Timing of decompressive hemicraniectomy for stroke: a nationwide inpatient sample analysis

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Timing of Decompressive Hemicraniectomy for Stroke

A Nationwide Inpatient Sample Analysis

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Background and Purpose—Previous clinical trials were not designed to discern the optimal timing of decompressive craniectomy for stroke, and the ideal surgical timing in patients with space-occupying infarction who do not exhibit deterioration within 48 hours is debated.

Methods—Patients undergoing decompressive craniectomy for stroke were extracted from the Nationwide Inpatient Sample (2002–2011). Multivariable logistic regression evaluated the association of surgical timing with mortality, discharge to institutional care, and poor outcome (a composite end point including death, tracheostomy and gastrostomy, or discharge to institutional care). Covariates included patient demographics, comorbidities, year of admission, and hospital characteristics. However, standard stroke severity scales and infarct volume were not available.

Results—Among 1301 admissions, 55.8% (n=726) underwent surgery within 48 hours. Teaching hospital admission was associated with earlier surgery (P=0.02). The timing of intervention was not associated with in-hospital mortality. However, when evaluated continuously, later surgery was associated with increased odds of discharge to institutional care (odds ratio, 1.17; 95% confidence interval, 1.05–1.31, P=0.005) and of a poor outcome (odds ratio, 1.12; 95% confidence interval, 1.02–1.23; P=0.02). When evaluated dichotomously, the odds of discharge to institutional care and of a poor outcome did not differ at 48 hours after hospital admission, but increased when surgery was pursued after 72 hours. Subgroup analyses found no association of surgical timing with outcomes among patients who had not sustained herniation.

Conclusions—In this nationwide analysis, early decompressive craniectomy was associated with superior outcomes. However, performing decompression before herniation may be the most important temporal consideration.

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Key Words: cerebral infarction ■ decompressive craniectomy ■ early intervention ■ middle cerebral artery ■ stroke ■ time

The original randomized, controlled clinical trials that established the efficacy of decompressive hemicraniectomy after space-occupying, malignant cerebral artery infarction were neither designed nor powered to evaluate the optimal timing of intervention. Because of the time frame used as enrollment criteria in these clinical trials, the initial pooled analysis was restricted to patients treated within 48 hours[1–3]; therefore, subsequent guidelines recommended intervention be pursued within 2 days of the onset of stroke symptoms.[4] However, few patients in these randomized controlled trials underwent surgery after 48 hours, limiting assessment of outcomes based on the timing of surgery.

Several factors influence the timing of decompressive hemicraniectomy, including the severity of infarction, antithrombotic medications, and the tempo of developing malignant cerebral edema.[5] Previous publications have found that the progression of cerebral edema after acute infarction ranges between 2 and 5 days: while 68% of patients exhibit clinical deterioration within 48 hours of symptom onset, almost one third of patients experience worsening of sensorium after 48 hours.[6] In such cases, clinicians are faced with a dilemma of pursuing a hemicraniectomy before significant neurological deterioration from mass effect has transpired, or performing surgery outside of the recommended interval. In addition, inappropriate patient selection and overutilization of surgery is suboptimal, as decompressive craniectomy carries a risk of additional perioperative complications, including infection and reoperation.

The utilization of decompressive craniectomy in the setting of stroke is increasing,[7] and authors have highlighted the need

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for additional data analyzing the optimal timing of surgery.[8,9] The goal of this study is to use the Nationwide Inpatient Sample (NIS), the largest all-payer inpatient database in the United States, to evaluate (1) what are the predictors of the timing of decompressive craniectomy after stroke? (2) What is the association of the timing of surgery with postoperative outcomes? (3) Can an optimal time period be discerned for surgical intervention? and (4) Does the association of timing of intervention with outcomes vary based on herniation or patient age?

Methods

Data Source

Data were extracted from the NIS (Healthcare Cost and Utilization Project, Agency Healthcare Research and Quality). A 20% stratified sample of hospital admissions in the United States, the NIS has previously been used to evaluate patients undergoing craniectomy for acute ischemic stroke. The NIS underwent a redesign in 2012, prohibiting appropriate variance calculations of populations from before and after the redesign—therefore, the study population was restricted to 2002 to 2011. Our institutional review board has exempted the NIS from individual study review.

Inclusion Criteria

Patients were included who met the specified inclusion criteria: (1) had a primary *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) diagnosis code of acute ischemic stroke (433.11, 433.31, 433.81, 433.91, 434.01, 434.11, and 434.91); (2) had an ICD-9-CM procedure code indicating a craniectomy (01.25) or craniotomy (01.24), with or without concomitant lobectomy (01.39, 01.53, and 01.59); (3) were aged at least 18 years; and (4) the hospital admission was nonelective. Similar diagnosis and procedure codes have been utilized in other ICD-9-CM–based studies of decompressive craniectomy for stroke.[10] However, admissions with the following secondary diagnoses were excluded: arteriovenous malformation (747.81), brain tumor (191.x, 192.0, 192.1, 194.3 198.3, 198.4, 199.0, 200.5, 225.x, 227.3, 237.0, 237.5, and 237.6), cerebral arteritis (437.4), extra-axial hematoma (432.0, 432.1, and 432.9), head trauma (80x.xx and 85x.xx), intracranial abscess (324.0), Moyamoya disease (437.5), subarachnoid hemorrhage (430), unruptured cerebral aneurysm (437.3), venous sinus thrombosis (437.6), vertebral artery dissection (443.24), or vertebrobasilar infarction (433.01 and 433.21). In addition, admissions with the following procedure codes were excluded: arteriovenous malformation repair (39.53), carotid artery stent placement (00.63), carotid endarterectomy (38.12), cranioplasty (02.03–02.07), microsurgical clipping of a cerebral aneurysm (39.51, 39.52), stereotactic radiosurgery (92.3x), or laminectomy (as a C1 laminectomy is a common component of a suboccipital craniectomy, 03.09). Because the goal of this analysis was to examine the optimal timing of decompressive craniectomy after hospital admission among patients presenting with acute ischemic stroke, patients who underwent surgery more than 7 days after admission were excluded (n=70), as these patients were unlikely to have been admitted with space-occupying infarction.

Timing of Surgery

Procedure day is encoded in the NIS. To maximize available information, in the primary analysis, the timing of surgery was evaluated continuously. Thereafter, to increase clinical interpretability, the timing of surgery was examined dichotomously at 1, 2, and 3 days (24, 48, and 72 hours) after hospital admission.

Covariates

Patient age, sex, year of admission, and primary expected payer were extracted. The first age division was 50 years, as this was approximately the lower quartile of the interquartile range of the study population. Sixty years was selected as the second division to match the enrollment criteria of the initial randomized controlled trials.[11] Medical comorbidities were evaluated using the components of the Elixhauser scale. Comorbidities encoded in fewer than 20 patients were not evaluated individually; neurological disorders or paralysis were not considered comorbidities because of the potential misclassification with the primary diagnosis. Additional stroke risk factors that are not included in the Elixhauser score were extracted: atrial fibrillation (427.31), carotid dissection (443.21), carotid stenosis (433.10, 433.11), hypercoaguable state (289.81, 289.82), hyperlipidemia (272.x) and tobacco use (305.1).

Severity adjustment was estimated using relevant ICD-9 codes, as standard stroke severity scales and infarct volume were not available. To account for documented neurological examination, aphasia (438.1x and 784.3) and hemiplegia/paresis (438.2-5x and 342.xx) were included. Infarction severity was estimated by herniation (348.4) and cerebral edema (348.5). Coma (780.01 and 780.03) and mechanical ventilation (967.x) were used as markers of poor mental status. Treatment variables evaluated included weekend hospital admission, thrombolytic administration (99.10 and V45.88), mechanical thrombectomy (39.74), and ventriculostomy (02.2 and 02.21). Hospital characteristics encoded in the NIS include bed size, control, location, region, and teaching status.

Outcome Measures

Six outcomes were evaluated: inpatient mortality, neurological complications, tracheostomy (31.1 and 31.2x) and gastrostomy (43.1x, 46.32) placement, length of hospital stay, discharge disposition, and a poor outcome. Neurological complications included intracranial hemorrhage (431), postprocedure neurological complications (997.01 and 997.09), seizures (345.xx), and stroke (433.x and 434.x). An extended hospitalization was defined as a hospital stay longer than the upper quartile of the interquartile range for the entire population. Discharge to institutional care included discharge to a nursing facility, extended care facility, or hospice, but did not include rehabilitation or another acute care facility. Analyses of tracheostomy and gastrostomy, length of stay, and discharge disposition were only performed for patients discharged alive, to differentiate these measures from mortality. Finally, the composite NIS-subarachnoid hemorrhage outcome measure (NIS-SOM) was analyzed, which defines a poor outcome by in-hospital mortality, tracheostomy and gastrostomy placement, or discharge to institutional care. The NIS-SOM has been externally validated against physician review and shown (in the subarachnoid hemorrhage population) to have 91% agreement with a modified Rankin Scale score of >3.

Missing Data

Some variables in the NIS are not reported by every state, and the timing of procedures was not reported from Hawaii, Ohio, Oklahoma, Wisconsin, and West Virginia during the duration of the study, and from Illinois, Kansas, and Washington during some of the years evaluated; these patients were excluded from the primary analysis. In addition, data on to institutional care placement are not recorded from California, Maryland, or Maine, who comprised 20.8% (n=205) of patients in the primary analysis and were excluded from the analysis of this outcome and of the NIS-SOM.

Subgroup and Sensitivity Analyses

A subgroup analysis exclusively evaluated patients who did not have a diagnosis of herniation. In addition, sensitivity analyses were performed with an interaction between the timing of intervention (when evaluated continuously) and patient age, as well as between the timing of surgery and herniation. Finally, another sensitivity analysis compared the demographics and outcomes of patients with a known day of intervention to those without a documented timing of surgery, to evaluate if missing data introduced a selection bias.

Statistical Analyses

Statistical analyses were performed using STATA 13.0 (StataCorp, College Station, TX), after accounting for the survey design of the

NIS, including the NIS strata and discharge weights. First, regression models evaluated the predictors of timing of surgery: logistic regression was used when time was evaluated dichotomously, and linear regression was used when time was analyzed continuously. Univariable regression screened potential predictors, and those with a $P<0.25$ were included in the final model. Subsequently, logistic regression models evaluated the association of timing of intervention with the 6 outcomes evaluated. All described patient and hospital characteristics were included as covariates in these models, due to their potential association with the timing of surgery and outcomes. Subsequently, a sensitivity analysis was performed of outcomes using a propensity score (modeled with a spline with 5 knots) as a covariate. Concordance (C) statistics assessed the discriminatory capacity and the Hosmer–Lemeshow test the calibration of logistic regression models. Probability values <0.05 were considered significant.

Results

Baseline Characteristics

A total of 1301 admissions were included: 22.1% (n=287) underwent surgery within 24 hours, 55.8% (n=726) within 48 hours, and 76.8% (n=999) within 72 hours of hospital admission. The demographics of the study population are stratified by the performance of surgery within 48 hours in Table 1.

Predictors of the Timing of Intervention

Multivariable logistic regression models evaluated the predictors of surgical timing: linear regression analyzed the timing of decompression continuously, and logistic regression examined the timing of surgery dichotomously, stratified at 48 hours. In both analyses, admission to a teaching hospital and atrial fibrillation were associated with earlier surgery, whereas carotid stenosis was associated with later surgery (Table 2). In addition, in the dichotomous analysis, cardiac valvular disease was associated with later surgery. Notably, the proportion of patients with carotid stenosis did not differ by teaching hospital admission ($P=0.66$).

Outcomes

The association of the timing of intervention with outcomes is reported in Table 3; the timing of surgery was evaluated continuously and dichotomously at 24, 48, and 72 hours after hospital admission. In-hospital mortality did not differ significantly by surgical timing when evaluated continuously or dichotomously (Figure). When the timing of surgery was evaluated continuously, later surgery was associated with greater odds of discharge to institutional care (odds ratio [OR], 1.17; 95% confidence interval [CI], 1.05–1.31; $P=0.005$) and of sustaining a poor outcome (OR, 1.12; 95% CI, 1.02–1.23; $P=0.02$). Subsequently, in dichotomous analyses, surgery within 24 or 48 hours was not associated with differential outcomes. However, surgery after 72 hours was associated with increased odds of discharge to institutional care and of a poor outcome (Table 3). A sensitivity analysis was performed of outcomes using propensity score adjustment in regression analyses, which showed similar statistical analyses as the primary analysis (data not shown).

Subgroup and Sensitivity Analyses

A subgroup analysis was performed exclusively of patients who did not have a diagnosis of herniation ($n=931$), and the timing of surgery (when evaluated continuously) was not associated with differential outcomes (data not shown). Subsequently, multivariable regression constructs evaluated outcomes after including an interaction between patient age and the timing of surgery in addition to other covariates included in other multivariable models. However, no effect measure modification of outcomes was seen by patient age, suggesting that the association of the timing of surgery with outcomes did not vary by patient age. When multivariable regression models included an interaction between herniation and the timing of surgery, herniation was associated with increased odds of mortality (OR, 1.70; 95% CI, 1.14–2.56; $P=0.009$). Moreover, the interaction was significant for discharge to institutional care (OR, 1.36; 95% CI, 1.06–1.75; $P=0.02$) and sustaining a poor outcome (OR, 1.31; 95% CI, 1.01–1.71; $P=0.045$), indicating that the association of surgical timing with these outcomes differs based on herniation.

Missing Data

A total of 1631 patients were included in the initial sample, of whom 4.2% (n=69) were excluded for undergoing surgery more than 7 days after admission, and 16.0% (n=261) were excluded because of missing procedure day. The baseline characteristics of patients with known and unknown timing of surgery were compared (Table I in the online-only Data Supplement). Year of admission, hospital region, and hospital bed size differed significantly by known timing of intervention, attributable to the design of the NIS. In addition, patients with known timing of intervention were less likely to have drug use and more likely to have hypothyroidism as a comorbidity; however, no significant differences were seen in other measures, including stroke risk factors and severity measures. A sensitivity analysis was performed comparing the outcomes of patients with a known timing of intervention to those without a documented day of intervention. The crude rates of mortality (26.2% versus 25.3%), discharge to institutional care (35.0% versus 32.5%), and a poor outcome (70.2% versus 67.2%) were similar between patients with known and missing timing of surgery; likewise, no significant differences in outcomes were seen in multivariable regression constructs (data not shown), suggesting that missing data on the timing of intervention does not introduce a selection bias.

Discussion

In the present analysis, 1301 patients from across the United States were extracted from the National Inpatient Sample to evaluate the predictors of surgical timing and analyze the association of the timing of surgery with outcomes after decompressive craniectomy for space-occupying infarction. First, multivariable regression evaluated the predictors of surgical timing and admission to a teaching hospital was associated with earlier surgery. Increased decompressive hemicraniectomy utilization at academic centers has been reported, hypothesized to be because of specialized stroke units and increased neurological, and neurosurgical staff available for emergent cases.[7] However, this analysis suggests that teaching hospitals also have increased efficiency of stroke care. In addition, atrial fibrillation was associated with

Table 1. Univariable Analysis of Patient and Hospital Characteristics, Stratified by the Timing of Surgery After Hospital Admission

Variable	Total Population (n=1301)	Early Surgery (<48 h; n=726)	Late Surgery (>48 h; n=575)	*P* Value
Patient characteristics				
Age, y				
18–50	35.0	36.4	33.2	Ref.
51–60	27.3	27.4	27.1	0.61
>60	37.7	36.2	39.7	0.18
Sex				
Male	60.5	60.5	61.5	Ref.
Female	39.5	39.5	38.5	0.84
Year of admission				
2002–2005	21.6	19.8	23.8	Ref.
2006–2008	28.5	29.1	27.8	0.13
2009–2011	49.9	51.1	48.4	0.12
Payer status				
Private/other	44.7	43.3	46.6	Ref.
Medicare	29.4	28.1	29.7	0.71
Medicaid	17.1	17.9	16.2	0.29
Self-pay/No-charge	8.8	9.8	7.5	0.19
Comorbidities				
Alcohol abuse	7.4	7.3	7.5	0.96
Anemia deficiency	16.8	16.9	16.7	0.90
Congestive heart failure	9.9	11.7	9.9	0.35
Chronic pulmonary disease	9.5	9.6	9.2	0.77
Coagulopathy	7.8	7.9	7.8	1.00
Diabetes mellitus	25.3	23.4	27.7	0.08
Diabetes mellitus with complications	3.2	2.9	3.5	0.52
Drug abuse	5.8	5.7	6.1	0.70
Hypertension	62.4	62.8	61.9	0.78
Hypothyroidism	5.2	4.4	6.3	0.11
Obesity	8.6	7.7	9.7	0.21
Perivascular disease	8.3	7.9	8.9	0.48
Pulmonary hypertension	3.5	3.9	3.0	0.36
Renal failure	5.2	5.2	5.2	0.95
Valvular disease	5.8	4.8	6.9	0.09
Weight loss	11.2	12.1	9.9	0.22
Stroke risk factors				
Anticoagulation	2.9	3.7	1.9	0.08
Atrial fibrillation	22.0	24.2	19.1	0.03*
Carotid dissection	3.9	3.7	4.2	0.68
Carotid stenosis	17.4	14.3	21.2	0.002*
Hypercoagubility	2.7	2.8	2.6	0.81
Hyperlipidemia	26.2	24.5	28.4	0.13
Tobacco use	18.8	17.5	20.4	0.22
Severity indices				
Aphasia	16.3	16.4	16.2	0.92
Cerebral edema	40.0	39.8	40.2	0.82
Coma	10.5	11.2	9.6	0.28
Hemiparesis/ hemiplegia	54.6	53.3	56.2	0.27
Herniation	28.4	30.3	26.1	0.10
Mechanical ventilation	69.0	70.1	67.7	0.46
Treatment variables				
Weekend admission	28.7	28.0	29.6	0.50
Intravenous thrombolysis	21.1	20.0	22.8	0.21
Intra-arterial therapy	5.3	5.9	4.5	0.40
Ventriculostomy	21.3	23.7	18.4	0.02*
Hospital characteristics				
Hospital bed size				
Small/medium	18.6	19.6	17.4	Ref.
Large	81.4	80.4	82.6	0.41
Hospital location				
Rural	2.7	1.9	3.7	Ref.
Urban	97.3	98.1	96.4	0.09
Hospital teaching				
Nonteaching	23.2	19.7	27.7	Ref.
Teaching	76.8	80.3	72.4	0.001*
Hospital control				
Government/private	82.0	84.6	78.8	Ref.
Private/nonprofit	11.3	10.5	12.4	0.19
Other	6.7	5.0	8.9	
Hospital region				
Northeast	24.6	24.7	24.5	Ref.
Midwest	15.8	16.3	15.3	0.73
South	37.3	36.1	38.8	0.73
West	22.3	23.0	21.4	0.72

*Statistically significant differences with univariable logistic regression.

Table 2. Multivariable Logistic and Linear Regression Models Evaluating the Predictors of Surgical Timing

	Logistic Regression: Timing of Surgery Evaluated Dichotomously at 48 h			Linear Regression: Timing of Surgery Evaluated Continuously		
Variable	OR	95% CI	*P* Value	Coefficient, d	95% CI	*P* Value
Age, y						
<50	Ref.	…	…	Ref.	…	…
51–60	1.12	0.82 to 1.54	0.47	0.08	−0.15 to 0.31	0.50
>60	1.40	0.99 to 1.99	0.06	0.20	−0.04 to 0.45	0.10
Year of admission						
2002–2005	Ref.	…	…	…	…	…
2006–2008	0.77	0.56 to 1.06	0.11	…	…	…
2009–2011	0.73	0.52 to 1.02	0.06	…	…	…
Payer status						
Private/other	Ref.	…	…	Ref.	…	…
Medicare	0.84	0.61 to 1.16	0.29	0.12	−0.13 to 0.37	0.35
Medicaid	0.94	0.67 to 1.31	0.70	0.06	−0.19 to 0.30	0.66
Self-Pay/No-charge	0.74	0.47 to 1.19	0.22	−0.21	−0.50 to 0.08	0.16
Diabetes mellitus	1.26	0.97 to 1.65	0.08	0.16	−0.03 to 0.36	0.10
Hypothyroidism	1.41	0.87 to 2.29	0.17	0.38	−0.04 to 0.79	0.07
Valvular disease	1.73*	1.05 to 2.83*	0.03*	…	…	…
Weight loss	0.81	0.55 to 1.22	0.32	−0.17	−0.44 to 0.09	0.19
Anticoagulation	0.54	0.25 to 1.18	0.12	−0.20	−0.73 to 0.32	0.44
Atrial fibrillation	0.69*	0.51 to 0.93*	0.02*	−0.27*	−0.50 to −0.04*	0.02*
Carotid stenosis	1.61*	1.17 to 2.20*	0.003*	0.32*	0.09 to 0.54*	0.006*
Hyperlipidemia	1.17	0.88 to 1.56	0.27	…	…	…
Tobacco use	1.12	0.82 to 1.52	0.48	…	…	…
Coma	0.86	0.60 to 1.24	0.43	−0.10	−0.35 to 0.15	0.44
Hemiplegia	1.01	0.80 to 1.29	0.92	…	…	…
Herniation	0.91	0.70 to 1.19	0.49	−0.06	−0.24 to 0.12	0.54
Mechanical ventilation	…	…	…	−0.16	−0.35 to 0.02	0.08
Weekend admission	…	…	…	0.11	−0.09 to 0.30	0.28
Thrombolysis	1.18	0.87 to 1.58	0.28	…	…	…
Ventriculostomy	0.74*	0.55 to 1.00*	0.05*	−0.16*	−0.37 to 0.04*	0.12*
Urban hospital	0.45	0.16 to 1.22	0.12	−0.70	−1.49 to 0.08	0.08
Teaching hospital	0.58*	0.37 to 0.91*	0.02*	−0.42*	−0.75 to −0.09*	0.01*
Hospital control						
Government/private	Ref.	…	…	Ref.	…	…
Private/nonprofit	0.72	0.42 to 1.25	0.24	−0.20	−0.61 to 0.21	0.34
Other	1.00	0.54 to 1.83	0.99	0.02	−0.46 to 0.50	0.94
	Concordance statistic: 0.63Hosmer–Lemeshow Test: 0.66			R^2: 0.05		

Logistic regression models are evaluating the odds of undergoing late surgery (after 48 h), with early intervention as the reference group. Linear regression models are analyzing the association with the timing of intervention, with negative values denoting earlier intervention and positive later surgery. CI indicates confidence interval; OR, odds ratio; and Ref., reference.

*Statistically significant differences.

Table 3. Association of the Timing of Surgery With Outcomes After Decompressive Craniectomy for Stroke

Timing of Surgery: Continuous Analysis	Total Population (n=1301)			OR	95% CI	*P* Value	HL	C
In-hospital mortality				1.06	0.97–1.15	0.21	0.48	0.77
Neurological complications				1.04	0.96–1.13	0.37	0.09	0.68
Tracheostomy or gastrostomy				1.07	0.98–1.17	0.12	0.76	0.77
Extended hospitalization				1.08	0.98–1.20	0.13	0.66	0.75
Institutional care placement				1.17*	1.05–1.31*	0.005*	0.11	0.75
Poor outcome				1.12*	1.02–1.23*	0.02*	0.57	0.79
Within 24 h of admission	%	Early surgery (<24 h; n=287)	Late surgery (>24 h; n=1014)					
In-hospital mortality	26.2	26.5	26.1	1.03	0.74–1.42	0.87	0.96	0.77
Neurological complications	26.0	27.1	25.6	0.91	0.68–1.21	0.50	0.42	0.68
Tracheostomy or gastrostomy	49.0	50.7	48.5	0.94	0.68–1.30	0.71	0.28	0.77
Extended hospitalization	24.6	23.2	25.0	1.35	0.87–2.09	0.18	0.98	0.75
Institutional care placement	35.0	34.1	35.2	1.12	0.71–1.77	0.63	0.26	0.75
Poor outcome	70.2	70.6	70.1	1.01	0.66–1.56	0.95	0.99	0.79
Within 48 h of admission	%	Early surgery (<48 h; n=726)	Late surgery (>48 h; n=575)					
In-hospital mortality	26.2	26.0	26.4	1.00	0.76–1.33	0.98	0.96	0.77
Neurological complications	26.0	26.7	25.0	0.95	0.74–1.21	0.67	0.48	0.68
Tracheostomy or gastrostomy	49.0	47.3	51.1	1.27	0.97–1.67	0.08	0.84	0.77
Extended hospitalization	24.6	23.5	26.0	1.35	0.97–1.87	0.07	0.99	0.75
Institutional care placement	35.0	33.0	37.4	1.22	0.89–1.68	0.22	0.27	0.75
Poor outcome	70.2	69.6	70.9	1.10	0.81–1.50	0.52	0.73	0.79
Within 72 h of admission	%	Early surgery (<72 h; n=999)	Late surgery (>72 h, n=302)					
In-hospital mortality	26.2	25.8	27.5	1.11	0.80–1.55	0.53	0.77	0.77
Neurological complications	26.0	25.8	26.5	1.07	0.81–1.42	0.63	0.63	0.68
Tracheostomy or gastrostomy	49.0	48.2	51.6	1.26	0.91–1.74	0.16	0.69	0.77
Extended hospitalization	24.6	24.6	24.7	1.24	0.82–1.87	0.30	0.98	0.75
Institutional care placement	35.0	32.2	43.7	1.59*	1.08–2.34*	0.02*	0.40	0.75
Poor outcome	70.2	68.7	74.9	1.52*	1.07–2.16*	0.02*	0.50	0.79

An extended hospitalization was longer than 26 days (greater than the upper quartile for the entire population). A poor outcome was defined using the Nationwide Inpatient Sample-subarachnoid hemorrhage outcome measure, which defines a poor outcome as death, discharge to institutional care, or tracheostomy or gastrostomy placement. All multivariable logistic regression included patient characteristics, number of comorbidities, stroke risk factors, severity indices, treatment variables, and hospital characteristics as covariates. C indicates concordance statistic; CI, confidence interval; HL, Hosmer–Lemeshow test; and OR, odds ratio.

*Statistically significant differences.

earlier surgery, whereas carotid stenosis was associated with later surgery. These differences may be related to the severity of infarction, with atrial fibrillation having a predilection for proximal strokes, leading to earlier deterioration from larger territorial infarction. In addition, the year of operation was not predictive of early intervention, indicating that recommendations from clinical trials did not significantly change practice between 2009 and 2011 (compared with 2002–2005) in the United States.

Notably, patient age was not associated with the timing of surgery. Moreover, patient age was not found to be an effect measure modifier of the association of surgical timing with outcomes. This suggests that relationship between surgical timing and outcomes does not vary by patient age, but instead

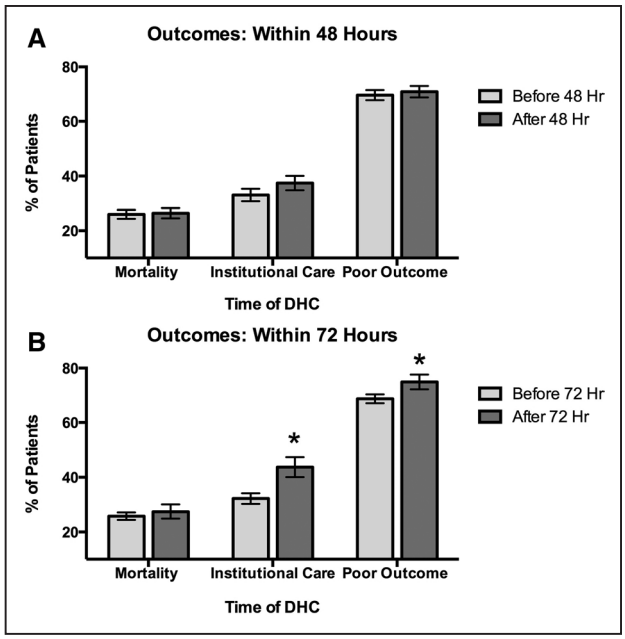

Figure. Differences in the crude rates (and SE) in mortality, discharge to institutional care, and of a poor outcome stratified by the timing of surgery: within 48 hours (**A**) and within 72 hours (**B**). A poor outcome was defined using the Nationwide Inpatient Sample-subarachnoid hemorrhage outcome measure (death, tracheostomy and gastrostomy placement, or discharge to institutional care). Statistically significant differences from multivariable logistic regression are designated with an asterisk. DHC indicates decompressive hemicraniectomy.

depends on other factors, such as the relationship between surgery and transtentorial herniation. However, the direct association of patient age with surgical outcomes was not analyzed in this study and has been the topic of other research.[12,13]

Thereafter, logistic regression analyzed the association of the timing of surgery with postoperative outcomes. No significant differences in in-hospital mortality were seen when surgical timing was evaluated continuously or dichotomously; the timing of surgery was also not associated with neurological complications, tracheostomy and gastrostomy placement, or length of hospital stay. However, patient functional capacity and quality of life are critical end points for physicians, patients, and families. The composite NIS-SOM has been previously used to evaluate neurological outcomes, which defines a poor outcome by death, tracheostomy and gastrostomy placement, or discharge to institutional care, and has been externally validated, with strong concordance with a modified Rankin Scale score of >3.

The importance of the timing of intervention is underscored by the results of this analysis: when surgical timing was evaluated continuously, later surgery was associated with increased odds of discharge to institutional care and of a poor outcome. Subsequently, the timing of surgery was analyzed dichotomously to determine whether a point of inflection about outcomes could be discerned. In this population, pursuing surgery within 72 hours from hospital admission—rather than 48 hours—emerged as the time point after which inferior outcomes were seen. However, in a subgroup analysis, there was no association between surgical timing and outcomes among patients without a diagnosis of herniation, and there was a statistically significant interaction between surgical timing and herniation in outcomes in the entire population. Therefore, pursuing surgical decompression before herniation may be the most critical temporal factor, especially in patients who do not deteriorate within 48 hours.

The limitations of this study merit further elaboration. The NIS is an administrative claims database, where data are collected from billing records (rather than primarily for the purpose of research) and thereby analyses are limited to variables encoded by ICD-9-CM identifiers. Therefore, a major limitation of this study is that preoperative functional status, National Institutes of Health stroke scale and other standard stroke severity scales, arterial distribution of the infarction, infarct volume, hemispheric lateralization, and medical treatment of cerebral edema could not be evaluated, due to a lack of corresponding ICD-9-CM indicators. Moreover, only data on the timing of surgery from hospital admission was available, and therefore, the time between symptom onset and hospital admission, as well as the time to clinical deterioration, could not be evaluated. The ICD-9 procedure codes do not differentiate between supratentorial and suboccipital craniectomy, and therefore exclusion of posterior fossa infarction relied upon diagnosis codes (for vertebrobasilar infarction or dissection) or the procedure code for a laminectomy (as a C1 laminectomy is common during a posterior fossa craniectomy). In addition, as the NIS only includes in-hospital data, long-term outcomes could not be assessed. Finally, data on the NIS are both collected and analyzed retrospectively.

Nevertheless, this nationwide analysis provides insight into treatment practices and outcomes of decompressive hemicraniectomy for space occupying infarction in the United States. The use of nationally representative data reduces institutional bias, particularly of academic medical centers, and increases the generalizability of findings. Moreover, data are available on many patient characteristics (including demographics, insurance status, comorbidities, and stroke risk factors) as well as treatment variables and hospital characteristics—which were included as covariates in multivariable regression models evaluating outcomes. Moreover, the large sample size allowed for outcomes to be evaluated at several different time points. Overall, this study suggests that patients with space-occupying infarction who do not experience clinical deterioration within 48 hours may benefit from surgery if pursued before herniation. Nonetheless, additional prospective data are needed specifically evaluating the optimal timing of decompressive craniectomy in space-occupying cerebral infarction.

Disclosures

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