SUPPLEMENTAL MATERIAL

Safety Outcomes after Thrombolysis for Acute Ischemic Stroke in Patients with Recent Stroke

Alexander E. Merkler, MD; Setareh Salehi Omran, MD; Gino Gialdini, MD; Michael P. Lerario, MD; Shadi Yaghi, MD; Mitchell S.V. Elkind, MD, MS; Babak B. Navi, MD, MS

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Supplemental Methods

Design

The Agency for Healthcare Research and Quality provides standardized, de-identified, and quality-checked discharge data from all patient visits to nonfederal acute care hospitals. These data are publicly available. A personal linkage number is assigned to all patients in order to allow them to be followed over time within each state in a de-identified manner throughout subsequent hospitalizations.[1] The three states that we studied represent a geographically and demographically-diverse cohort of patients, as reflected by the racial and payer breakdowns of the cohort (Supplemental Tables, Pages 4-5).

Ascertainment of Covariates

To control for potential confounders between history of ischemic stroke and intracerebral hemorrhage (ICH) after intravenous tissue plasminogen activator (IV-tPA) treatment, we used previously utilized *International Classification of Diseases, 9th Revision, Clinical Modification* (*ICD-9-CM)* diagnostic codes to identify the following demographics and vascular risk factors: age, sex, race, insurance status, hypertension, diabetes mellitus, coronary heart disease, congestive heart failure, atrial fibrillation, peripheral vascular disease, chronic kidney disease, history of transient ischemic attack, chronic obstructive pulmonary disease, tobacco use and alcohol use.[2]

Sensitivity Analysis

We performed four sensitivity analyses to test the validity of our results. First, in order to ensure that we captured all cases of post-tPA ICH, we expanded our cohort to include patients who had *ICD-9-CM* codes for ICH and IV-tPA, but lacked an *ICD-9-CM* code for ischemic stroke. Second, we adjusted our multivariable model to include both mechanical ventilation and length of stay, as these factors could affect the rates of ICH. Third, we excluded patients with limitations in care, which we defined using the palliative care code V66.7 in someone who died within 48 hour of admission.[3] Fourth, as the *ICD-9-CM* code for IV-tPA does not specify the indication and route of delivery, we excluded all patients with claims for myocardial infarction, pulmonary embolus, and end-stage renal disease requiring dialysis at the time of IV-tPA administration.

Supplemental Results

Secondary Analysis

Among patients with recent ischemic stroke treated with IV-TPA for AIS, the risk of ICH did not significantly vary when stratified by 1-month time intervals from the time of prior stroke (Supplemental Table 3). However, both inpatient death and unfavorable discharge disposition were higher in only the subgroup of patients who received IV-tPA within 1 month of prior ischemic stroke as compared to patients who received thrombolysis in later time intervals.

Sensitivity Analysis

In sensitivity analyses, the risk of ICH in patients with a recent ischemic stroke was unchanged after including patients who had *ICD-9-CM* codes for ICH and IV-tPA but lacked codes for ischemic stroke (an additional 336 patients) (odds ratio [OR], 1.0; 95% confidence interval [CI], 0.7-1.5), after further adjusting for length of stay and use of mechanical ventilation (OR, 0.9; 95% CI, 0.6-1.3), after excluding patients with limitations in care (OR, 0.8; 95% CI, 0.6-1.3) and after excluding patients who could have received IV-tPA for reasons other than acute ischemic stroke (i.e., myocardial infarction, pulmonary embolus, or hemodialysis) (OR, 0.9; 95% CI, 0.6-1.2).

Supplemental Table I. Characteristics of Patients, Stratified by History of Ischemic Stroke in the Previous Three Months

Characteristic[*]	Previous History of Recent Stroke (N = 568)	No Previous History of Recent Stroke (N = 36,031)
Age, mean (SD), y	69.0 (14.1)	70.9 (14.6)
Female	278 (48.9)	18,444 (51.2)
Race[†]		
White	363 (65.2)	24,415 (68.7)
Black	73 (13.1)	4,447 (12.5)
Hispanic	58 (10.4)	3,706 (10.4)
Asian	32 (5.8)	1,417 (4.0)
Other	31 (5.6)	1,535 (4.3)
Payment source[‡]		
Medicare	355 (62.5)	23,938 (66.4)
Medicaid	61 (10.7)	2,983 (8.3)
Private	124 (21.8)	6,996 (19.4)
Self-pay	15 (2.6)	1,158 (3.2)
Other	13 (2.3)	954 (2.7)
Hypertension	451 (79.4)	28,474 (79.0)
Diabetes	191 (33.6)	11,036 (30.6)
Coronary heart disease	195 (34.3)	11,556 (32.1)
Congestive heart failure	118 (20.8)	6,644 (18.4)
Peripheral vascular disease	56 (9.9)	2,557 (7.1)
Chronic obstructive pulmonary disease	74 (13.0)	3,790 (10.5)
Chronic kidney disease	77 (13.6)	4,018 (11.2)
Atrial fibrillation	197 (34.7)	13,045 (36.2)
Tobacco use	56 (9.9)	3,913 (10.9)
Alcohol use	85 (15.0)	5,535 (15.4)
Elixhauser comorbidities[§], mean (SD)	3.4 (1.8)	3.2 (1.8)

Abbreviations: SD, standard deviation

[*]Data are presented as number (%) unless otherwise specified

[†]Self-reported by patients or their surrogates. Numbers do not sum to group totals because of missing race/ethnicity data in 1.9% of patients

[‡]Numbers do not sum to group totals because of missing payment-source data in <0.01% of patients

[§]Numbers represent the number of Elixhauser comorbid conditions, which comprise a comprehensive set of 28 comorbidity measures for use with large administrative datasets

Supplemental Table II. Characteristics of Patients, Stratified by Development of ICH

Characteristic[*]	ICH (N = 1,792)	No ICH (N = 34,807)
Age, mean (SD), y	74.6 (12.4)	70.7 (14.6)
Female	956 (53.4)	17,766 (51.0)
Race[†]		
White	1,232 (69.5)	23,546 (68.6)
Black	189 (10.7)	4,331 (12.6)
Hispanic	189 (10.7)	3,575 (10.4)
Asian	85 (4.8)	1,364 (4.0)
Other	77 (4.4)	1,489 (4.3)
Payment source[‡]		
Medicare	1,363 (76.1)	22,930 (65.9)
Medicaid	128 (7.1)	2,916 (8.4)
Private	231 (12.9)	6,889 (19.8)
Self-pay	40 (2.2)	1,133(3.3)
Other	30 (1.7)	937 (2.7)
Hypertension	1,445 (80.6)	27,480 (79.0)
Diabetes	599 (33.4)	10,628 (30.5)
Coronary heart disease	644 (35.9)	11,107 (31.9)
Congestive heart failure	400 (22.3)	6,362 (18.3)
Peripheral vascular disease	126 (7.0)	2,487 (7.2)
Chronic obstructive pulmonary disease	188 (10.5)	3,676 (10.6)
Chronic kidney disease	217 (12.1)	3,878 (11.1)
Atrial fibrillation	920 (51.3)	12,322 (35.4)
Tobacco use	183 (10.2)	3,786 (10.9)
Alcohol use	213 (11.9)	5,407 (15.5)
Elixhauser comorbidities[§], mean (SD)	3.7 (1.8)	3.2 (1.8)

Abbreviations: ICH, intracerebral hemorrhage; SD, standard deviation

[*]Data are presented as number (%) unless otherwise specified

[†]Self-reported by patients or their surrogates. Numbers do not sum to group totals because of missing race/ethnicity data in 1.4% of patients

[‡]Numbers do not sum to group totals because of missing payment-source data in <0.01% of patients

[§]Numbers represent the number of Elixhauser comorbid conditions, which comprise a comprehensive set of 28 comorbidity measures for use with large administrative datasets

Supplemental Table III. Risk of ICH, Death, and Poor Discharge Disposition in Patients with Prior Ischemic Stroke, Stratified into Monthly Intervals before Thrombolysis for Acute Ischemic Stroke

	Number of patients	Risk of ICH*	Risk of Death*	Risk of Poor Discharge Disposition*
Within 1 Month of Thrombolysis	387	1.0 (0.6-1.6)	1.6 (1.2-2.2)	1.6 (1.1-2.2)
Between 1-2 Months before Thrombolysis	100	1.0 (0.4-2.6)	1.4 (0.8-2.5)	1.3 (0.8-2.2)
Between 2-3 Months before Thrombolysis	81	0.5 (0.1-2.0)	1.1 (0.6-2.3)	0.7 (0.4-1.2)

Abbreviations: ICH, intracerebral hemorrhage

*Data are presented as odds ratios (95% Confidence Interval)

Supplemental Table IV. Characteristics of Patients with Claims for Acute Ischemic Stroke Not Treated with Intravenous Thrombolysis, Stratified by History of Recent Stroke

Characteristic[*]	Previous History of Recent Stroke (N = 32,632)	No Previous History of Recent Stroke (N = 552,395)
Age, mean (SD), y	71.4 (14.2)	72.2 (14.2)
Female	16,879 (51.2)	291,038 (52.7)
Race[†]		
White	19,901 (62.1)	350,096 (64.6)
Black	5,005 (15.6)	80,082(14.8)
Hispanic	4,730 (14.8)	69,247 (12.8)
Asian	1,363 (4.3)	24,526 (4.5)
Other	1,060 (3.2)	17,993 (3.3)
Payment source[‡]		
Medicare	21,867 (67.0)	378,625 (68.6)
Medicaid	2,854 (8.8)	45,184 (8.2)
Private	5,945 (18.2)	91,066 (16.5)
Self-pay	1,127 (3.5)	20,871 (3.8)
Other	838 (2.5)	16.621 (2.9)
Hypertension	26,902 (82.4)	447,381 (81.0)
Diabetes	12,512 (38.3)	196,064 (35.5)
Coronary heart disease	9,313 (28.5)	155,647 (28.2)
Congestive heart failure	4,179 (12.8)	73,951 (13.4)
Peripheral vascular disease	2,680 (8.2)	42,797 (7.8)
Chronic obstructive pulmonary disease	3,287 (10.1)	58,312 (10.6)
Chronic kidney disease	3,539 (10.8)	60,946 (11.0)
Atrial fibrillation	7,491 (23.0)	130,245 (23.6)
Tobacco use	3,046 (9.3)	54,284 (9.8)
Alcohol use	5,003 (15.3)	81,945 (14.8)
Elixhauser comorbidities, mean (SD)[§]	2.6 (1.5)	2.6 (1.6)
ICH[‖]	119 (0.4)	2,109 (0.4)
Unfavorable discharge disposition[#]	18,576 (68.5)	338,633 (62.6)
Inpatient mortality	3,024 (9.3)	28,214 (5.1)

Abbreviations: SD, standard deviation; ICH, intracerebral hemorrhage

[*]Data are presented as number (%) unless otherwise specified

[†]Self-reported by patients or their surrogates. Numbers do not sum to group totals because of missing race/ethnicity data in 2.0% of patients

[‡]Numbers do not sum to group totals because of missing payment-source data in <0.01% of patients

[§]Numbers represent the number of Elixhauser comorbid conditions, which comprise a comprehensive set of 28 comorbidity measures for use with large administrative datasets

[‖]Represents the development of ICH during the index visit for acute ischemic stroke

[#]Includes discharge to a skilled nursing facility, subacute care center, chronic rehabilitation center, hospice, or death

Supplemental References

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3. Murthy SB, Moradiya Y, Hanley DF, Ziai WC. Palliative care utilization in nontraumatic intracerebral hemorrhage in the united states. *Crit Care Med*. 2016;44:575-582