Direct thrombectomy versus bridging thrombolysis with mechanical thrombectomy in middle cerebral artery stroke: a real-world analysis through National Inpatient Sample data

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OBJECTIVE A paradigm shift in the management of acute ischemic stroke (AIS) due to large-vessel occlusion (LVO) occurred after 2015 when 7 randomized controlled trials demonstrated better outcomes using second-generation thrombectomy devices combined with best medical management than did stand-alone intravenous thrombolysis (IVT) with tissue plasminogen activator (tPA). All recently published landmark trials were designed to study the outcome of mechanical thrombectomy (MT); therefore, the majority of the patients enrolled in these trials received intravenous tPA. Currently, initiating IVT before MT is a matter of debate. Recent trials (DIRECT-MT, DEVT) exploring this clinical question showed noninferiority of MT alone compared with the combined treatment. With this uncertainty, the authors aimed to explore real-world data through the latest National Inpatient Sample (NIS) to compare the safety and outcomes of MT alone with bridging IVT and MT in AIS due to LVO in the middle cerebral artery (MCA).

METHODS NIS data from 2017 to 2018 were analyzed to compare the outcomes and safety profiles of patients who underwent MT+IVT with those who underwent MT alone.

RESULTS A total of 2895 patients were included in the final analysis (MT, n = 1669; MT+IVT, n = 1226). The mean National Institutes of Health Stroke Scale score was 16.2 (SD 6.1) in the MT group and 16.6 (SD 5.97) in the MT+IVT group (p = 0.04). With respect to comorbidities, the two groups did not differ in rates of hypertension (p = 0.730), atrial fibrillation/flutter (p = 0.828), and smoking status (p = 0.914). The rate of diabetes mellitus was significantly higher in the MT group (28%) than in the MT+IVT group (22.1%) (p < 0.001). The frequency of intracerebral hemorrhage (ICH) in the MT group was 17.7% (n = 296) and 21.5% (n = 263) in the MT+IVT group (p = 0.012). Intraventricular hemorrhage (p = 0.875), subarachnoid hemorrhage (p = 0.99), and vasospasm (p = 0.976) did not differ significantly between the groups. The primary outcome considered was disability status between the groups; 23.8% of patients in the MT+IVT group had minimal disability versus 18.2% in the MT group (p = 0.001). The risk of progressing to severe disability from minimal disability decreased with the addition of IVT to MT (OR 0.762, 95% CI 0.637–0.912). The adjusted odds ratio for ICH in the MT+IVT group was 1.28 (95% CI 1.043–1.571, p = 0.018) and 2.676 (95% CI 1.259–5.686, p = 0.01) for access-site hemorrhages.

CONCLUSIONS In the analysis of the NIS database, the MT+IVT group had significantly higher rates of minimal disability at the time of hospital discharge versus the MT-alone group, despite a higher rate of ICH. The question of whether to treat patients with MT+IVT rather than MT alone is currently being addressed in ongoing prospective clinical trials (SWIFT-DIRECT [NCT03494920], MR CLEAN-NO IV [ISRCTN80619088], and DIRECT-SAFE [NCT03494920]). The results of these studies will contribute to greater understanding and progressive improvement in outcomes for AIS patients.

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KEYWORDS mechanical thrombectomy; intravenous thrombolysis; intracerebral hemorrhage; atrial fibrillation; hypertension

ABBREVIATIONS AIS = acute ischemic stroke; ICH = intracerebral hemorrhage; IVH = intraventricular hemorrhage; IVT = intravenous thrombolysis; LVO = large-vessel occlusion; MCA = middle cerebral artery; MT = mechanical thrombectomy; NIHSS = National Institutes of Health Stroke Scale; NIS = National Inpatient Sample; SAH = subarachnoid hemorrhage; tPA = tissue plasminogen activator.

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THE global burden of stroke is a persistent and escalating problem. It is estimated that 4% of US adults will have had a stroke by 2030, increasing the direct annual costs from \$71.55 billion to \$186 billion (USD).^{1,2} Approximately 85% of all strokes are ischemic, and large-vessel occlusion (LVO) accounts for half of them.³ A paradigm shift in the management of acute ischemic stroke (AIS) due to LVO occurred after 2015 when 7 randomized controlled trials demonstrated better outcomes using second-generation thrombectomy devices combined with best medical management than did stand-alone intravenous thrombolysis (IVT) with tissue plasminogen activator (tPA).^{4–10} The advantages of IVT include early recanalization before mechanical thrombectomy (MT), thus obviating the need for MT; altering the thrombus composition, thus facilitating MT; and dissolving thrombotic debris in downstream vessels, thus facilitating reperfusion. Despite the potential benefit of intravenous tPA in achieving recanalization, there is a potential increased risk of systemic and intracranial hemorrhage. All recently published landmark trials were designed to study the outcome of MT, and therefore the majority of the patients enrolled in these trials received intravenous tPA. The pooled post hoc analysis of major trials did not show better recanalization rates for IVT combined with MT.¹¹ Currently, initiating IVT before MT is a matter of debate. Recent trials (DIRECT-MT, DEVT) exploring this clinical question showed noninferiority of MT alone compared with the combined treatment.^{12,13} The DIRECT-MT trial was conducted in China, and the applicability of those results to the US population needs to be studied further. Also, the sample size was small, and prespecified noninferiority margins were generous. The SKIP trial also showed similar outcomes between MT and combined treatment, although it failed to meet the noninferiority margin.¹⁴ With this uncertainty, we aimed to explore the real-world data through the latest National Inpatient Sample (NIS) to compare the safety and outcomes of MT alone with bridging IVT and MT in AIS because of an LVO in the middle cerebral artery (MCA). The limitations in using the NIS database for this study are that the data do not provide the time of onset of stroke to hospitalization or an objective scale of functional status at discharge, or whether each case met eligibility criteria for IVT. Acknowledging these limitations, we explored the NIS data to provide meaningful analysis to answer the above clinical question.

Methods

Study Population

Data were extracted from the NIS database for 2017 to 2018; this database is the largest publicly available all-payer database in the US (<https://www.hcup-us.ahrq.gov/nisoverview.jsp>). The unweighted data contain more than 7 million hospitalizations. These were coded in the form of diagnostic and procedural ICD-10 codes. Inclusion criteria for the study were 1) MCA stroke as the primary cause of admission, 2) the presence of National Institutes of Health Stroke Scale (NIHSS) score in the form of an ICD-10 diagnostic code, 3) age > 18 years, 4) an NIHSS score ≥ 5 and ≤ 30 , and 5) patients who underwent MT alone or MT+IVT.

FIG. 1. Flow diagram showing inclusion and exclusion of the cases.

Patients were excluded from the study if 1) there was the presence of a tandem LVO, 2) an MCA stroke was not a primary cause of admission, 3) there was an absence of an NIHSS score or score < 5 or > 30, or 4) the patient did not undergo MT as the primary treatment procedure. Detailed inclusion and exclusion criteria are shown in Fig. 1.

Data Extraction and Patient Characteristics

The data were extracted from the NIS data (unweighted) based on the ICD-10 diagnostic and procedural codes. Following the adoption of ICD-10 data, the granularity of the diagnostic coding was significantly increased, giving the chance to explore more entities for the analysis. The codes used for the diagnosis of MCA stroke, internal carotid artery stroke, NIHSS score, presence of intracerebral hemorrhage (ICH), intraventricular hemorrhage (IVH), subarachnoid hemorrhage (SAH), hypertension, smoking status, atrial fibrillation/atrial flutter, diabetes, access-site hemorrhage, vasospasm, IVT injection (same hospital/elsewhere), ventilation status (< 24, 24–96, and > 96 hours), and contrast dye allergy are provided in Supplementary Table 1. The data were grouped based on the intervention (MT alone vs MT+IVT). Patient socioeconomic characteristics such as patient location (urban/rural), hospital location, patient zip code, and median income were also analyzed. As the NIS data did not provide any objective scale for measuring stroke severity, like the

TABLE 1. Demographics and disability status of the MT and MT+IVT patient groups

Variable	MT (n = 1669)	MT+IVT (n = 1226)	p Value
Mean age, yrs	69.9 (14.8)	69.23 (4.4)	0.09
Sex			0.96
M	765 (45.8)	563 (45.9)	
F	904 (54.2)	663 (54.1)	
Diabetes	467 (28)	271 (22.1)	<0.001
Hypertension	1117 (66.9)	828 (67.5)	0.730
Atrial fibrillation/flutter	671 (40.2)	488 (39.8)	0.828
Smoking	575 (34.5)	420 (34.3)	0.914
Mean NIHSS score	16.2 (6.1)	16.6 (5.97)	0.04
Race			
White	1117 (69.7)	807 (68.9)	
Black	263 (16.4)	167 (14.3)	
Hispanic	124 (7.7)	110 (9.4)	
Asian/Pacific Islander	41 (2.6)	39 (3.3)	
Native American	5 (0.3)	4 (0.3)	
Other	53 (3.3)	44 (3.8)	
Missing	66 (3.95)	55 (4.4)	
Discharge destination			
Routine	304 (18.2)	292 (23.8)	
Transfer to short-term hospital	49 (2.9)	41 (3.3)	
Transfer to other*	991 (59.4)	658 (53.7)	
Home healthcare	174 (10.4)	122 (10)	
Against medical advice	5 (0.3)	3 (0.2)	
Died	144 (8.6)	109 (8.9)	
Disability based on discharge destination			
Minimal disability	304 (18.2)	292 (23.8)	0.001
Moderate to severe disability	1219 (73.1)	824 (67.3)	
Died	144 (8.6)	109 (8.9)	
Mean hospital charges, USD	\$173,544.32 (\$133,158.19)	\$184,908.22 (\$132,582.25)	<0.001

Values represent the number of patients (%) or the mean (SD) unless stated otherwise. Boldface type indicates statistical significance.

* Hospital, short-term skilled facility, or hospice care.

modified Rankin Scale or postprocedural perfusion status (Thrombolysis in Cerebral Infarction), the current study considered disability status as its primary outcome. Disability status was defined based on the discharge disposition and grouped into mild, moderate to severe, and in-hospital death. Discharge to home was considered a mild disability; discharge to any other facility (hospital, short-term skilled facility, or hospice care) was considered moderate to severe disability. Patients who died during hospital admission were categorized as a third discharge category. Secondary outcomes analyzed were the presence of ICH, IVH, SAH, vasospasm, and access-site hemorrhages.

Statistical Analysis

All variables are described in a standard descriptive fashion. Continuous variables are described as mean (SD), median as appropriate, and categorical variables as frequencies. Groups were compared using the chi-square test for categorical variables, the t-test, and the Mann-Whitney U-test for continuous variables where applicable. Ordinal

regression analysis was performed to predict the factors affecting the primary outcome (disability status) after adjusting for all the covariates and binary regression analysis for the secondary outcomes. Statistical significance was considered if the p value (two-tailed) was < 0.05. Statistical analysis was performed using IBM SPSS version 27 (IBM Corp.). Odds ratio and 95% confidence interval were derived and are presented for all outcomes after adjusting for the potential confounding factors. The intervention's effect was presented for the secondary outcomes after adjusting for covariate factors.

Results

Clinical Characteristics

A total of 2895 patients were included in the final analysis (MT, n = 1669; and MT+IVT, n = 1226). The mean ages were 69.9 years (SD 14.8 years) in the MT group and 69.23 years (SD 14.4 years) in the MT+IVT group (p = 0.09) (Table 1). The male-to-female ratio between the groups was not statistically significant (MT, 45.8% and

FIG. 2. Distribution of patient cohort based on hospital divisions across the US. Created using mapchart.net. CC BY-SA 4.0 (<https://creativecommons.org/licenses/by-sa/4.0/>).

54.2%; and MT+IVT, 45.9% and 54.1%) ($p = 0.96$). White (MT, 69.7%; and MT+IVT, 68.9%) and Black (MT, 16.4%; and MT+IVT, 14.3%) were the predominant race categories. The mean NIHSS score was 16.2 (SD 6.1) in the MT group and 16.6 (SD 5.97) in the MT+IVT group ($p = 0.04$). With respect to comorbidities, the two groups did not differ in rates of hypertension ($p = 0.730$), atrial fibrillation/flutter ($p = 0.828$), and smoking status ($p = 0.914$). Diabetes was significantly higher in the MT group (28%) versus the MT+IVT group (22.1%) ($p < 0.001$).

Socioeconomic Characteristics

The most common insurance was Medicare (MT, 64.9%; and MT+IVT, 61.1%) in both groups, followed by private insurance (MT, 19.6%; and MT+IVT, 24.3%). Patient location was stratified based on the 6-category urban-rural health scheme of the National Center for Health Statistics. Most patients lived in “central” counties of metro areas with a population ≥ 1 million people (MT, 31.9%; and MT+IVT, 30.2%), followed by “fringe” counties of metro areas with a population ≥ 1 million people (MT, 23.9%; and MT+IVT, 24.2%). The South Atlantic region was the most common area (MT, 24.2%; and MT+IVT, 21%) (Fig. 2). Complete details of the socioeconomic characteristics are presented in Table 2. Patients in the 0–25th percentile for median household income per zip code were slightly overrepresented compared with the other percentiles (MT, 29.3%; and MT+IVT, 28.9%) ($p = 0.824$). The mean hospital charges were \$173,544 (SD \$133,158.19) for the MT group and \$184,908.22 (SD \$132,582.25) for the MT+IVT group ($p < 0.001$).

Intervention and Complications

The frequencies of ICH were 17.7% ($n = 296$) in the

MT group and 21.5% ($n = 263$) in the MT+IVT group ($p = 0.012$). IVH ($p = 0.875$), SAH ($p = 0.999$), and vasospasm ($p = 0.976$) did not differ significantly between the groups. The MT+IVT group (1.7%) had more access-site hemorrhages compared with the MT group (0.7%) ($p = 0.013$). Mechanical ventilation status was not significantly different between the groups (Table 3). The mean hospital lengths of stay were 8.17 days (SD 9.91 days) in the MT group and 7.16 days (SD 6.9 days) in the MT+IVT group ($p = 0.002$).

Primary and Secondary Outcomes

The primary outcome considered was disability status; 23.8% of patients in the MT+IVT group had minimal disability versus 18.2% in the MT group ($p = 0.001$) (Fig. 3). The in-hospital death rate was similar in both groups (MT, 8.6%; and MT+IVT, 8.9%). An ordinal regression analysis was performed to calculate the OR and 95% CI for each independent variable's effect on the outcome (Table 4). The OR for secondary outcomes (IVH, ICH, SAH, vasospasm, and access-site hemorrhages) was calculated through binary regression analysis after adjusting the effect of all independent variables (Table 5). Ordinal regression analysis revealed multiple factors predicting the outcome. The risk of progressing to severe disability from minimal disability decreased with the addition of IVT to MT treatment (OR 0.762, 95% CI 0.637–0.912). The adjusted OR for ICH in the MT+IVT group was 1.28 (95% CI 1.043–1.571, $p = 0.018$) and 2.676 (95% CI 1.259–5.686, $p = 0.01$) for access-site hemorrhages.

Discussion

In the current study, we found a significantly higher rate

TABLE 2. Socioeconomic data of the patient cohort

Variable	MT	MT+IVT	p Value
Insurance			
Medicare	1082 (64.9)	749 (61.1)	
Medicaid	151 (9.1)	104 (8.5)	
Private	327 (19.6)	298 (24.3)	
Self-pay	64 (3.8)	56 (4.6)	
No charge	6 (0.4)	4 (0.3)	
Other	37 (2.2)	14 (1.1)	
Hospital division			
New England	83 (5)	63 (5.1)	
Middle Atlantic	252 (15.1)	139 (11.3)	
East North Central	268 (16.1)	177 (14.4)	
West North Central	98 (5.9)	92 (7.5)	
South Atlantic	408 (24.4)	258 (21)	
East South Central	140 (8.4)	105 (8.6)	
West South Central	131 (7.8)	132 (10.8)	
Mountain	82 (4.9)	68 (5.5)	
Pacific	207 (12.4)	192 (15.7)	
Patient location			
"Central" counties of metro areas of ≥ 1 million people	529 (31.9)	367 (30.2)	
"Fringe" counties of metro areas of ≥ 1 million people	397 (23.9)	294 (24.2)	
Counties in metro areas of 250,000–999,999 people	367 (22.1)	291 (23.9)	
Counties in metro areas of 50,000–249,999 people	128 (7.7)	107 (8.8)	
Metropolitan counties	131 (7.9)	95 (7.8)	
Not metropolitan or micro-political counties	107 (6.4)	62 (5.1)	
Missing	10 (0.59)	10 (0.81)	
Median household income for patient zip code, percentile			
0–25th	480 (29.3)	346 (28.9)	0.824
26th–50th	426 (26)	310 (25.9)	
51st–75th	398 (24.3)	307 (25.6)	
76th–100th	337 (20.5)	234 (19.5)	
Missing	28 (1.6)	29 (2.3)	

Values represent the number of patients (%) unless stated otherwise.

of minimal disability in patients who received MT+IVT versus MT alone for MCA LVO despite higher rates of intracranial hemorrhage. In contrast to these results, the recent DIRECT-MT,¹³ DEVT,¹² and SKIP¹⁴ trials all demonstrated noninferiority of MT alone compared with MT+IVT; however, the MT-alone group in our analysis does not include all patients within the 4.5-hour window after stroke onset for IVT. Similar to our study, the SKIP trial demonstrated a higher rate of any ICH (symptomatic and asymptomatic together) in the MT+IVT group (MT 33.7% vs MT+IVT 50.5%). After adjusting for all independent variables, the effect of adding IVT to MT reduced the chance of having moderate to severe disability by 34%

TABLE 3. Complications and ventilation of the MT and MT+IVT groups

Complication	MT (n = 1669)	MT+IVT (n = 1226)	p Value
ICH	296 (17.7)	263 (21.5)	0.012
IVH	22 (1.3)	17 (1.4)	0.875
SAH	98 (5.9)	72 (5.9)	0.999
Vasospasm	22 (1.3)	16 (1.3)	0.976
Access-site hemorrhage	12 (0.7)	21 (1.7)	0.013
Contrast allergy	13 (0.8)	10 (0.8)	0.912
Ventilation, hrs			
<24	81 (4.9)	65 (5.3)	0.586
24–96	136 (8.1)	102 (8.3)	0.868
>96	91 (5.5)	71 (5.8)	0.695
Mean LOS, days	8.17 (9.91)	7.16 (6.9)	0.002

LOS = length of stay.

Values represent the number of patients (%) or the mean (SD) unless stated otherwise. Boldface type indicates statistical significance.

(OR 0.762). In addition to IVT, an increase in age, presence of ICH, IVH, SAH, vasospasm, diabetes as a comorbidity, and a higher NIHSS score influenced the disability status.

The primary outcome considered in most of the trials was functional independence at 90 days posttreatment (shift of modified Rankin Scale score). In the DEVT trial, 54.3% of the MT-alone group achieved functional independence compared with 46.6% in the MT+IVT group.¹² These findings are in agreement with the DIRECT-MT trial as well. Similarly, in the SKIP trial, 59.4% of patients achieved functional independence at 90 days in the MT-alone group compared with 57.3% in the MT+IVT group (OR 1.09), a difference that was not significant.¹⁴ These three trials all used a binary outcome measure, whereas we separated outcome into three different groups, contributing to our different findings.

Secondary outcomes in our study were limited to ICH, access-site hemorrhages, SAH, and vasospasm due to limitations of the NIS database. As previously mentioned, we saw a higher ICH rate in our MT+IVT group, even though this group had a higher rate of minimal disability at discharge. This may be because many of these hemorrhages were not clinically significant, a characteristic that is impossible to determine with our methodology. The DEVT, DIRECT-MT, and SKIP trials all examined symptomatic ICH, finding no significant difference in this measure between the MT-alone and MT+IVT groups.^{12–14} The benefit of both IVT and MT in treating AIS has been established.^{4–10} The addition of bridging IVT to MT has pros and cons. Factors favoring thrombolysis initiation are good collaterals, more distal location of the thrombus, a low NIHSS score, infarcts of multiple territories, and any factor precluding rapid access to the MT. Factors favoring MT are proximal occlusions, use of anticoagulants/ineligibility for thrombolysis, and a higher risk of ICH.

Time as the Most Significant Influence

Time of intervention after the onset of a stroke is considered the most crucial factor for salvaging the ischemic

FIG. 3. Distribution of disability between the MT-alone and MT+IVT groups.

brain. Most trials considered 4.5 to 6 hours for the administration of IVT. Based on the HERMES group's meta-analysis,¹⁵ the median time from stroke onset to endovascular perfusion was 196 minutes (IQR 142–267 minutes). After the paradigm shift of stroke management from IVT alone to endovascular thrombectomy and bridging thrombolysis, two further trials, DEFUSE¹⁶ and DAWN,¹⁷ demonstrated improved functional outcomes in patients who received MT and IVT 6 to 16 hours after symptom onset. The DAWN trial concentrated on the clinical deficit and radiological infarct mismatch, whereas the DEFUSE trial selection was based on perfusion imaging. The results from these trials were promising in the means of care individualization. Unfortunately, the NIS database did not provide data regarding time from symptom onset to treatment, limiting our study. It is possible that the patients in our study in the MT+IVT group had better outcomes than the MT-alone group because the latter may have presented outside of the 4.5-hour window for IVT administration eligibility.

Limitations

There are several limitations to this study. The most significant limitation, as previously discussed, is the lack of data regarding time from symptom onset to interven-

TABLE 5. Binary regression analysis for secondary outcomes focusing on the intervention's effect on outcome after considering all covariate factors

Outcome	MT (n = 1669)	MT+IVT (n = 1226)	OR (95% CI)	p Value
ICH	296 (17.7)	263 (21.5)	1.280 (1.043–1.571)	0.018
SAH	98 (5.9)	72 (5.9)	1.020 (0.727–1.432)	0.90
IVH	22 (1.3)	17 (1.4)	1.00 (0.991–1.008)	0.932
Access-site hemorrhage	12 (0.7)	21 (1.7)	2.676 (1.259–5.686)	0.01
Vasospasm	22 (1.3)	16 (1.3)	0.927 (0.454–1.889)	0.834

Values represent the number of patients (%) unless stated otherwise. Boldface type indicates statistical significance.

tion. Hence, this data analysis cannot be compared with trials in which the patients were eligible for both treatment options. The patients in our MT group may or may not have been eligible for IVT. This analysis offers an insight into the safety profile for the MT+IVT group.

Also, we used discharge disposition as a surrogate for the functional outcome, though factors such as patient preference and family support may confound this measure. Again, the outcomes of the MT+IVT group would be influenced by the fact that they arrived in the treatment facility earlier (as they were eligible for IVT) versus the MT-alone group (in which patients may or may not have been eligible for IVT due to arrival at the treatment facility > 4.5 hours after stroke onset). We did not analyze our patients separately based on whether they initially presented to a community hospital versus a tertiary center (i.e., “drip and ship” vs “motherhood” model), though this may also contribute to the outcome. Other limitations include loss of data in exclusion due to missing data fields, interrater coding bias, inability to compare baseline degree of deficit (NIHSS), and extensive variability in ICD-10 codes.

Conclusions

Although ongoing clinical trials are best suited to address the clinical question of MT alone versus MT+IVT for treatment of AIS due to LVO, real-world data in terms of patient outcomes are essential for gaining a wider perspective. In our analysis of the NIS database, the MT+IVT group had significantly higher rates of minimal disability at the time of hospital discharge compared with the MT-alone group, despite a higher rate of ICH. The question of whether to treat patients with MT+IVT rather than MT alone is currently being addressed in ongoing prospective clinical trials (SWIFT-DIRECT [NCT03494920], MR CLEAN-NO IV [ISRCTN80619088], and DIRECT-SAFE [NCT03494920]). We look forward to the results of these studies and the progressive improvement in outcomes for AIS patients.

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TABLE 4. Generalized linear regression model for outcomes: ordinal regression analysis for the primary outcome (disability status)

Factor	OR	95% CI	p Value
Age	1.041	1.032–1.050	<0.001
MT+IVT	0.762	0.637–0.912	0.003*
IVH	2.597	1.192–5.657	0.016
SAH	1.708	1.168–2.497	0.006
Vasospasm	0.522	0.251–1.084	0.081
Diabetes	1.497	1.218–1.841	<0.001
ICH	1.974	1.553–2.510	<0.001
Ventilation, hrs			
<24	2.553	1.670–3.904	<0.001
24–96	4.829	3.462–6.735	<0.001
>96	4.768	3.143–7.231	<0.001
NIHSS score	1.076	1.059–1.092	<0.001

Boldface type indicates statistical significance.

* Note the effect of IVT on outcome.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Guthikonda, Kandregula, Savardekar, Kosty, Cuellar. Acquisition of data: Kandregula. Analysis and interpretation of data: Kandregula, Savardekar, McLarty. Drafting the article: Kandregula, Savardekar, Trosclair. Critically revising the article: Guthikonda, Kandregula, Savardekar, Sharma, Kosty, Trosclair, Cuellar. Reviewed submitted version of manuscript: Guthikonda, Kandregula, Savardekar, Sharma, Kosty, Trosclair, Cuellar. Approved the final version of the manuscript on behalf of all authors: Guthikonda. Statistical analysis: Kandregula, McLarty. Administrative/technical/material support: Guthikonda. Study supervision: Guthikonda, Savardekar, Sharma, Kosty, Cuellar.

Supplemental Information

Online-Only Content

Supplemental material is available online.

Supplementary Table 1. <https://thejns.org/doi/suppl/10.3171/2021.4.FOCUS21132>.

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