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Disparities in the Use of Mechanical Thrombectomy Alone Compared with Adjunctive Intravenous Thrombolysis in Acute Ischemic Stroke in the United States

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ABSTRACT

BACKGROUND AND PURPOSE: For patients with large-vessel occlusion, mechanical thrombectomy (MT) without IV-tPA is a proved strategy. The relative benefit of direct MT versus MT+IV-tPA for patients with indications for IV-tPA is being actively investigated. We used a national inpatient database to assess trends in use and patient profiles after MT+IV-tPA versus mechanical thrombectomy alone.

MATERIALS AND METHODS: The National Inpatient Sample was queried between 2013 and 2018 for patients undergoing mechanical thrombectomy for acute ischemic stroke. Patients who received mechanical thrombectomy alone were compared with those who underwent MT+IV-tPA. The Cochran-Armitage test was conducted to assess the linear trend of use of mechanical thrombectomy alone among the entire cohort and between admissions involving non-White and White patients. All estimates were nationalized using discharge weights.

RESULTS: A total of 89,645 weighted admissions were identified pertaining to mechanical thrombectomy for acute ischemic stroke from 2013 to 2018. Of these, 59,935 (66.9%) admissions involved mechanical thrombectomy alone. There was an increase in the trend toward the use of mechanical thrombectomy alone (trend: 3.26%; $P < .001$) per year. Multivariable regression analysis regarding patient profiles indicated that patients who identified as Black (OR = 0.83, $P = .001$) or Hispanic (OR = 0.79; $P < .001$) were more likely to undergo mechanical thrombectomy alone compared with those who identified as White. There was no statistically significant difference in the slope between non-White and White populations receiving mechanical thrombectomy alone (trend: +0.93% in favor of non-White; $P = .096$).

CONCLUSIONS: Our results indicated that mechanical thrombectomy alone was used more frequently than MT+IV-tPA among patients with acute ischemic stroke. The disparity between those who identify as White and non-White persisted across the years, though it is closing.

ABBREVIATIONS: ADSS = Administrative Data Stroke Scale; AIS = acute ischemic stroke; ASOV = Administrative Stroke Outcome Variable; ICD = International Classification of Diseases; MT = mechanical thrombectomy; NIS = Nationwide Inpatient Sample

Guidelines for acute ischemic stroke (AIS) are rapidly changing with the advent of 5 randomized trials in 2015 that supported the use of mechanical thrombectomy (MT) over alteplase alone for large-vessel occlusion.¹ The Highly Effective Reperfusion evaluated in Multiple Endovascular Stroke (HERMES) trial meta-analysis showed the superiority of the tPA along with MT over tPA alone and lowered rates of disability at the 3-month mark.¹

In 2018, American Heart Association/American Stroke Association released guidelines regarding early management of stroke, which recommended the use of MT within 16–24 hours of stroke onset. It also stressed that IV-tPA treatment should not be delayed.² In 2020 and 2021, three clinical trials, Direct Endovascular Thrombectomy vs Combined IVT and Endovascular Thrombectomy for Patients With Acute Large Vessel Occlusion in the Anterior Circulation (DEVT); Direct Intra-arterial Thrombectomy in Order to Revascularize AIS Patients with Large Vessel Occlusion Efficiently in Chinese Tertiary Hospitals: A Multicenter Randomized Clinical Trial (DIRECT-MT); and Direct Mechanical Thrombectomy in Acute LVO Stroke (SKIP), all investigated the efficacy of various combinations of endovascular and medical treatments for AIS. Two of the 3 trials (DEVT and DIRECT-MT) demonstrated noninferiority of MT alone compared with MT+IV-tPA.^{3–5}

While the trends in AIS are changing due to new research into treatment and management, other studies have found disparities

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in the use of MT for patients with AIS associated with race and ethnicity.⁶ To investigate whether the gap in the use of the aforementioned techniques between races is closing, we studied the trends in outcomes, use, and patient profiles of MT alone compared with MT+IV-tPA in the United States using a national inpatient database.

MATERIALS AND METHODS

Data Source

The Nationwide Inpatient Sample (NIS) database was queried from January 1, 2013, to December 31, 2018. The NIS is created by the Healthcare Cost and Utilization Project. It samples ~7 million hospitalized patients per year, representing 20% of all discharges annually. This database is the largest public national all-payer database, sponsored by the Agency for Healthcare Research and Quality.⁷ Furthermore, the NIS contains discharge weights that aid investigators in extrapolating discharges using the variable discharge weight (for data after 2012) and trend weight (for data before 2012). In turn, the cases in the NIS are converted to national estimates.

Cohort Selection

The 9th and 10th editions of the International Classification of Diseases (ICD-9 and -10) were used to identify patients with AIS who underwent MT from 2013 to 2018. These years were selected to include only the modern era of MT devices, mostly involving stent retrievers, because the first 2 stent retrievers received FDA approval in 2012.^{8,9} Patients with a primary diagnosis of subarachnoid hemorrhage or intracerebral hemorrhage or any diagnosis of head trauma were excluded. Diagnosis codes regarding postoperative hemorrhage were also selected. All included ICD-9 and ICD-10 codes are available in the Online Supplemental Data.

Outcomes and Variables of Interest

We recorded the following demographic variables: age, sex, race, insurance type, and Elixhauser Comorbidity Indices. Elixhauser Comorbidity Indices are based on 31 predefined comorbidities that use ICD-9 and -10 codes, which identify risks of poor outcomes.¹⁰ These comorbidities are listed in the Online Supplemental Data. We collected the following hospital data: bed size, location (rural/urban), teaching status, and region (Northeast, Midwest, South, West).

The Administrative Data Stroke Scale (ADSS) and Administrative Stroke Outcome Variable (ASOV) were both calculated in this study, both based on Patel et al.¹¹ The ADSS is a validated scale with a moderate correlation with the admission NIHSS with a Spearman correlation of 0.39 and a strong correlation with NIHSS >15 ($P < .001$) at discharge. The ADSS consists of the following variables: mechanical ventilation, coma, aphasia, stupor, cerebral edema, cerebral herniation, nasogastric tube placement, parenteral nutrition, dysphagia, and neglect. The ADSS is derived using the sum of the odds ratio of each variable in a multivariable regression model. The ASOV represents poor functional outcome if any of the following were present: in-hospital mortality, discharge to hospice care, discharge to long-term acute care facility, or discharge to skilled nursing facility. This has substantial agreement with a 90-day mRS > 3

cutoff (κ statistic = 0.69). Poor functional outcome is a surrogate for mRS > 3 at 90-day follow-up. More information can be seen in the study published by Patel et al.¹¹

Statistical Analysis

The cohort was divided into 2 groups: admissions involving MT alone and those involving MT+IV-tPA. The Cochran-Armitage test was conducted to assess linear trends in the proportions of use of MT alone compared with MT+IV-tPA among all admissions involving MT for AIS. The numerator of this proportion was MT alone, and the denominator was patients who underwent MT alone in addition to those who underwent MT+IV-tPA. This analysis was also conducted to assess trends in the use of MT alone between admissions involving non-White and White patients. For each group, the numerator was the number of those who received MT alone, and the denominator was those who received either treatment. Trend lines were compared between the 2 groups using the ANOVA test, which produces a mean difference in trend with its corresponding 95% CI. Linear trends in the proportion of admissions with poor functional outcome among the 2 groups were also assessed by the Cochran-Armitage test.¹² The Cuzick nonparametric test was used to assess linear trends in mean ADSS scores in the 2 groups.¹³ Results from this analysis are represented as a change in the slope of proportion per year with its 95% confidence interval. Multivariable stepwise logistic regression analysis, stratified by hospital region and year, was conducted to assess patient profiles for MT alone versus MT+IV-tPA. The Wald test was performed to investigate the evidence of whether the outcome of MT alone varied across the different groups for each categorical variable within the regression. A $P < .05$ for this test indicates that there is no difference between the groups regarding the outcome.

Regression results are represented as ORs and their respective 95% CIs. χ^2 tests were used to compare the proportion of each categorical variable between the 2 groups. A Student t test was used to compare the means of each continuous variable between the 2 groups. Statistical analysis was performed using STATA 16 (StataCorp).¹⁴ P values < .05 were considered statistically significant. All estimates were nationalized using discharge weights provided by the Healthcare Cost and Utilization Project.

RESULTS

Patient Characteristics

A total of 89,645 admissions were identified from 2013 to 2018, including 59,935 undergoing MT alone and 29,710 undergoing MT+IV-tPA. The mean age was 68.3 (standard error: ± 0.15) years for MT alone and 68.4 (± 0.18) years for MT+IV-tPA. There were 29,915 (49.9%) women in the cohort of MT alone and 15,070 (50.7%) in the cohort with MT+IV-tPA. The mean ADSS score was 4.46 (SE, 0.09) for MT alone and 4.63 (SE, 0.12) for MT+IV-tPA. There were 40,465 admissions (71.56%) involving patients who identified as White in the MT alone group and 19,100 (67.43%) in the MT+IV-tPA group ($P < .001$). Additional patient characteristics can be seen in the Online Supplemental Data.

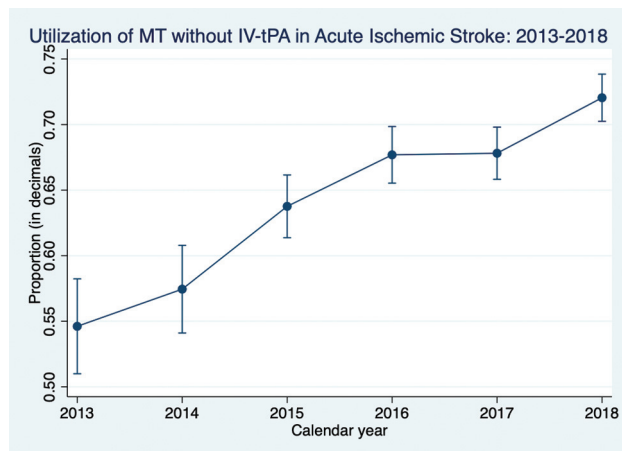


FIG 1. Use of MT alone among those with AIS undergoing MT.

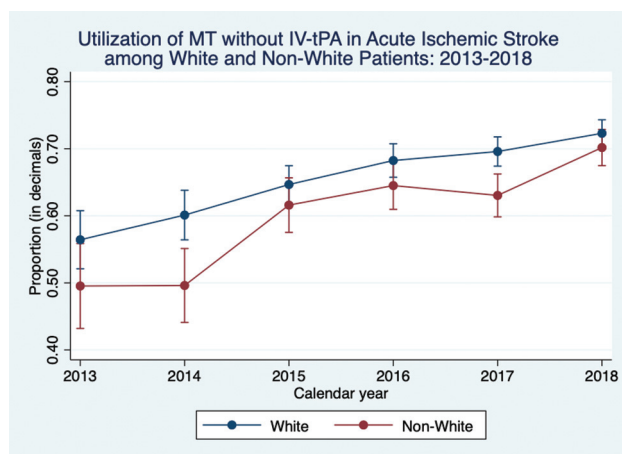


FIG 2. Use of MT alone among those who identify as White versus non-White among those with AIS.

Trend Analysis

The use of MT alone ranged from 3315 in 2013 (54.6% of all MT cases that year) to 20,230 (72.0%) in 2018. There was an increase in the trend toward the use of MT without IV-tPA among patients with AIS by an average of 3.26% per year (95% CI, 2.64%–3.87%; $P < .001$). This is also depicted as a line graph in Fig 1.

The prevalence of the use of MT alone among those who identified as White increased from 2259 (56.43% of all admissions involving those who identify as White) in 2013 to 13,535 (72.30%) in 2018. There was an average increase in the proportion of MT alone by 2.96% per year (95% CI, 2.25%–3.66%). The prevalence of the use of MT alone among those who identified as non-White ranged from 795 (49.53%) in 2013 to 5764 (70.18%) in 2018. There was an average increase in the proportion of MT alone by 3.89% per year (95% CI, 2.89%–4.89%). There was no statistically significant difference in slope between the 2 groups (difference in slope: +0.93% in favor of non-White; 95% CI: -0.17% – 2.03% ; $P = .096$). This analysis is also depicted as a line graph in Fig 2.

The proportion of poor functional outcome among admissions involving MT alone decreased from 83.1% ($n = 2755$) in 2013 to 78.1% ($n = 15,790$) in 2018. There was an average decrease in the proportion of poor functional outcomes by -0.67% per year (95%

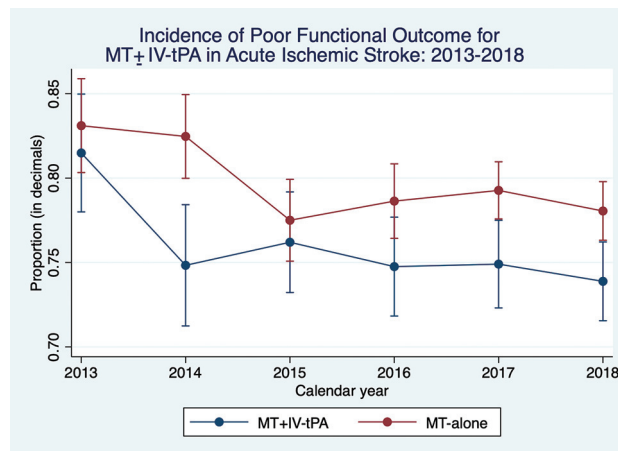


FIG 3. The incidence of poor functional outcome for MT versus MT+IV-tPA.

CI, -1.22 to -0.12). On the other hand, the proportion of poor functional outcomes among admissions involving MT+IV-tPA decreased from 2245 (81.5%) in 2013 to 5800 (73.9%) in 2018. There was an average decrease in the proportion of poor functional outcomes by -0.98% per year (95% CI, -1.69 to -0.27). There was no statistically significant difference in slope between the 2 groups (difference in slope: $+0.31\%$ in favor of MT alone; 95% CI, -0.54% – 1.16% ; $P = .47$). This analysis is also depicted as a line graph in Fig 3.

The mean ADSS among admissions involving MT alone decreased by an average of -0.41 per year (95% CI, -0.56 to -0.27). Meanwhile those involving MT+IV-tPA decreased from 2013 to 2018 (trend: -0.37 ; 95% CI, -0.51% to -0.22%). There was no significant statistical difference between the 2 slopes (difference in slope: MT alone lower by 0.046; 95% CI, -0.24 – 0.15 ; $P = .65$). This analysis is also depicted as a line graph in the Online Supplemental Data.

Multivariable Regression

Multivariable regression assessing the association between patient profiles and the type of therapy received (MT alone versus MT+IV-tPA) was conducted. Patients who identified as Black had lower odds of receiving MT alone compared with those who identified as White (OR = 0.83; 95% CI, 0.75–0.92; $P = .001$). Those who identified as Hispanic also had lower odds of receiving MT alone compared with those who identified as White (OR = 0.79; 95% CI, 0.70–0.89; $P < .001$). Those who identified as any of the other races had similar odds of receiving MT alone compared with those who identified as White (OR = 0.90; 95% CI, 0.79–1.02; $P = .10$). Admissions in urban teaching hospitals had higher odds of receiving MT alone compared with those in urban nonteaching hospitals (OR = 1.44; 95% CI, 1.29–1.61; $P < .001$). Admissions in rural hospitals had similar odds of patients undergoing MT alone compared with those in urban nonteaching hospitals (OR = 0.80; 95% CI, 0.37–1.72; $P = .57$). Additional results can be seen in the Table.

DISCUSSION

Based on our analysis, there was an increasing trend in the use of MT alone over MT+IV-tPA. Our multivariable regression

Multivariable regression on patient profiles of MT alone (versus MT+IV-tPA)

Outcome: MT Alone (vs MT+IV-tPA)	Odds Ratio	P Value	95% CI	
Race		<.001 ^a		
White	1.000	—	—	—
Black	0.830	.001	0.747	0.922
Hispanic	0.788	<.001	0.698	0.890
Other	0.899	.102	0.792	1.021
Region of hospital		<.001 ^a		
Northeast	1.000	—	—	—
Midwest	0.979	.783	0.845	1.135
South	0.886	.064	0.779	1.007
West	0.826	.008	0.716	0.952
Median household income national quartile for patient ZIP code		.032 ^a		
0–25th Percentile	1.000	—	—	—
26th–50th Percentile	1.078	.111	0.983	1.183
51st–75th Percentile	1.022	.666	0.926	1.127
>75th Percentile	0.934	.221	0.838	1.042
Location/teaching status of hospital		<.001 ^a		
Urban nonteaching	1.000	—	—	—
Urban teaching	1.442	<.001	1.286	1.616
Rural	0.802	.571	0.374	1.721
ADSS score	0.998	.267	0.994	1.002
Elixhauser Comorbidity Index score	1.017	.050	1.000	1.034

Note:—indicates not available (reference group).

^a P value for Wald test.

indicated that those who identified as Black or Hispanic were more likely to receive MT+IV-tPA over MT alone compared with those who identified as White. The Midwest and South had similar odds of using MT alone compared with the Northeast, while those in the West had higher odds of receiving MT alone. Our analysis also revealed that the trends in the use of MT alone were increasing at a similar rate for both White and non-White populations with AIS receiving MT. The overall rate of the use of MT alone was still higher in Whites than in Hispanics, Blacks, and other races/ethnicities, showing a possible presence of disparities.

Brinjikji et al⁶ found that among the patients with a primary diagnosis of AIS, the use of MT among Black patients was less than among White patients. This finding was similar to ours, though they used the NIS from 2006 to 2010. Our analysis showed no difference in the use of MT among differing insurance statuses, which contradicted their findings. Brinjikji et al indicated a significant reduction in the use of MT in uninsured patients compared with those with private insurance.⁶ Golnari et al¹⁵ investigated thrombectomy rates, outcomes, and readmission across the United States between 2016 and 2017 using the NIS and National Readmission Database (NRD) and compared the results with those of the HERMES collaboration meta-analysis.¹⁶ Golnari et al also found a similar rate of nonroutine discharge to our cohort of NIS from 2013–2018 (78.2% versus 78.0% for all thrombectomies, respectively). They indicated that a racial disparity existed for thrombectomy; those who identified as Black were less likely to receive MT than those who identified as White (OR = 0.88; $P < .001$). Our study also shows a racial disparity in the differences between MT alone and MT+IV-tPA; those who identified as a minority were less likely to receive MT alone (versus MT+IV-tPA) compared with those who identified as White. Moreover, this finding was contradictory to the findings of

Rinaldo et al.¹⁷ Among those who underwent MT, there was no difference in the odds of tPA administration among those who identified as Black or Hispanic compared with those who identified as White.¹⁷ This difference may be due to the fewer number of years in a different database that Rinaldo et al analyzed. Last, our results show that MT alone has a lower rate of postoperative hemorrhage than MT+IV-tPA, which was similar to the findings of Rinaldo et al.

Nagaraja et al¹⁸ also analyzed racial disparities among those who underwent MT, MT+IV-tPA, and tPA alone in the NIS in 2016. They reported that there was no disparity in use, but there were differences in outcomes.¹ Non-White patients were less likely to be discharged to home compared with White patients if they underwent tPA alone or MT alone.¹⁸ On the contrary, we identified disparities in use. This difference may be due to the inclusion of a single year in the study of Nagaraja et al.¹⁸ This can be seen in Fig 2 of our study, which shows that the proportion of the use of MT alone in 2016 was similar among White and Non-White patients.

Additionally, our analysis shown in Fig 2 indicates that the gap in racial disparities for use of MT alone and MT+IV-tPA is closing across the years. This finding is supported by Otite et al,¹⁹ who analyzed the 10-year trend in racial disparity in tPA and MT use in the NIS. Although they analyzed tPA and MT use separately, the conclusion was similar to ours. They concluded that the use of both stroke treatments was lower among non-White patients compared with White patients, but the gap is closing.

Future Implications

The HERMES collaboration helped shed light on the efficacy of thrombectomy for AIS, while the 3 recent clinical trials (DIRECT-MT, DEVT, and SKIP) contributed to the literature by investigating the efficacy of MT alone compared with

MT+IV-tPA.^{4,5,15,20} Moreover, 3 additional clinical trials are ongoing with more countries being involved (A Randomized Controlled Trial of DIRECT Endovascular Clot Retrieval Versus Standard Bridging Thrombolysis With Endovascular Clot Retrieval [DIRECT-SAFE], NCT03494920; Bridging Thrombolysis Versus Direct Mechanical Thrombectomy in Acute Ischemic Stroke [SWIFT-DIRECT], NCT03192332; and Intravenous Treatment followed by Endovascular Treatment versus Direct Endovascular Treatment for Acute Ischemic Stroke Caused by a Proximal Intracranial Occlusion Trial [MR CLEAN NO-IV], ISRCTN80619088).²¹⁻²³ These results may further increase the use of MT alone during the next several years. We hope that future studies will evaluate trends and disparities of use as more data from randomized controlled trials become available. We intend to conduct further subanalysis regarding relevant comorbidities with our current data for this study.

Strengths and Limitations

Our study has strengths that are worth highlighting. The NIS is a validated national database that contains all-payer information and is widely used for studies on inpatient trends and analyses.⁷ It is not limited by selection bias, and it is representative of all types of hospitals in the United States. However, our study also has limitations that need to be considered. Administrative databases depend on the quality of data entry, which may be variable.^{6,11,16,24-26} We based our selection of ICD codes for this study on previously published studies and clinicians' expertise.^{6,11,16,25,26} Additionally, ICD codes cannot differentiate between the different MT devices, which have shown heterogeneity.²⁷ The modern era of mechanical thrombectomies mostly involves stent retrievers. Two of these devices received FDA approval in 2012, Trevor Pro (Stryker) and Solitaire (Covidien).¹¹ Thus, the cohort of our study begins in 2013. The NIS is also limited in terms of identifying the timing of tPA delivery. Therefore, the increased use of MT alone could be partially due to the longer time window for its use.

The choice of treatment is confounded by the onset of stroke presentation, which is not captured in the NIS. It is also confounded by the lack of information on the incidence of large-vessel occlusions, which reflects the prevalence of patients eligible for these treatments. The MT and MT+IV-tPA cohorts in our analysis may represent, at least in part, 2 different types of patients (with patients with MT alone having later presentation); consequently, the comparison of outcomes with the 2 strategies must be interpreted with caution. However, this limitation does not affect our results regarding trends in use and racial/ethnic disparities. Although we used novel stroke scales for the administrative databases, ADSS and ASOV have shown strong concordance with the NIHSS score and 90-day mRS >3 in the authors' institutional cohort, respectively.¹¹ We did not use mRS > 2 as a cutoff because it showed a low-to-moderate correlation with ASOV in the aforementioned study.

CONCLUSIONS

Our results indicated that MT alone was used more frequently than MT+IV-tPA among patients with AIS. The disparities between those who identify as White and non-White persisted

across the years, though the gap is closing. Regression analysis indicated that MT alone was less likely to be received by Blacks and Hispanics compared with Whites. MT alone was also less common in urban nonteaching hospitals compared with urban teaching hospitals.

Disclosure forms provided by the authors are available with the full text and PDF of this article at www.ajnr.org.

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