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ORIGINAL COMMUNICATION

Endovascular thrombectomy versus medical management for moderate-to-severe anterior cerebral artery occlusion stroke

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Abstract

Background There are no established patient selection criteria for endovascular thrombectomy (EVT) for anterior cerebral artery (ACA) stroke.

Methods This was a retrospective cohort study of the 2016–2020 National Inpatient Sample in the United States. Isolated ACA-occlusion stroke patients with moderate-to-severe stroke symptoms (NIH stroke scale [NIHSS] ≥ 6) were included. Primary outcome was hospital discharge to home with self-care. Secondary outcomes include in-hospital mortality and intracranial hemorrhage (ICH). Confounders were accounted for by multivariable logistic regression.

Results 6685 patients were included; 335 received EVT. Compared to medical management (MM), EVT patients were younger (mean 67.2 versus 72.2 years; $p = 0.014$) and had higher NIHSS (mean 16.0 versus 12.5; $p < 0.001$). EVT was numerically but not statistically significantly associated with higher odds of home discharge compared to MM (aOR 2.26 [95%CI 0.99–5.17], $p = 0.053$). EVT was significantly associated with higher odds of home discharge among patients with NIHSS 10 or greater (aOR 3.35 [95%CI 1.06–10.58], $p = 0.039$), those who did not receive prior thrombolysis (aOR 3.96 [95%CI 1.53–10.23], $p = 0.005$), and those with embolic stroke etiology (aOR 4.03 [95%CI 1.21–13.47], $p = 0.024$). EVT was not significantly associated with higher rates of mortality (aOR 1.93 [95%CI 0.80–4.63], $p = 0.14$); however, it was significantly associated with higher rates of ICH (22.4% vs. 8.5%, $p < 0.001$).

Conclusion EVT was associated with higher odds of favorable short-term outcomes for moderate-to-severe ACA-occlusion stroke in select patients. Future studies are needed to confirm the efficacy of EVT in terms of longer term neurological outcomes.

Keywords Stroke · Thrombectomy · Anterior cerebral artery · Hemorrhage · Thrombolysis

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Introduction

Endovascular thrombectomy (EVT) is now standard of care for the treatment of select patients with large vessel occlusion stroke [1, 2]; however, its efficacy and safety for distal and medium vessel occlusion (DMVO) is less clear [3, 4], and clinical data on EVT for isolated anterior cerebral artery (ACA) occlusion strokes are particularly scarce [5]. To date, only two retrospective studies have specifically investigated the comparative effectiveness of EVT and medical management (MM) for ACA-occlusion strokes. In a multicenter retrospective study, Meyer et al. [6] suggested that EVT for isolated ACA stroke ($n = 90$) yielded similar rates of favorable functional outcomes, mortality, and hemorrhagic complications. Similarly, in another multicenter cohort study, Filioglo et al. [7] also suggested that EVT ($n = 37$) may yield similar results compared to medical management alone.

While findings were consistent between the two studies, both investigations were limited by sample size, and lack of efficacy may have been due to lack of statistical power. Thus, the comparative effectiveness of EVT and MM for isolated ACA occlusions strokes remains unclear.

To address the dearth of clinical data on the safety and efficacy of ACA-EVT, we conducted this retrospective nationwide analysis of real-world data in the Unites States. We investigated the comparative efficacy and safety of EVT and MM for the treatment of moderate-to-severe isolated ACA-occlusion strokes measured by short-term hospitalization outcomes. Our hypothesis is that EVT may yield significant clinical benefit over MM in terms of favorable outcomes.

Methods

Study design

This study was a retrospective analysis of the 2016–2020 National Inpatient Sample (NIS) database. The NIS, part of the Healthcare Cost and Utilization Project (HCUP), provides stratified discharge information in the United States representing 20% of all inpatient admissions in real-world practice. The NIS does not contain patient identifiers; thus, this study was exempt from informed consent or institutional review board approval under the Health Insurance Portability and Accountability Act.

Patient population

Adult patients (18 years or older) with cerebral infarction due to the anterior cerebral artery were identified using International Classifications of Diseases–Tenth Revision–Clinical Modification (ICD-10-CM) codes. To ensure that included patients did not have chronic ACA infarction as a premorbid diagnosis, we included only patients with ACA stroke in the top diagnosis code, and we also excluded patients with missing NIH stroke scale (NIHSS) information. The Center of Medicare Services instructs that NIHSS should be coded as close as possible to the time of stroke onset, so the presence of an NIHSS code is likely indicative of acute ischemic stroke. Patients with concomitant cerebral infarction due to internal carotid or middle cerebral artery occlusion were excluded, since concomitant large vessel occlusion would be expected to significantly confound patient outcomes. Finally, patients with minor stroke (NIHSS less than 6) were excluded, as EVT is of uncertain benefit and patients with minor stroke are subject to high treatment selection bias [8, 9]. All ICD-10 codes used in this study are detailed in Supplementary Table 1.

Exposure

The study exposure was endovascular thrombectomy, which was identified using ICD-10-Procedural Coding System (ICD-10-PCS) codes (Supplementary Table 1). Patients were separated into the EVT and the non-EVT (MM) arms.

Outcomes

The primary efficacy endpoint of this study was rate of excellent neurological outcomes, defined as routine hospital discharge to home or self-care without inpatient rehabilitation needs. Safety endpoints include in-hospital mortality as well as intracranial hemorrhage (ICH), intraparenchymal hemorrhage (IPH), and subarachnoid hemorrhage (SAH) identified by ICD-10-CM codes (Supplementary Table 1). Length of hospital stay was also recorded and compared.

Other variables of interest

Patient demographics (age, sex, and race) and hospital characteristics (size, location, and teaching status) were recorded. Stroke characteristics, such as NIHSS, prior intravenous thrombolysis (IVT) treatment, and stroke etiology, were captured with ICD-10-CM codes. Embolic stroke etiology was defined as the presence of I63.42 or I48 codes; the stroke etiology was considered non-embolic for all other patients. Stroke risk factors, such as atrial fibrillation, hypertension, hyperlipidemia, diabetes, smoking history, heart failure, coagulopathy, and drug use, were also captured with ICD-10-CM codes. Elixhauser comorbidity index was calculated for each patient to estimate overall medical comorbidity burden [10]. The timing of EVT procedure relative to day of hospital admission was also recorded.

Statistical methods

Patient numbers were calculated using discharge-level weights. Continuous data were expressed as mean ± SD and compared via Student's *t* test. Length of stay data were expressed as median and interquartile range and compared using the Mann–Whitney *U* test. Categorical data were represented as percentages and compared with Rao–Scott Chi-square tests. To best account for selection/treatment bias and confounding of study outcomes, multivariate binary logistic or negative binomial regression models were used to adjust for all clinical variables captured in this study including patient demographics (age, sex, and race), stroke etiology, NIHSS, stroke risk factors (atrial fibrillation/flutter, hypertension, hyperlipidemia, diabetes, chronic heart failure, drug use, smoking, and coagulopathy), hospital characteristics, and overall comorbidity burden (as measured by Elixhauser comorbidity index) to identify independent associations of EVT for various outcome variables compared to MM. Variable selection for inclusion was done *a priori* based on prior literature on significant drivers for patient outcomes following acute ischemic stroke [11]. The rates and odds of the primary efficacy endpoint were also assessed in patient subgroups stratified by NIHSS, prior IVT use, and stroke etiology. Mediation analyses were performed per methods described by Baron and Kenny [12]. Average direct effect (ADE), average causal mediation effect (ACME), total effect, and proportion mediated (ACME divided by total effect) by ICH, IPH, and SAH on excellent outcomes were calculated (with multivariable adjustments for variables included in the main multivariable logistic regression models as described above), and the bootstrapping method described by Preacher and Hayes [13] with 1000 simulations per analysis was used to generate confidence intervals and test for statistical significance. Negative values for ACME and proportion mediated were interpreted as net suppression effects. P values less than 0.05 were deemed statistically significant. All statistical analyses were performed using R, Version 3.6.2.

Results

Patient characteristics

A total of 2,635,594 hospitalizations for ischemic stroke were identified, of whom 32,930 had isolated ACA occlusions, and 6,685 were included in our study. Overall, 6350 (95.0%) patients were treated with MM, and 335 patients (5.0%) were treated with EVT. 96.9% of patients received EVT within 1 day of hospital admission. Compared to MM patients, EVT patients were significantly younger (mean age 67.2 vs 72.2 years, respectively; $p = 0.014$), were numerically more likely to have suffered embolic stroke (58.2% vs. 47.4%, respectively; $p = 0.077$), and had significantly higher rates of smoking (47.8% vs. 31.7%, respectively; $p = 0.005$), drug abuse (13.4% vs. 4.6%, respectively; $p < 0.001$), and coagulopathy (11.9% vs. 5.7%, respectively; $p = 0.032$). EVT patients also had significantly higher NIHSS compared to MM (mean 16.0 vs. 12.5, respectively; $p < 0.001$). EVT patients had numerically but non-significantly higher rates of prior IVT treatment compared to MM (26.9% vs. 18.9%, respectively; $p = 0.097$). Patient characteristics are outlined in Table 1.

Efficacy outcomes

In unadjusted analysis, EVT was numerically but not significantly associated with higher rates of excellent outcomes compared to MM (13.4% vs. 7.5%, respectively, $p = 0.063$; Table 2). However, in subgroup analysis, EVT was significantly associated with higher rates of excellent outcomes compared to MM among patients who did not receive prior IVT (16.3% vs. 6.3%, respectively, $p = 0.004$; Table 2) and those with embolic stroke etiology (12.8% vs. 4.5%, respectively, $p = 0.018$; Table 2). These statistical trends persisted after multivariable adjustments for confounders—EVT remained numerically but not significantly associated with higher odds of excellent outcomes (aOR 2.26 [95%CI 0.99–5.17], $p = 0.053$; Table 2, Fig. 1), while EVT was significantly associated with higher odds of excellent outcomes among patients with NIHSS 10 or greater (aOR 3.35 [95%CI 1.06–10.58], $p = 0.039$; Table 2, Fig. 1), those who did not receive prior IVT (aOR 3.96 [95%CI 1.53–10.23], $p = 0.005$; Table 2, Fig. 1), and those with embolic stroke etiology (aOR 4.03 [95%CI 1.21–13.47], $p = 0.024$; Table 2, Fig. 1).

Length of hospital stay

In terms of length of stay (LOS), EVT patients had significantly higher number of hospital days compared to MM in unadjusted comparisons (median 5 vs. 7 days, respectively, $p < 0.001$; Supplementary Table 2); and this association remained significant after multivariable adjustments using a negative binomial regression model (estimate 1.293 [95%CI 1.01– 1.65], $p = 0.040$; Supplementary Table 2). EVT was significantly associated with longer LOS for patients treated with IVT and for patients with non-embolic etiology, whereas it was not associated with different LOS for those not treated with IVT or those with embolic etiology (Supplementary Table 2).

Safety outcomes

In unadjusted analysis, EVT was significantly associated with higher rates of in-hospital mortality (13.4% vs. 4.1%, $p < 0.001$), ICH (22.4% vs. 8.5%, $p < 0.001$), IPH (16.4% vs. 6.7%, $p = 0.003$), and SAH (7.5% vs. 1.3%, $p < 0.001$) compared to MM (Table 3). After multivariable adjustments, EVT was numerically but non-significantly associated with higher odds of in-hospital mortality (aOR 1.93 [95%CI 0.8–4.63], $p = 0.14$) and significantly associated with higher odds of ICH (aOR 2.6 [95%CI 1.27–5.32], $p = 0.009$; Table 3). Multivariable analyses for differential odds of IPH and SAH were not performed due to limited sample size.

Mediation analyses

Next, we performed mediation analyses to assess whether the higher rates of hemorrhagic complications associated with EVT may have suppressed EVT's association with excellent outcomes in the overall population and among

Table 1 Patient characteristics

Patient characteristics Mean ± SD or % (*n*)	All patients (*N* = 6685)	MM (*N* = 6350)	EVT (*N* = 335)	*p* value
Age (years)	71.9 ± 13.7	72.2 ± 13.5	67.2 ± 16.6	0.014
Female sex	56.5 (3780)	56.9 (3615)	49.3 (165)	0.20
Race				
White	59.0 (3945)	58.6 (3720)	67.2 (225)	0.69
Black	25.9 (1730)	26.2 (1665)	19.4 (65)	
Hispanic	6.9 (460)	6.9 (440)	6.0 (20)	
Other	5.8 (385)	5.7 (365)	6.0 (20)	
Unknown	2.5 (165)	2.5 (160)	1.5 (5)	
Stroke etiology				
Embolic	47.9 (3205)	47.4 (3010)	58.2 (195)	0.077
Non-embolic	52.1 (3480)	52.6 (3340)	41.8 (140)	
Risk factors				
Hypertension	89.4 (5975)	89.3 (5670)	91.0 (305)	0.65
Hyperlipidemia	63.4 (4235)	63.8 (4050)	55.2 (185)	0.16
Uncomplicated diabetes	14.8 (995)	15.0 (995)	11.9 (40)	0.49
Complicated diabetes	24.4 (1625)	24.3 (1540)	25.4 (85)	0.84
Atrial fibrillation or flutter	26.4 (1765)	26.0 (1650)	34.3 (115)	0.12
Smoking	32.5 (2175)	31.7 (2015)	47.8 (160)	0.005*
Drug abuse	5.0 (335)	4.6 (290)	13.4 (45)	< 0.001*
Coagulopathy	6.0 (400)	5.7 (360)	11.9 (40)	0.03*
Chronic heart failure	22.0 (1470)	21.7 (1380)	26.7 (90)	0.31
NIH stroke scale	12.7 ± 6.4	12.5 ± 6.4	16.0 ± 6.4	< 0.001*
Elixhauser comorbidity index	15.8 ± 8.8	15.7 ± 8.8	17.4 ± 8.3	0.092
Received intravenous thrombolysis	19.3 (1290)	18.9 (1200)	26.9 (90)	0.097

*Statistically significant

Table 2 Efficacy of EVT vs MM in terms of rates and odds of excellent outcomes in the study cohort and key subgroups

	Unadjusted analyses			Multivariable analyses	
	MM	EVT	*p* value	Adjusted OR for EVT [95%CI]	*p* value
All patients	7.5 (475/6350)	13.4 (45/335)	0.063	2.26 [0.99 to 5.17]	0.053
Age (years)					
Less than 80	10.0 (410/4105)	17.0 (40/235)	0.12	2.37 [0.92 to 6.10]	0.26
80 years or older	2.9 (65/2245)	< 10.0% (< 10/100)	0.59	3.82 [0.55 to 26.34]	0.17
NIHSS					
6–9	10.5 (290/2755)	23.1 (15/65)	0.14	1.72 [0.32 to 9.17]	0.52
10 or greater	5.1 (185/3595)	11.1 (30/270)	0.059	3.35 [1.06 to 10.58]	0.039*
Thrombolysis					
Yes	12.5 (150/1200)	5.6 (5/90)	0.38	0.49 [0.05 to 5.19]	0.55
No	6.3 (325/5150)	16.3 (40/245)	0.004*	3.96 [1.53 to 10.23]	0.005*
Stroke etiology					
Embolic	4.5 (135/3010)	12.8 (25/195)	0.018*	4.03 [1.21 to 13.47]	0.024*
Non-embolic	10.2 (340/3340)	14.3 (20/140)	0.47	1.82 [0.57 to 5.80]	0.31

Data represented as % (*n*) or aOR [95%CI]

*Statistically significant

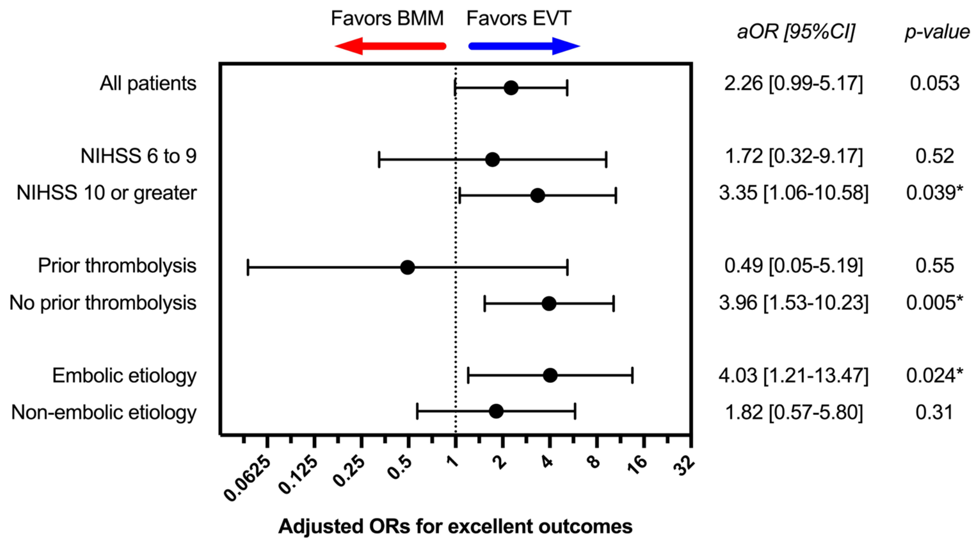

Fig. 1 Adjusted odds ratios (ORs) of excelent discharge outcomes for isolated ACA occlusion stroke patients treated with EVT vs. best medical management (BMM). Analyses were conducted using binary logistic regression models accounting for patient demographics, stroke characteristics, stroke risk factors, stroke etiology, medical comorbidities, and hospital characteristics. *P-values less than 0.05 were deemed statistically significant

Table 3 EVT vs. MM safety outcomes

	Unadjusted analyses			Multivariable analyses	
	MM ($n=6350$)	EVT ($n=335$)	p value	Adjusted OR for EVT [95%CI]	p value
In-hospital mortality	4.1 (260)	13.4 (45)	< 0.001*	1.93 [0.80 to 4.63]	0.14
Intracranial hemorrhage	8.5 (540)	22.4 (75)	< 0.001*	2.60 [1.27 to 5.32]	0.009*
Intraparenchymal hemorrhage	6.7 (425)	16.4 (55)	0.003*	–	–
Subarachnoid hemorrhage	1.3 (80)	7.5 (25)	< 0.001*	–	–

Data represented as % (n) or aOR [95%CI]

those with low NIHSS, those who received prior IVT, and those with non-embolic stroke etiology. Here, we found that EVT's association with higher odds of excellent outcomes was significantly suppressed by both IPH (− 5.8% [95%CI − 10.8 to − 0.1%] proportion mediated, $p=0.042$) and SAH (− 9.7% [95%CI − 17.6 to − 0.7%] proportion mediated, $p=0.046$) in the overall population (Supplementary Table 3). SAH was a significant suppressor of EVT's association with higher odds of excellent outcomes among patients with non-embolic stroke etiology (− 9.1% [95%CI − 22.1 to − 0.1%] proportion mediated, $p=0.050$; Supplementary Table 3), whereas IPH was a possible suppressor among patients treated with IVT (− 10.4% [95%CI − 31.3 to 1.4%] proportion mediated, $p=0.066$; Supplementary Table 3).

Discussion

In this nationwide retrospective study of 6685 patients with moderate-to-severe isolated ACA strokes in the United States, we showed that (1) EVT was seldom performed for isolated ACA occlusions strokes in routine US clinical practice, (2) EVT was overall numerically associated with higher rates of excellent outcomes compared to MM, (3) the efficacy of EVT for isolated ACA strokes appears sensitive to patient and stroke characteristics such as NIH stroke scale, prior thrombolysis use, and stroke etiology, and (4) EVT was significantly associated higher rates of hemorrhagic complications, which suppressed its overall efficacy. Our study is the largest to date on the comparative effectiveness of EVT and medical management of ACA occlusions strokes, and it is the first to demonstrate a significant benefit of EVT for select patient populations.

EVT has been established as the gold standard treatment for select patients with large vessel occlusion strokes [1, 2]; however, its efficacy and safety for DMVOs are less clear [3, 4]. On the one hand, the current literature generally suggests that EVT may be efficacious for DMVOs, but on the other hand, data also suggest an increased risk of hemorrhagic complications, particularly for patients with mild neurological deficits [14]. EVT for the ACA-occlusion strokes may be uniquely challenging due to its anatomic characteristics of a sharp turn from the internal carotid artery terminus to the A1 segment, an often-short A1 segment, followed by another sharp turn from the A1 to the A2 segment [5]. This series of abrupt turns present challenges for navigating across the vascular occlusion in the absence of contrast opacification, which can limit the deployment of EVT devices. Thus, clot retrieval may be riskier for ACA strokes than for strokes in other vascular territories. Furthermore, ACA territory strokes are generally associated with milder neurological deficits [15]. Multiple ongoing randomized trials for medium vessel EVT allow enrollment of ACA-occlusion strokes and their results may reveal valuable insight [4]; however, it remains to be seen whether the ultimate recruitment of ACA strokes into these trials will reach sufficiently large numbers for meaningful subgroup analyses. Currently, EVT for ACA-occlusion stroke is not guideline recommended nor routinely offered in clinical practice. Thus, it is unsurprising that our study revealed a low rate of EVT utilization for patients with isolated ACA-occlusion strokes.

Despite a low number of EVT procedures for ACA-occlusion strokes in the United States, which may reflect stringent patient selection in routine clinical practice, EVT treatment was not associated with significant clinical benefit over MM overall. However, a strong numerical trend toward better outcomes was observed, and subgroup analyses revealed significant clinical benefit among select patient populations. These results suggest that while ACA-EVT may not be beneficial for unselected patients, more formalized treatment eligibility criteria based on stroke severity, prior IVT treatment, and stroke etiology may help optimize the risk–benefit tradeoffs of ACA-EVT. Our findings contrast with those of previously published reports of smaller cohort studies [6, 7], which demonstrated no benefit of EVT over medical management. The reasons underlying these differences in study outcomes are unclear, but it is possible that these prior studies were not sufficiently sensitive in detecting EVT's clinical benefit due their limited sample size and statistical power [6, 7]. Importantly, results from our subgroup analyses are consistent with previously reported trends regarding posterior cerebral artery (PCA) thrombectomy, which also suggested that NIHSS and IVT use may modulate the effectiveness of EVT [16, 17]. Thus, given the similarity of our results with known trends for DMVO-EVT, the efficacy signals observed for ACA-EVT in our study are unlikely due to spurious statistical associations. Nevertheless, larger prospective studies are needed to confirm the benefit of EVT over MM in select patient populations.

It is also important to recognize that while EVT appears efficacious in certain patient subgroups, it did not demonstrate benefit in patients with non-embolic stroke etiology. Mediation analyses conducted in our study suggested that ACA-EVT's efficacy was significantly suppressed by high rates of subarachnoid hemorrhage, particularly among the non-embolic subgroup. This phenomenon may reflect the potential for procedural harm of EVT treatment for ACA-occlusion strokes, which is generally not a major consideration for large vessel occlusion EVT procedures. One possible explanation is that ACA strokes are clinically milder [15]; thus, the potential clinical benefit of EVT may be limited from the outset of ACA strokes. Another explanation is that risks of endothelial damage and subarachnoid hemorrhage may be heightened for ACA-EVT due to its challenging anatomy and medium vessel caliber, particularly for non-embolic strokes which may require multiple thrombectomy passes [18]. Regardless of their explanations, the associations of ACA-EVT with hemorrhage and their potentially harmful effects speak to the importance of careful patient selection for ACA-EVT as well as the need for better devices (e.g., shorter and smaller devices) and techniques tailored for DMVOs. The overall efficacy of ACA-EVT was also significantly suppressed by higher rates of intraparenchymal hemorrhage, particularly among patients treated with intravenous thrombolysis; this association also highlights the importance of carefully stratifying the risk of hemorrhagic transformation when making treatment decisions, particularly for high risk populations such as the elderly and those with coagulopathies [19–21].

Our study has several limitations. First, the NIS only provides hospitalization data, and therefore, only short-term outcomes as measured by discharge destinations are available. Moreover, other important post-procedural outcomes, such as early neurological deterioration or incomplete recanalization [22], are not reported in the NIS. However, given that (1) NIHSS 5 or less is strongly correlated with discharge to home without inpatient rehabilitation need [23] and (2) our study only included patients with admission NIHSS 6 or greater, the routine discharge outcome captured in our study can be a surrogate marker for NIHSS improvement and early neurological improvement, which are closely associated with favorable 90-day neurological outcomes after stroke thrombectomy [24]. Second, the study period was 2016–2020, during which EVT procedures in the United States primarily employed stent-retriever devices. Stent-retriever passes may be associated with endothelial damage and thus hemorrhagic complications, particularly for DMVOs [25]. Whether the safety profile of aspiration EVT is more favorable and whether its increased use in more recent years may have contributed to improved performance of ACA-EVT require further investigation. Third, as a retrospective study, our analysis is inherently subject to confounding from uncaptured variables. The NIS also does not report detailed information regarding the segment of ACA occlusion (which is an important factor for endovascular treatments), treatment time windows or timing of treatment decision, or radiographic biomarkers (e.g., core size, penumbra size, collateral status, etc.); it is likely that consideration of these factors in future studies would help to further optimize patient selection criteria for ACA-EVT. Furthermore, compared to large vessel occlusions, DMVOs are more likely to achieve early recanalization with IVT treatment [26]; thus, it is possible that the lack of significant efficacy ACA-EVT's observed among IVT-treated patients may have been due to an enrichment of the MM cohort with patients who achieved early recanalization. This possibility further emphasizes the importance of considering the competing therapeutic efficacy of IVT for ACA-occlusion strokes when making decisions regarding EVT treatment. Additionally, the NIS does not report detailed information regarding EVT procedures, such as number of passes, occurrence of embolism to new territories, and final degree of revascularization, which may also impact and confound the study outcomes. Finally, as ACA-EVT is not standard of care, our study is subject to selection bias which could only be partially accounted for with the available information available in the NIS.

Conclusions

EVT is seldom performed for ACA-occlusion strokes in the United States. For patients with moderate-to-severe stroke symptoms, EVT may be an effective treatment. However, EVT's comparative efficacy over MM appears sensitive to patient and stroke characteristics and is likely suppressed by higher rates of hemorrhagic complications. Future prospective studies with longer term data are needed to confirm the efficacy and safety of ACA-EVT and formalize patient selection criteria based on stroke severity, prior IVT administration, and stroke etiology as well as careful consideration of hemorrhage risk and further refinement of EVT devices and techniques for DMVOs.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00415-024-12582-z.

Author contributions HC and MC conceived the study idea and designed the study. HC and MK acquired and analyzed the data. HC and MC wrote the manuscript. AM and DG revised the manuscript. All authors approve the final submission. HC and MK contributed equally to this work and are co-first authors.

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Data availability The National Inpatient Sample is a publicly available database that can be acquired at https://hcup-us.ahrq.gov/

Declarations

Conflicts of interest HC, MK, AM, DG, and MC have no potential conflicts of interest to declare.

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