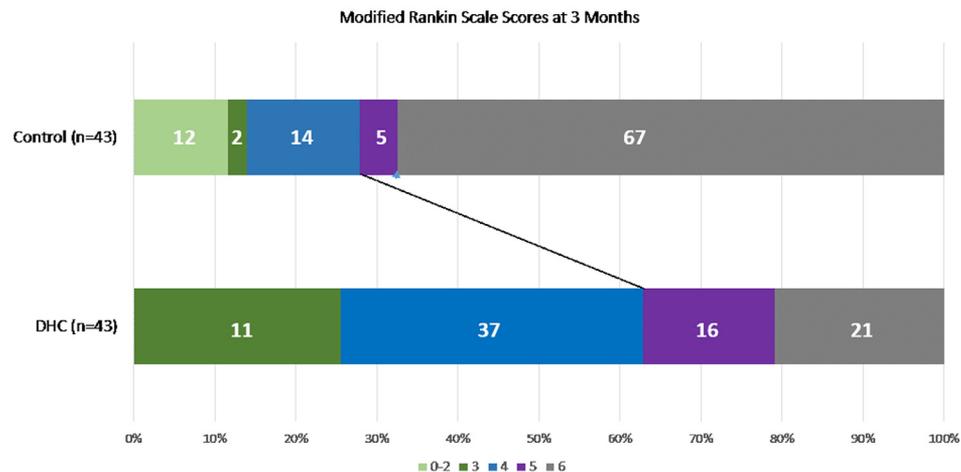

Figure 1. *Functional outcome after decompressive hemicraniectomy and after medical management alone. The primary outcome was poor neurologic function at 3 months, defined as modified Rankin scale score of 5 (severe disability; bedridden, incontinent and requiring constant nursing care and attention) or 6 (deceased). Abbreviations: DHC, decompressive hemicraniectomy.*

Discussion

Our findings demonstrate safety and benefit of DHC for selected patients with spontaneous supratentorial ICH. Though previous randomized studies have not shown a significant benefit on functional outcome with surgical intervention, patients in our cohort generally had more severe strokes than those in clinical trials. Specifically, ICH volumes were considerably larger and more participants were in a comatose state on presentation. Importantly, we excluded patients with early withdrawal of care. Just as DHC is reserved for patients with malignant MCA ischemic stroke, our data suggest that DHC may be an appropriate consideration for large volume hemorrhagic strokes with resultant significant mass effect. We found that DHC with or without hematoma evacuation resulted in a significant reduction in the odds of both in-hospital mortality and poor functional outcome at 3 months, without an increased rate of complications.

Data on DHC for ICH remain mostly limited to case series and small case-control studies. In a preclinical mouse model of ICH, DHC was shown to reduce early and late mortality.[12] In a case series of 12 consecutive patients with hypertensive ICH who received DHC with clot evacuation, Murthy et al found in-hospital mortality was only 8% despite nearly all patients having a predicted mortality of 72% based on their ICH score.[13] There were no controls as a part of this study and the time point for outcome assessment was variable, ranging from 2 to 39 months. The largest published case series to date consists of 73 patients from a single institution, in which the average hematoma volume was 81 mL and one third of patients were in coma on presentation. At 3 months, 27% of patients had died and 29% had a favorable outcome (Glasgow Outcome Scale ≥4), but there was no nonsurgical comparison group.[8] A retrospective case-control study of 5 patients matched on age, side of lesion, lesion volume, and GCS found improvement in functional independence (mRS ≤3) at 6 months.[14] Similarly, in a study of 12 patients with spontaneous supratentorial ICH matched to concurrent controls on age, GCS, hematoma volume, degree of midline shift, and signs of herniation, Fung et al found no difference in good neurologic outcome (mRS ≤4) at 6 months between the 2 groups.[15] They have since embarked on the Swiss Trial of Decompressive Craniectomy Versus Best Medical Treatment of Spontaneous Supratentorial Intracerebral Hemorrhage (SWITCH, NCT02258919), a randomized controlled study of 300 patients to assess the benefit of DHC in spontaneous deep (basal ganglia and thalamus) ICH. More recently, a retrospective case-control study of spontaneous ICH comparing DHC to medical management found reduced mortality at 1 month, 6 months, and 12 months in the surgical group, but there was no difference in functional outcome at discharge, 3, 6, or 12 months.[16] However, this study was performed at a single center and the authors acknowledged potential selection bias in the decision for a patient to undergo surgery.

Our 3-month mRS results demonstrate that in this condition with high morbidity and mortality, treatment with DHC may be lifesaving with the trade-off of survival with a high degree of disability. In ischemic stroke trials of hemicraniectomy, this dilemma becomes more relevant with increasing age.[17] Our findings highlight the importance of the randomized controlled trial, SWITCH, to address these and other important issues in this patient population.

A strength of our case-control analysis is our use of a propensity score model that consisted of variables which may affect physicians' decision to proceed with DHC. These variables not only included those known to be associated with prognosis in ICH (e.g., age, GCS, ICH volume), but also anticoagulant use and side of lesion, which some may view as prognostic as well. Anticoagulant use increases risk of hematoma expansion, which is associated with worse outcome.[18] Aphasia and other language deficits accompany dominant side lesions, which can contribute to less independence.[19]

There are several limitations to our study. Despite the propensity score matched method, our study is small and retrospective in nature. Our surgical cohort consisted of 43 patients from a single center and results may not be generalizable. Functional outcomes for our surgical cohort were extrapolated from chart review, which is subject to bias. In contrast, the control cohort included all participants in an observational clinical trial where outcome data were prospectively collected. Although our surgical protocol required the presence of mass effect on imaging, which can be an important variable in the decision to pursue DHC, we did not include the presence of mass effect in our analysis. This could be considered a limitation; however, the geometric means for ICH volume were 55.3 and 61.1 cc for the DHC and medically managed groups, respectively. These large hematoma sizes in our relatively young cohort imply that mass effect was probably present in most patients. Last, the majority of the surgical patients received DHC with clot evacuation, and thus we were not able to assess for differential effects of DHC with and without clot evacuation.

Summary

In our study, DHC reduced in-hospital mortality and poor functional outcome at 3 months in patients with supratentorial spontaneous ICH without increased complications. Results from a randomized controlled trial of DHC with or without hematoma evacuation versus standard treatment are needed to confirm these findings to support implementation into routine clinical practice.

Declaration of Competing Interest

The authors declare no conflicts of interest.

References

1. Morgenstern LB, Hemphill 3rd. JC, Anderson C, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2010;41(9):2108-2129.
2. Dey M, Stadnik A, Awad IA. Spontaneous intracerebral and intraventricular hemorrhage: advances in minimally invasive surgery and thrombolytic evacuation, and lessons learned in recent trials. Neurosurgery 2014;74(Suppl 1):S142-S150.
3. Qureshi AI, Palesch YY. Antihypertensive treatment of acute cerebral hemorrhage (ATACH) II: design, methods, and rationale. Neurocrit Care 2011;15(3):559-576.
4. Mendelow AD, Gregson BA, Fernandes HM, et al. Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral haematomas in the International Surgical Trial in Intracerebral Haemorrhage (STICH): a randomised trial. Lancet 2005;365(9457):387-397.
5. Mendelow AD, Gregson BA, Rowan EN, et al. Early surgery versus initial conservative treatment in patients with spontaneous supratentorial lobar intracerebral haematomas (STICH II): a randomised trial. Lancet 2013;382 (9890):397-408.
6. Mendelow AD, Gregson B. Surgery for intracerebral hemorrhage. In: Mohr J, Wolf P, Grotta JC, Moskowitz M, Mayberg M, von Kummer R, eds. Stroke: Pathophysiology, Diagnosis, and Management, 5th ed., Philadelphia, PA: WB Saunders; 2011.
7. Hanley DF, Thompson RE, Muschelli J, et al. Safety and efficacy of minimally invasive surgery plus alteplase in intracerebral haemorrhage evacuation (MISTIE): a randomised, controlled, open-label, phase 2 trial. Lancet Neurol 2016;15(12):1228-1237.
8. Esquenazi Y, Savitz SI, El Khoury R, McIntosh MA, Grotta JC, Tandon N. Decompressive hemicraniectomy with or without clot evacuation for large spontaneous supratentorial intracerebral hemorrhages. Clin Neurol Neurosurg 2015;128:117-122.
9. Vahedi K, Hofmeijer J, Juettler E, et al. Early decompressive surgery in malignant infarction of the middle cerebral artery: a pooled analysis of three randomised controlled trials. Lancet Neurol 2007;6(3):215-222.
10. Rahbar MH, Gonzales NR, Ardjomand-Hessabi M, et al. The University of Texas Houston Stroke Registry (UTHSR): implementation of enhanced data quality assurance procedures improves data quality. BMC Neurol 2013;13:61.
11. Woo D, Rosand J, Kidwell C, et al. The ethnic/racial variations of intracerebral hemorrhage (ERICH) study protocol. Stroke 2013;44(10):e120-e125.
12. Omary R, Chernoguz D, Lasri V, Leker RR. Decompressive hemicraniectomy reduces mortality in an animal model of intracerebral hemorrhage. J Mol Neurosci 2013;49(1):157-161.
13. Murthy JM, Chowdary GV, Murthy TV, Bhasha PS, Naryanan TJ. Decompressive craniectomy with clot evacuation in large hemispheric hypertensive intracerebral hemorrhage. Neurocrit Care 2005;2(3):258-262.
14. Heuts SG, Bruce SS, Zacharia BE, et al. Decompressive hemicraniectomy without clot evacuation in dominant-sided intracerebral hemorrhage with ICP crisis. Neurosurg Focus 2013;34(5):E4.
15. Fung C, Murek M, Z'Graggen WJ, et al. Decompressive hemicraniectomy in patients with supratentorial intracerebral hemorrhage. Stroke 2012;43(12):3207-3211.
16. Lo YT, See AAQ, King NKK. Decompressive Craniectomy in Spontaneous Intracerebral Hemorrhage: A Case-Control Study. World Neurosurg 2017;103:815-820. e2.
17. Juttler E, Bosel J, Amiri H, et al. DESTINY II: DEcompressive Surgery for the Treatment of malignant INfarction of the middle cerebral arterY II. Int J Stroke 2011;6(1):79-86.
18. Cucchiara B, Messe S, Sansing L, Kasner S, Lyden P, Investigators C. Hematoma growth in oral anticoagulant related intracerebral hemorrhage. Stroke 2008;39 (11):2993-2996.
19. Lazar RM, Boehme AK. Aphasia as a predictor of stroke outcome. Curr Neurol Neurosci Rep 2017;17(11):83.