

# Rates and Outcomes of Neurosurgical Treatment for Postthrombolytic Intracerebral Hemorrhage in Patients with Acute Ischemic Stroke

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## Key words

- Craniotomy
- Hematoma
- Medical management
- Postthrombolytic intracerebral hemorrhage

## Abbreviations and Acronyms

**APR-DRG:** All Patient Refined Diagnosis Related Group

**CI:** Confidence interval

**ICD-9-CM:** International Classification of Diseases, 9th Revision, Clinical Modification

**ICH:** Intracerebral hemorrhage

**NIS:** Nationwide Inpatient Sample

**OR:** Odds ratio



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## INTRODUCTION

Postthrombolytic intracerebral hemorrhage (ICH) is an infrequent but potentially life-threatening complication of thrombolytic therapy for acute ischemic stroke (18, 20, 31). Radiographically, the spectrum of postthrombolytic ICH varies considerably, ranging from benign petechial hemorrhage to large parenchymal hemorrhage with prominent mass effect (14, 19). The frequency of symptomatic ICH (leading to neurologic deterioration) after thrombolytic treatment ranges from 5.9%–8.8% (8, 10, 18, 19, 27, 32). With the increased use of combined intravenous and intraarterial thrombolytic therapy for acute stroke along with mechanical thrombectomy for delayed arrival, the incidence of postthrombolytic ICH is likely to increase.

Postthrombolytic ICH is associated with excessively high mortality. In-hospital

■ **OBJECTIVE:** Postthrombolytic intracerebral hemorrhage (ICH) is an infrequent occurrence in patients with acute ischemic stroke. There is controversy surrounding the value of neurosurgical treatment of symptomatic hematomas in these patients and whether availability of neurosurgical treatment is a necessary prerequisite for administration of thrombolytic agents. We report the frequency and outcomes of patients who undergo craniotomy for postthrombolytic ICH.

■ **METHODS:** Patients with acute ischemic stroke who experienced postthrombolytic ICH were identified using the Nationwide Inpatient Sample from 2002–2010 and International Classification of Diseases, 9th Revision, Clinical Modification codes. Patients were divided into patients who received craniotomy and patients who received medical management alone. Discharge destination and mortality were primary endpoints.

■ **RESULTS:** An estimated 7607 patients experienced postthrombolytic ICH; 125 (1.6%) patients underwent craniotomy, and 7482 patients (98.4%) received medical treatment alone. Patients in the craniotomy group were younger (53.7 years old  $\pm$  36 vs. 72.4 years old  $\pm$  29,  $P = 0.09$ ) and were frequently in the extreme severity All Patient Refined Diagnosis Related Group category compared with patients in the medical management group (92.2% vs. 55.5%,  $P = 0.001$ ). The mean length of stay was also longer in the craniotomy group (21.5 days vs. 10 days,  $P < 0.0001$ ). In-hospital mortality was greater in the medical management group (30.5% vs. 24.2%,  $P = 0.5$ ). After adjusting for age, gender, and All Patient Refined Diagnosis Related Group severity index, the odds ratios of in-hospital mortality, discharge to extended care facility, and discharge to home or self-care were 0.8 (95% confidence interval [CI] 0.3–2.0,  $P = 0.5$ ), 5.4 (95% CI 0.6–52.0,  $P = 0.1$ ), and 0.2 (95% CI 0.02–1.8,  $P = 0.1$ ) for the craniotomy group compared with the medical management group.

■ **CONCLUSIONS:** Emergent craniotomy for postthrombolytic ICH in patients with acute stroke is a salvage treatment offered to a small proportion of patients. Although biases introduced by patient selection cannot be excluded in our analysis, the excessively high rates of death or disability associated with surgical evacuation limit the value of such a procedure in current practice.

mortality approaches 47% with intravenous thrombolytic agents (5), and 3-month mortality can be 83% after intraarterial thrombolytic treatment (15). Although considerable emphasis has been placed on identifying patients at risk for ICH related to thrombolytic therapy (13), little effort has been focused on determining the effectiveness of treatment protocols. In particular, few data exist on outcomes of neurosurgical

intervention for postthrombolytic ICH. Guidelines from the American Heart Association concluded that there is lack of evidence to support any specific therapy for postthrombolytic ICH at this time (9). In the current study, we analyzed Nationwide Inpatient Sample (NIS) data to evaluate the impact of neurosurgical intervention on outcome of patients with acute ischemic stroke and postthrombolytic ICH.

## METHODS

We used NIS data files from 2002–2010. The NIS, as part of the Healthcare Cost and Utilization Project sponsored by the Agency for Healthcare Research and Quality, is the largest all-payer inpatient care database in the United States (28). Data from 5–8 million hospital stays, representing approximately a 20% stratified sample of U.S. hospitals, are collected. Detailed information on the design of the NIS is available at <http://www.hcup-us.ahrq.gov>. The NIS database contains data on >100 clinical and nonclinical variables associated with hospital stays, including primary and secondary diagnoses, primary and secondary procedures, patient admission and discharge status, patient demographic information, and individualized financial statistics.

### Patient Selection

We used the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) primary diagnosis codes 433, 434, 436, 437.0, and 437.1 to identify patients admitted with ischemic stroke. Patients who underwent thrombolytic treatment were identified by procedure code 99.10. If patients with ischemic stroke who received thrombolytic treatment had a secondary diagnosis of ICD-9-CM code 431 or 432, they were considered to have postthrombolytic ICH. We used ICD-9-CM procedure codes 012 and 012.4 to identify patients who underwent craniotomy. These patients were categorized as “craniotomy group.” All remaining selected patients with postthrombolytic ICH were categorized as “medical management group.”

### Variables Analyzed

We obtained information regarding patient age, sex, race and ethnicity, length of stay, discharge status, and hospitalization charges and characteristics of the admission hospitals (teaching vs. nonteaching hospitals). Data on comorbid conditions, including hypertension, diabetes mellitus, congestive heart failure, and chronic renal failure, were acquired from the comorbidity data files. ICD-9-CM secondary diagnosis codes were used to identify complications, such as pneumonia (486, 481, 482.8, and 482.3), urinary tract infection (599.0, 599.9), sepsis (995.91, 996.64, 038, 995.92, and 999.3), deep venous thrombosis (451.1,

**Table 1.** Comparison Between the Craniotomy Group and Medical Management Group

	Craniotomy Group	Medical Management Group	OR (95% CI)	P Value
Overall number (%)	125	7482		
Mean age (CI)	53.7 ± 36	72.4 ± 29		0.09
Women	39.3 (31.4)	3916 (52.3)		0.1
Race/ethnicity				
White	90.5 (81.9)	4488 (74)		0.4
Black	5.1 (4.6)	818.3 (13.5)		
Hispanic	10.1 (9.2)	369.8 (6.1)		
Other	4.8 (4.3)	388.9 (6.4)		
Comorbid conditions				
Hypertension	86.3 (68.8)	5553 (74.4)	0.7 (0.3–2.0)	0.5
Diabetes mellitus	34.5 (27.5)	1810 (24.3)	1.2 (0.4–3.3)	0.7
Dyslipidemia	9.5 (7.6)	586 (7.8)	1 (0.2–4.3)	0.9
Atrial fibrillation	29.8 (23.7)	3010 (40.2)	0.5 (0.2–1.3)	0.1
Congestive heart failure	15 (12)	1391 (18.6)	0.6 (0.1–2.8)	0.4
Chronic lung disease	24.9 (19.9)	901.4 (12.1)	1.8 (0.5–5.8)	0.4
Renal failure	15.3 (12.2)	728.6 (9.8)	1.2 (0.3–6.0)	0.7
Alcohol	9.8 (7.8)	325.1 (4.4)	1.8 (0.5–7.1)	0.4
Smokers	4.7 (3.8)	745.7 (10)	0.3 (0.05–2.3)	0.2
In-hospital complications				
Pneumonia	19.6 (15.7)	511.3 (6.8)	2.5 (0.8–7.3)	0.08
Deep venous thrombosis	9.9 (7.9)	187.2 (2.5)	3.3 (0.4–27.0)	0.4
Urinary tract infection	15 (12)	1451 (19.4)	0.6 (0.2–2.0)	0.3
Sepsis	15.2 (12.1)	291 (3.9)	3.4 (0.7–15.3)	0.1
Pulmonary embolism	4.7 (3.7)	118.5 (1.6)	2.4 (0.3–19.5)	0.5
Myocardial infarction	4.7 (3.7)	335.9 (4.5)	0.8 (0.1–6.1)	0.8
In-hospital procedure				
Angiography	48.4 (38.6)	2176 (29.1)	1.5 (0.6–4.1)	0.4
Gastrostomy	59.9 (47.8)	1252 (16.7)	4.5 (1.7–12.2)	0.002
CAS	4.5 (3.6)	223 (3)	1.2 (0.1–9.4)	0.8
Mechanical ventilation	69 (55)	1034 (13.8)	7.6 (3.0–19.0)	<0.0001
Tracheostomy	4.7 (3.7)	30.6 (0.4)	9.4 (1.0–87.9)	0.04
Intubation	50.2 (40)	2003 (26.8)	1.8 (0.7–4.8)	0.2
Transfusion	15.8 (12.6)	402.4 (5.4)	2.5 (0.7–9.4)	0.2
APR-DRG disease severity scale				
Moderate to major loss of function	9.8 (7.8)	3321 (44.5)	0.1 (0.02–0.4)	0.001
Extreme loss of function	115.6 (92.2)	4141 (55.5)	9.5 (2.4–37.1)	

OR, odds ratio; CI, confidence interval; APR-DRG, All Patient Refined Diagnosis Related Group.

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