

## In-Hospital Strokes Demonstrate Improved Outcomes with Mechanical Thrombectomy

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### Abstract

**Objective**— Patients with in-hospital stroke often have contraindications to intravenous alteplase(1), (2). Mechanical thrombectomy is a treatment option, even for patients otherwise ineligible for intravenous alteplase. We compare outcomes between mechanical thrombectomy performed in patients with strokes that occurred in-hospital versus community-onset strokes.

**Methods**— This is an Institutional Review Board-approved, retrospective cross-sectional study analyzing patients who underwent thrombectomy for acute ischemic stroke with large vessel occlusion between January 2012 and November 2017 at Tampa General Hospital. We performed logistic regression analysis to compare the outcomes between patients with in-hospital stroke and community-onset stroke after adjusting for potential confounders.

**Results**— A total of 334 patients received mechanical thrombectomy for acute ischemic stroke: 13.2% were in-hospital and 86.8% were community-onset. Patients who presented with strokes that occurred in-hospital were significantly younger (mean age 60.7 vs. 70.4 years;  $p < 0.001$ ). In-hospital stroke treated with mechanical thrombectomy had lower pretreatment with intravenous alteplase (14% vs. 34%;  $p = 0.006$ ). Patients with in-hospital stroke had a significantly shorter time interval between symptom recognition and groin puncture ( $p = 0.039$ ). Also, in-hospital stroke patients had significantly higher rates of favorable outcomes at discharge as measured by the modified Rankin scale 0–3 (52% vs. 32%;  $p = 0.009$ ) and continued to have favorable outcomes (adjusted odds ratios = 4.832; 95% CI, (1.207-19.348);  $P = 0.026$ ) after adjustment for age and National Institute of Health Stroke Scale which were felt to be potential confounders.

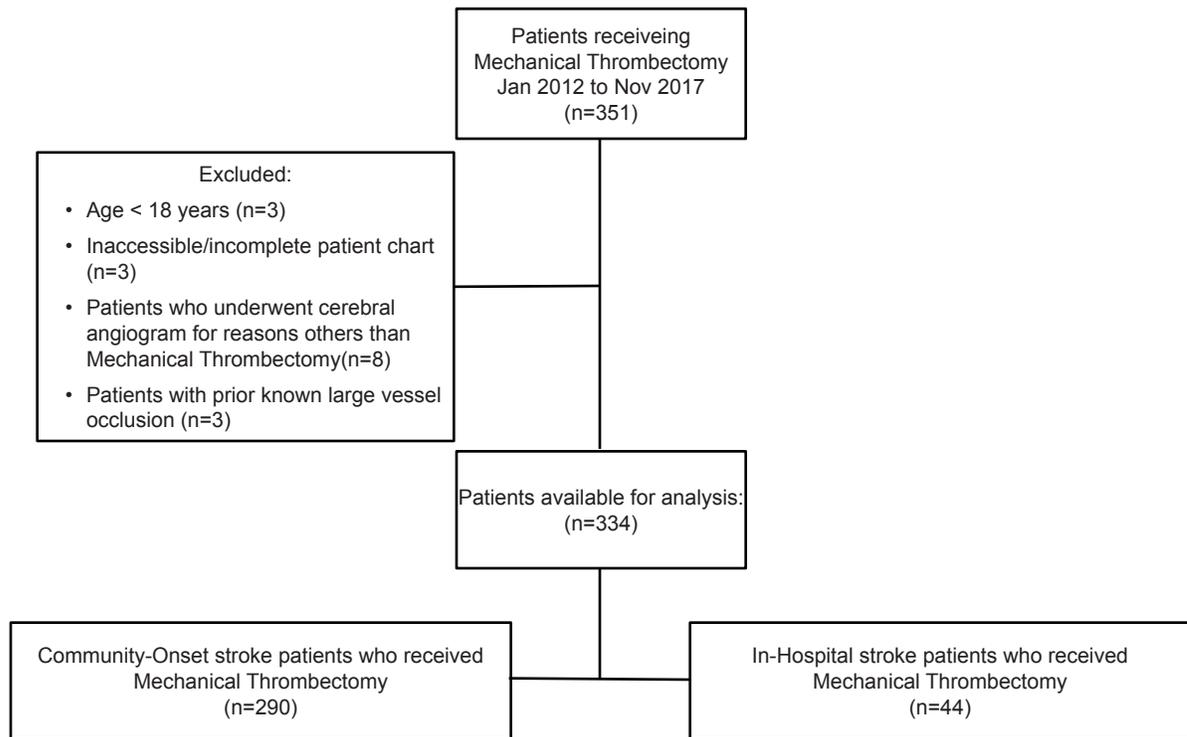
**Conclusions**— Compared with patients with community-onset stroke, patients with in-hospital stroke who underwent thrombectomy had higher rates of favorable outcomes at discharge.

**Search Terms**— All Cerebrovascular disease/Stroke, Outcome research, All Clinical Neurology.

### INTRODUCTION

Approximately 2.2-17% of ischemic strokes occur in patients who are hospitalized for other reasons.<sup>1</sup> Despite having numerous stroke risk factors, hospitalized patients are often ineligible to receive intravenous alteplase due to contraindications such as active use of anticoagulation, blood dyscrasias, coagulopathy, and recent major surgery or trauma.<sup>1,2</sup> Approximately 70% of patients who presented with in-hospital hospital stroke were ineligible to receive alteplase due to these aforementioned (or other) contraindications or a delay in

stroke discovery.<sup>3</sup> Therefore, in-hospital strokes are associated with overall worse outcomes.<sup>4</sup> Paradoxically, studies have also shown that alteplase-treated in-hospital strokes have a longer time interval between symptom onset and treatment than those who present to the emergency room with community-onset stroke.<sup>5</sup> Additionally, in-hospital treated patients had lower rates of favorable outcomes than community-onset patients.<sup>6,7</sup> Mechanical thrombectomy in acute ischemic stroke is a treatment option for patients with large vessel occlusion, including those otherwise ineligible for alteplase.<sup>8</sup> Essentially, in-hospital patients with a contraindication to



**FIGURE 1: Flowsheet of patient selection.**

alteplase may benefit from thrombectomy. Therefore, we compared the outcomes of in-hospital strokes with community-onset strokes in patients with large vessel occlusion who underwent thrombectomy at our hospital.

## METHODS

We performed an Institutional Review Board-approved, retrospective cross-sectional study on thrombectomy patients at our large, tertiary comprehensive stroke center for acute ischemic stroke between January 2012 and November 2017. Outcomes were determined by the modified Rankin Scale at discharge, which measures patient level of disability with higher scores indicating greater disability.<sup>9,10</sup> A score from 0-3 was considered as a favorable outcome and conversely a score from 4-6 was considered an unfavorable outcome. We considered 0-3 a favorable outcome as it reflects the patient's ability to remain independent/ walk without the assistance of another individual.<sup>11</sup>

### Data Source

We obtained our initial patient population from "Get with the Guidelines" database from Tampa General Hospital, a 1,018-bed tertiary care center and the primary academic teaching facility for the University of South Florida Morsani College of Medicine. The American Heart Association / American Stroke Association developed the database to help improve stroke care nationwide by encouraging and monitoring hospitals' adherence to their most recent and updated national guidelines for optimal care in stroke and heart disease.<sup>12</sup> Variables including patient demographics, vascular risk factors, stroke location, symptom recognition time, groin puncture time, symptom recognition to groin puncture time, discharge

disposition, and disability as measured by the modified Rankin Scale were extracted from the database. Data absent from the registry was obtained by reviewing the patient's electronic medical record.

### Case Selection

We identified 351 patients who received thrombectomy during this timeframe at our hospital through the registry. After exclusion of patients <18 years of age, those with inaccessible/incomplete patient charts, those who received an angiogram for reasons other than thrombectomy and those with a prior known large vessel occlusion, we were left with 334 patients who met our study criteria (Figure 1).

### Statistical Analysis

Descriptive statistics for patient demographics, clinical characteristics, stroke location, symptoms recognition to groin puncture time, discharge disposition, and disability as measured by the modified Rankin Scale are presented as mean (standard deviation) for continuous variables and counts (percentages) for categorical variables. We identified differences between patients with community-onset stroke and those with in-hospital stroke using t-tests for continuous variables and chi-square tests for categorical variables. We performed logistic regression analysis to compare the outcomes between patients with strokes that occurred in the hospital versus the community after adjusting for potential confounders. Results are presented as adjusted odds ratios (AOR) and corresponding 95% confidence intervals (95% CI). Statistical significance was defined as a p-value of <0.05. All analyses were conducted using the SAS System (Version 9.4, SAS Institute Inc, Cary, NC).

**TABLE 1: Characteristics of Patients with In-Hospital Stroke and Community-Onset Strokes.**

	Community Onset Stroke patients (n=290)	In-Hospital Stroke patients (n=25)	Total (n=334)	P value
Age, Mean(SD)	70.4 (15.3)	60.7 (17.7)	69.1(15.9)	<0.001
<b>Gender, %</b>				0.652
Men	51	48	51	
Women	49	52	49	
Admission NIHSS score, Mean (SD) <sup>a</sup>	17.1 (6.4)	14.4(5.4)	16.7(6.3)	0.007
<b>Site of occlusion, %</b>				0.704
Internal carotid artery	17	25	18	
Middle cerebral artery	73	68	73	
Posterior cerebral artery	1	0	1	
Vertebral artery	1	0	1	
Basilar artery	7	5	6	
Anterior cerebral artery	1	2	1	
Cigaretter smoking, % <sup>b</sup>	16	32	19	0.032
Coronary artery disease, % <sup>c</sup>	25	48	19	0.003
Atrial fibrillation, % <sup>d</sup>	42	20	40	0.005
Hypertension, %	71	77	72	0.391
Diabetes mellitus, %	25	32	26	0.323
Dyslipidemia, % <sup>e</sup>	37	39	37	0.911

a Data available on 333 patients.

b Data available on 328 patients.

c Data available on 329 patients.

d Data available on 332 patients.

e Data available on 330 patients.

#### Abbreviations used:

N	number
SD	Standard Deviation
NIHSS	National Institute of Health Stroke Scale
%	percent

### Data Availability

The de-identified data for the current study is available from the corresponding author on reasonable request until 5 years after the close of the study (2024).

### Results

Of the 334 ischemic stroke patients who received mechanical thrombectomy for acute large vessel occlusion, 290 (87%) presented with community-onset stroke, and 44 (13%) with in-hospital strokes (Figure 1). Clinical and demographic data for these patients are shown in (Table 1). The mean age of the study population was 69.1 years, and 51% were men.

Patients who presented as in-hospital stroke were younger; mean age for community-onset patients was 70.4 versus 60.7 years for those that presented in-hospital ( $p < 0.001$ ). There was no significant difference in gender between the two groups ( $p = 0.652$ ). In-hospital stroke patients were more likely to have a history of coronary artery disease (48% versus 25%;  $p = 0.003$ ) and cigarette smoking (32% versus 16%;

**TABLE 2: Outcome of Patients with In-Hospital Stroke and Community-Onset Strokes.**

	Community Onset Stroke patients (n=290)	In-Hospital Stroke patients (n=25)	P value
mRS at discharge, mean (SD)	30.9(1.6)	3.5(1.8)	0.162
<b>mRS at discharge, n (%)</b>			0.009
0-3	93(32)	23(52)	
4-6	197(68)	21(48)	
<b>TICI Score, n (%)<sup>a</sup></b>			0.807
0-2	112(39)	16(36)	
3	174(60)	27(61)	
Thrombectomy treatment time (minutes), mean (SD) <sup>b</sup>	277.3 (184.1)	215.0 (169.5)	0.039
Alteplase administered, n (%)	100 (34)	6 (14)	0.006

a Data available on 329 patients.

b Data available on 331 patients.

#### Abbreviations used:

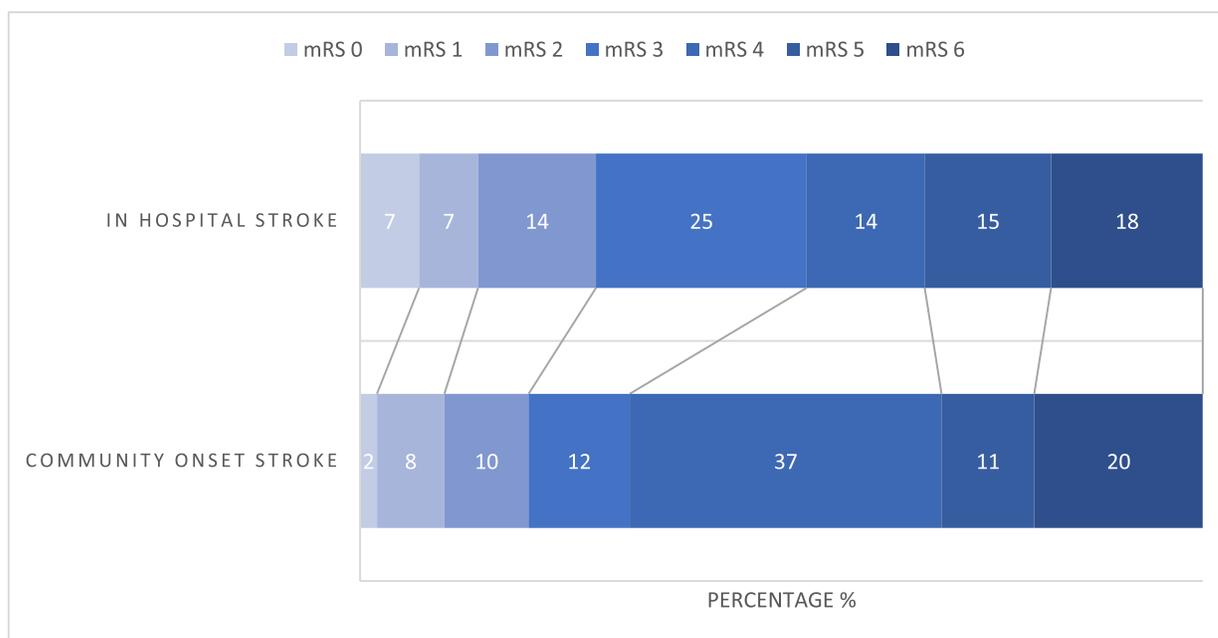
SD	Standard Deviation
%	percent
mRS	modified Rankin Scale
TICI	Thrombolysis in Cerebral Infarction. Thrombectomy treatment time is defined as symptom recognition to groin puncture time

$p = 0.032$ ) but lower rates of atrial fibrillation (20% versus 42%;  $p = 0.005$ ). In both cohorts, most occlusions occurred in the anterior circulation (in-hospital stroke 95%, community-onset stroke 91%) (Table 1). In-hospital stroke patients had lower National Institute of Health Stroke Scale score, indicating less severe (stroke-related) neurologic deficits ( $p = 0.007$ ). In-hospital stroke also had significantly lower alteplase use than community-onset stroke patients (14% versus 34%;  $p = 0.006$ ).

Patients with in-hospital strokes had a significantly shorter thrombectomy treatment time (symptom recognition to groin puncture time), compared with community patients ( $p = 0.039$ ). Favorable outcomes at discharge (modified Rankin Scale 0-3) occurred more frequently for in-hospital patients than community patients (52% versus 32%;  $p = 0.009$ ) (Table 2). The distribution of modified Rankin Scale scores for the two groups are presented in (Figure 2). After adjustment for age and National Institute of Health Stroke Scale, in-hospital stroke patients had higher rates of a favorable outcome at discharge (AOR=4.832; 95% CI, (1.207-19.348);  $P = 0.026$ ).

### DISCUSSION

We found that patients with in-hospital stroke were significantly younger than those with community-onset stroke. This observation is distinct from previous studies that had not identified much difference in age between the two groups.<sup>5,6</sup> Patients with in-hospital stroke in our study had significantly lower National Institute of Health Stroke Scale scores than those with stroke from the community. A previous study reported that the patients with stroke that occurred in-hospital had higher National Institute of Health Stroke Score scores, with a mean value of 9.5 versus 7.0 for community-onset stroke patients.<sup>1</sup> Another study found that patients with



**FIGURE 2: Distribution of modified Rankin Scale grades at discharge.**

Abbreviations used:

mRS      modified Rankin Scale

in-hospital strokes had a higher average National Institute of Health Stroke Score of 9 versus 4 in patients with community-onset strokes.<sup>13</sup> We postulate that the lower National Institute of Health Stroke Score in patients with strokes in-hospital is because our study is limited to those presenting with large vessel occlusion who were candidates for mechanical thrombectomy. We also found that patients with in-hospital stroke were significantly less likely to receive alteplase, which is consistent with previous studies.<sup>5,6</sup> The lower utilization is related to multiple contraindications to alteplase in hospitalized patients, as mentioned earlier.<sup>1,2</sup>

The thrombectomy treatment time in our study was significantly lower for in-hospital patients than for community-onset stroke patients. We found no difference in the thrombolysis in cerebral infarction score between the two groups. Interestingly, however, patients with strokes that occurred in-hospital had less disability as measured by an increased favorable outcome of modified Rankin Scale 0-3 compared to community-onset stroke. After adjustment for age and National Institutes of Health Stroke Scale scores, in-hospital patients had higher rates of a favorable outcome at discharge. We postulate that the higher rates of favorable outcomes in these patients is secondary to a smaller time interval to groin puncture.<sup>14</sup>

A study by Moradiya et al. utilizing the Nationwide Inpatient Sample from 2005-2010 reported that patients with in-hospital strokes had higher rates of unfavorable discharge outcomes (compared with patients with community-onset stroke) among those treated with thrombolysis as well as the endovascular therapy group.<sup>6</sup> Another study by Caparros et al. published in 2017 did not identify any differences in outcome in patients with stroke that occurred in-hospital that were treated with intravenous thrombolysis or mechanical throm-

bectomy (compared with patients with community-onset stroke); however, patients with in-hospital stroke had shorter time interval between symptom onset and groin puncture.<sup>15</sup> An analysis of stroke registry data from the National Taiwan University Hospital found no difference in rates of favorable outcomes between patients with stroke that occurred in-hospital or the community receiving thrombectomy. However, patients with in-hospital stroke had a shorter time interval between symptom onset and groin puncture.<sup>16</sup> The faster treatment time observed in patients with in-hospital stroke may be a result of increased training of hospital staff, strict adherence to national guidelines, stroke database-incentivized hospitals, and routine protocolization for quickly identifying and treating patients with in-hospital stroke vis-a-vis “code stroke.”

The primary limitation of this study is that data is derived from a single center and thus may not be generalizable to institutions without similar protocols. Our institution has well-designed and vetted protocols with multiple interdisciplinary stakeholder involvement (neurology, emergency medicine, critical care medicine, nursing, pharmacy staff, and others), which helps streamline care for hospitalized patients who develop acute stroke symptoms. If a new stroke is recognized, a “code gold” can be activated by any staff member on any floor of the hospital at any time immediately. Once the code is activated, the neurology team will arrive at the bedside as fast as possible, and the scanner is quickly cleared for urgent brain imaging. A pharmacist is on standby to calculate the weight-based dose and mix alteplase if needed.

## CONCLUSION

In conclusion, patients with in-hospital stroke had a significantly shorter time interval between symptom onset and groin puncture time. Subsequently, the rates of favorable outcomes

were significantly higher in patients with in-hospital stroke than those with community-onset stroke.

## DISCLOSURES

None.

## SOURCES OF FUNDING

None.

## REFERENCES

- Cumbler Ethan, Wald Heidi, Bhatt Deepak L., et al. Quality of Care and Outcomes for In-Hospital Ischemic Stroke. *Stroke* 2014;45(1):231–8.
- Re-examining Acute Eligibility for Thrombolysis (TREAT) Task Force., Levine SR, Khatri P, et al. Review, historical context, and clarifications of the NINDS rt-PA stroke trials exclusion criteria: Part 1: rapidly improving stroke symptoms. *Stroke* 2013;44(9):2500–5.
- Bunch ME, Nunziato EC, Labovitz DL. Barriers to the use of intravenous tissue plasminogen activator for in-hospital strokes. *J Stroke Cerebrovasc Dis* 2012;21(8):808–11.
- Farooq MU, Reeves MJ, Gargano J, et al. In-hospital stroke in a statewide stroke registry. *Cerebrovasc Dis* 2008;25(1–2):12–20.
- Masjuan J, Simal P, Fuentes B, et al. In-hospital stroke treated with intravenous tissue plasminogen activator. *Stroke* 2008;39(9):2614–6.
- Moradiya Y, Levine SR. Comparison of short-term outcomes of thrombolysis for in-hospital stroke and out-of-hospital stroke in United States. *Stroke* 2013;44(7):1903–8.
- Emiru T, Adil MM, Suri MFK, Qureshi AI. Thrombolytic treatment for in-hospital ischemic strokes in United States. *J Vasc Interv Neurol* 2014;7(5):28–34.
- Zivelonghi C, Tamburin S. Mechanical thrombectomy for acute ischemic stroke: the therapeutic window is larger but still “time is brain”. *Funct Neurol* 2018;33(1):5–6.
- Wilson JTL, Hareendran A, Grant M, et al. Improving the assessment of outcomes in stroke: use of a structured interview to assign grades on the modified Rankin Scale. *Stroke* 2002;33(9):2243–6.
- Saver JL, Filip B, Hamilton S, et al. Improving the reliability of stroke disability grading in clinical trials and clinical practice: the Rankin Focused Assessment (RFA). *Stroke* 2010;41(5):992–5.
- The Joint Commission: Specifications Manual for Joint Commission National Quality Measures v2018A. Illinois. [accessed Feb 2018]; Available from: <https://manual.jointcommission.org/releases/TJ-C2018A/>
- Schwamm LH, Fonarow GC, Reeves MJ, et al. Get With the Guidelines-Stroke is associated with sustained improvement in care for patients hospitalized with acute stroke or transient ischemic attack. *Circulation* 2009;119(1):107–15.
- Cumbler E, Wald H, Bhatt DL, et al. Quality of care and outcomes for in-hospital ischemic stroke: findings from the National Get With The Guidelines-Stroke. *Stroke* 2014;45(1):231–8.
- Saver JL. Time is brain--quantified. *Stroke* 2006;37(1):263–6.
- Caparros, F., Ferrigno, M., Decourcelle, A. et al. In-hospital ischaemic stroke treated with intravenous thrombolysis or mechanical thrombectomy. *J Neurol* 2017;264:1804–1810.
- Lu M-Y, Chen C-H, Yeh S-J, et al. Comparison between in-hospital stroke and community-onset stroke treated with endovascular thrombectomy. *PLoS One* 2019;14(4):e0214883.