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Original Article

Safety and efficacy of mechanical thrombectomy for acute ischemic stroke with volume over 50 mL and significant perfusion mismatch

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ABSTRACT

Background: This study aims to address the safety and efficacy of mechanical thrombectomy (MT) in acute ischemic stroke with an established infarction equal to or >50 mL with a significant difference between penumbra and established infarction detected by perfusion cerebral computed tomography (CT) with the Rapid® system.

Methods: This was a retrospective case–control study. Patients diagnosed with established and extensive ischemic stroke, defined by an ischemic volume equal to or >50 mL on CT or magnetic resonance imaging perfusion using the RAPID® system, were examined. The intervention group received endovascular interventional treatment with or without recombinant tissue plasminogen activator (rt-PA) in addition to standard therapy, and the control group received conservative treatment with or without rt-PA plus standard therapy.

Results: A total of 59 patients were enrolled, including 38 in the intervention group and 21 in the control group. Baseline characteristics were similar between groups. Patient National Institutes of Health Stroke Scale at discharge was significantly different between the control (median 30, interquartile range [IQR] 13) and intervention group (median 8, IQR 14) ($P < 0.001$). Modified Rankin scale (mRS) scores were significantly different at discharge between intervention (median mRS 2, IQR 3) and controls (median mRS 5, IQR 1) ($P = 0.002$). These mRS differences remained significant at 90 days, with median (IQR) values of 2 (2.75) and 5 (1), respectively ($P < 0.001$).

Conclusion: MT is safe and effective for large-core ischemic strokes with significant perfusion mismatch, leading to better functional outcomes without significant complications compared to the best medical treatment.

Keywords: Ischemic stroke, Reperfusion, Stroke, Thrombectomy, Endovascular

INTRODUCTION

Ischemic stroke remains a major global cause of morbidity and mortality despite advancements in medical therapy.[5,6,9] Particularly in cases of large-core ischemic strokes characterized by a significant volume of cerebral infarct, traditional therapies such as intravenous thrombolysis

are often insufficient to optimize patient outcomes.[4] Over the past decade, mechanical thrombectomy (MT) has emerged as an effective treatment modality for such strokes, leading to improved functional outcomes.[7] Yet, the use of MT in large-core strokes has been debated due to concerns about potential harm, including the risk of symptomatic intracranial hemorrhage and futile reperfusion.[3,14]

In this evolving landscape, recent clinical trials such as RESCUE-Japan LIMIT, SELECT2, and ANGEL-ASPECT2 have provided significant insights into the use of MT for large-core ischemic strokes.[8,13,16] These trials have explored the nuances of patient selection, safety parameters, and functional outcomes following MT, extending our understanding of this treatment modality's applicability in this high-risk patient cohort. However, consistent findings across these trials and the definition of clear clinical guidelines for MT in large-core ischemic strokes remain a challenge, necessitating further research to optimize patient outcomes.

This study aims to address the safety and efficacy of MT in acute ischemic stroke with an established infarction equal to or >50 mL with a significant difference between penumbra and established infarction detected by perfusion cerebral computed tomography (CT) with the Rapid® system.

MATERIALS AND METHODS

This study was a retrospective case–control. Patients diagnosed with established and extensive ischemic stroke, defined by an ischemic volume equal to or >50 mL on CT or magnetic resonance imaging (MRI) perfusion using the RAPID® system, were examined. Two groups were studied: One group received endovascular interventional treatment with or without recombinant tissue plasminogen activator (rt-PA) in addition to standard therapy, and the other group received conservative treatment with or without rt-PA plus standard therapy. Data collection occurred at the Baptist Medical Center in Jacksonville, FL, USA, from January 2016 to December 2019. The Local Institutional Review Board approved the study (study 16–58 of the North Florida Stroke Patient Registry).

All patients received pre-hospital care from a highly trained team, either by ground or air, arriving at the Baptist Medical Center's emergency department. A code stroke was declared when a possible cerebral ischemia/hemorrhage was suspected, at which point a nurse practitioner from the interventional neurosurgery department would conduct a clinical assessment (National Institutes of Health Stroke Scale [NIHSS] and modified Rankin scale [mRS]) and immediately send the patient for imaging, including unenhanced CT, perfusion CT, and brain AngioCT. The Rapid® system was used to analyze all data and images, alerting the team through a mobile application when a Code Stroke was declared. The team would then assess whether endovascular intervention was warranted.

Inclusion and exclusion criteria

Inclusion criteria were patients over 18 years old with acute occlusion of the internal carotid artery, middle cerebral artery, anterior cerebral artery, or vertebrobasilar system. Patients with a baseline mRS 0–2 were included in the study. NIHSS equal to or >5. Symptom onset up to 24 h or unknown. CT or MRI images for ASPECTS evaluation and collaterals were evaluated by two independent neuroradiologists blind to patient information.

Exclusion criteria included patients with a cerebral infarct volume equal to oligemia, pregnancy, suspicion of intracranial arterial dissection, inability to follow-up for mRS at 90 days, and patients with severe diseases that interfere with patient management and follow-up.

Data analysis

Descriptive analyses were used to describe and characterize the two groups: the intervention group (n = 38) and the control group (n = 21). The normality of distribution was assessed using a histogram and the Shapiro-Wilk test. Continuous variables were presented as mean and SD or median and interquartile range (IQR) (if not normally distributed). Categorical variables were presented as numbers and frequencies. Clinical and imaging variables between the two groups were compared using the χ^2 test (Categorical variable) or G-test when npq <5. The Mann-Whitney U-test was used to compare non-normally distributed quantitative variables. For text similarity analysis, the Iramuteq version 7.0 program was used,[11] with 105 texts extracted from the database. Statistical significance was considered with $P < 0.05$. Statistical hypothesis testing was performed using SPSS Statistics version 27 and BioEstat version 5.3.

RESULTS

Between January 2016 and December 2019, a total of 38 cases required endovascular intervention through thrombectomy, and 21 cases were treated conservatively on patients with ischemic stroke with an established infarct volume equal to or >50 mL, based on cranial CT or MRI perfusion using the RAPID® system.

Baseline characteristics

Baseline characteristics are described in Table 1. In the intervention group, there were 21 male patients (55.3%) and 17 female patients (44.7%) with a mean age of 66.2 ± 14.8 years and a median of 64.5 years, ranging from 43 to 88 years. Left

Table 1: Baseline characteristics.

	Intervention		Control		*P*-value
	n	%	*n*	%	
Hypertension	32	84.2	14	66.7	0.23
Diabetes	7	18.4	5	23.8	0.88
Heart failure	7	18.4	1	4.8	0.26
Smoker	6	15.8	0	0.0	0.10
Alcohol abuse	4	10.5	0	0.0	0.28
Atrial fibrillation	13	34.2	4	19.0	0.34
Coronary artery disease	8	21.1	4	19.0	0.88
Previous stroke	3	7.9	1	4.8	0.93
Transient ischemic attack	2	5.3	1	4.8	0.60
Dementia	4	10.5	1	4.8	0.78
Dyslipidemia	4	10.5	3	14.3	0.99
Obesity	3	7.9	0	0.0	0.46
Cancer	3	7.9	1	4.8	0.93
Pulmonary embolism	4	10.5	0	0.0	0.28
Endarterectomy	0	0.0	1	4.8	0.77
Moya-Moya	0	0.0	2	9.5	0.25
Lung disease	1	2.6	3	14.3	0.26
Chronic kidney disease	3	7.9	0	0.0	0.46

middle cerebral artery syndrome (M1 segment) was found in 29% of the cases. The mean NIHSS at admission was 20.9 (10–31), and the mean pre-intervention definitive cerebral infarct volume was 85.5 mL (51–271 mL) [Table 2]. Infarct with oligemia averaged 182.5 mL (80–384 mL), and the difference (mismatch) between the total volume that could potentially be preserved (penumbra) averaged 83.5 mL (05–278 mL). The mean ASPECTS score on CT or MRI was 8.0 (3–10).

In the control group, there were 9 male patients (42.9%) and 12 female patients (57.1%) with a mean age of 68.9 ± 17.5 years and a median age of 73 years (50–89). In 47.6% of the cases, a left middle cerebral artery syndrome (M1 segment) occurred. The mean NIHSS at admission was 22.0 (0–28). The mean pre-intervention definitive cerebral infarct volume was 97.0 mL (52–281.3 mL), and infarct with oligemia averaged 193.0 mL (65–423 mL). The mismatch between the total volumes that could potentially be preserved (penumbra) was 94 mL (12–326 mL). The mean ASPECTS score on CT or MRI was 4 (2–9). Table 3 shows the location of the lesions, and there was no difference between the intervention and control groups. Table 4 shows perfusion imaging characteristics.

Treatment and outcomes

In the intervention group, thrombectomy with aspiration using a stent retriever was performed in 100% of cases, achieving Thrombolysis in Cerebral Infarction (T1C1) 2b-3 in 84.2% of cases. The rate of mRS 0–2 at 90 days was 65.8%, and the 90-day mortality rate was 10.5%. There was one case of non-significant hemorrhagic transformation, which required surgical treatment.

Table 2: Patient symptoms.

Symptoms	Intervention		Control		*P*-value
	(*n*=38)	%	(*n*=21)	%	
Paresis					0.80
Left	15	39.5	7	33.3	
Right	13	34.2	9	42.9	
None	10	26.3	5	23.8	
Conjugate gaze deviation					0.81
Left	6	15.8	4	19.0	
Right	8	21.1	3	14.3	
None	24	63.2	14	66.7	
Facial paresis					0.83
Left	7	18.4	3	14.3	
Right	5	13.2	2	9.5	
None	26	68.4	16	76.2	
Negligence					0.27
Left	7	18.4	1	4.8	
Right	3	7.9	3	14.3	
None	28	73.7	17	81.0	
Hemiplegia					0.46
Left	1	2.6	2	9.5	
Right	4	10.5	1	4.8	
None	33	86.8	18	85.7	
Dysarthria	3	7.9	2	9.5	0.78
Aphasia	22	57.9	10	47.6	0.63
mRS					0.79
Zero	27	71.0	15	71.5	
1 a 4	11	29.0	6	28.5	

Table 3: Lesion location.

	Intervention		Control		*P*-value
	(*n*=38)	%	(*n*=21)	%	
M1					0.17
Left	11	29.0	10	47.6	
Right	23	60.5	9	42.9	
None	4	10.5	2	9.5	
M2					0.98
Left	23	60.5	12	57.1	
Right	11	29.0	6	28.6	
None	4	10.5	3	14.3	
ICA					0.87
Left	24	63.1	12	57.1	
Right	9	23.7	7	33.4	
None	5	13.1	2	9.5	
Tandem occlusion					0.74
Yes	8	21.0	6	28.7	
No	30	79.0	15	71.4	

ICA: Internal carotid artery

In the control group, the treatment was the optimization of clinical parameters in a neurological intensive care

Table 4: Perfusion imaging.

	Core volume (mL)		Perfusion volume (Tmax >6 s) ml		Mismatch volume (mL)		Mismatch ratio	
	Study	Control	Study	Control	Study	Control	Study	Control
Sample size	38	21	38	21	38	20	36	18
Mean	96.3	108.7	200.2	216.0	103.2	108.4	2.3	2.2
Standard deviation	43.8	57.3	78.6	95.4	68.3	74.9	1.1	0.8
P-value (U-test)	0.52		0.65		0.53		0.77	

unit, followed by rehabilitation center treatment. The rate of mRS 0–2 at 90 days was 0%, and the 90-day mortality rate was 28.6%. There were ten cases of cerebral ischemic enlargement, and all the patients were discharged to an inpatient rehabilitation facility for clinical treatment.

Table 5 summarizes interventional results. Patient NIHSS at discharge was significantly different between the control (median 30, IQR 13) and intervention group (median 8, IQR 14) ($P < 0.001$). mRS scores were also significantly different between groups, both at discharge ($P = 0.002$) and at 3 months ($P < 0.001$) [Table 6]. The median mRS at discharge was 2 (IQR = 3) for the MT group and 5 (1) for the control group [Figure 1]. At 3 months, the median mRS was 2 (IQR 2.75) for the MT group and 5 (IQR 1) for the control group [Figure 2].

Table 5: Post-procedure results.

	Intervention		Control group		*P*-value
	n	%	*n*	%	
Stroke core volume					0.02*
Post-procedure					
CTP	4	10.5	1	4.8	
MRI	15	39.5	2	9.5	
Not (or other)	19	50.0	18	85.7	
Hemorrhagic transformation					0.74
24–48 h					
Yes	1	2.6	1	4.8	
No	37	97.4	20	95.2	
Retrieval attempts					<0.0001*
0	1	2.6	21	100.0	
1	19	50.0	0	0.0	
2	10	26.3	0	0.0	
3	4	10.5	0	0.0	
4	3	7.9	0	0.0	
5	1	2.6	0	0.0	
TICI					<0.0001*
0	0	0.0	21	100.0	
2a	4	10.5	0	0.0	
2b	16	42.1	0	0.0	
3	16	42.1	0	0.0	
Collaterals score					0.02*
0	8	21.1	1	4.8	
1	10	26.3	15	71.4	
2	7	18.4	2	9.5	
3	11	28.9	3	14.3	
4	2	5.3	0	0.0	

MRI: Magnetic resonance imaging, CTP: Computed tomography with perfusion study, T1C1: Thrombolysis in Cerebral Infarction,*P-value < 0.05

DISCUSSION

The present study aimed to evaluate the results of MT for large-core ischemic strokes with significant perfusion mismatch. The results demonstrated a significant benefit in terms of functional outcomes without a significant difference in unfavorable complication rates.

Prior studies such as MR CLEAN,[1] EXTEND-IA,[2] and REVASCAT[15] have offered outcomes akin to the present study in terms of recanalization rates, TICI 2b-3, functional independence based on the mRS scale, and rates of complications and mortality. The early studies employed similar protocols. For instance, MR CLEAN used CT and brain angio-CT, whereas EXTEND-IA and SWIFT PRIME[15] utilized CT, angio-CT, and brain perfusion CT for diagnosis and therapeutic decisions.

Our analysis reveals superior outcomes for patients undergoing MT, especially when performed within 6 h of symptom onset, despite the acceptance of endovascular intervention up to 24 h as indicated by the DAWN trial.[11] This treatment attained the desirable TICI 2b-3 in 84.2% of patients in the present study. There is, however, a lack of international studies considering infarctions larger than 50 mL, which are deemed extensive ischemic areas. The EXTEND-IA study targeted definitive ischemia areas smaller than 70 mL, which is less commonly seen in previous research. Prior studies often provided ambiguous guidance on thrombectomy in patients with extensive definitive ischemia areas.

In 2017, Rebello *et al.*[12] published a study in JAMA aiming at MT intervention for ischemia above 50 mL, yielding satisfactory results. In comparison to Rebello's study, our study had slightly superior success rates with MT (89.6% vs. 79%) and significantly better favorable outcome rates, mRS

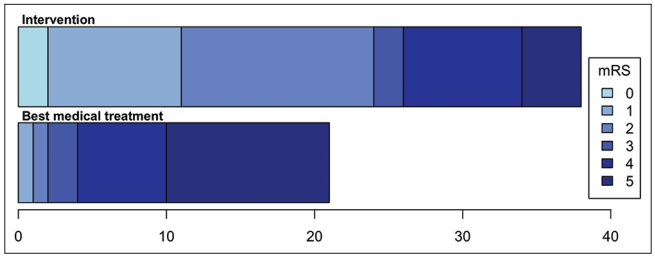

Figure 1: mRS at discharge. The bar plots show the distribution of mRS scores at discharge. The upper bar represents the intervention group, and the lower bar represents the control group (best medical treatment). The difference was statistically significant (P = 0.002). mRS: Modified Rankin scale.

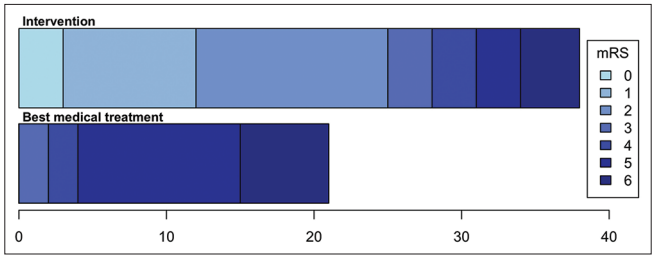

Figure 2: mRS at 90 days. The bar plots show the distribution of mRS scores reevaluated at 3 months. The upper bar represents the intervention group, and the lower bar represents the control group (best medical treatment). The difference was statistically significant (P < 0.001). mRS: Modified Rankin scale.

Table 6: Patient outcomes.

mRS	Intervention (*n*=38)		Control group (*n*=21)		*P*-value
	n	%	*n*	%	
Discharge					0.0020*
0	2	5.3	0	0.0	
1	9	23.7	1	4.8	
2	13	34.2	1	4.8	
3	2	5.3	2	9.5	
4	8	21.1	6	28.6	
5	4	10.5	11	52.4	
6	0	0.0	0	0.0	
After 90 days					<0.0001*
0	3	7.9	0	0.0	
1	9	23.7	0	0.0	
2	13	34.2	0	0.0	
3	3	7.9	2	9.5	
4	3	7.9	2	9.5	
5	3	7.9	11	52.4	
6	4	10.5	6	28.6	

mRS: Modified Rankin scale, *P-value < 0.05

0–2, at 90 days (65.8% vs. 25%). However, the mortality rates in the control groups were 48% in Rebello's study and 28.6% in the present study. Our study, therefore, underscores the importance of early diagnosis, suggesting that patients with larger infarction areas can still benefit from endovascular intervention.

Interestingly, patients with an established infarction (core) equal to or >50 mL are not frequently studied. However, our study has shown evidence of MT benefits for patients at this infarction level. Often, patients with this level of established infarction present with smaller penumbral areas, creating a mismatch between the potential salvageable brain tissue and the established infarction.[10] Yet, 3 months post-MT, many patients showed smaller infarction areas than initially presented during the ischemic stroke, with entirely preserved penumbral areas.

While the study offers valuable insights, it is not without limitations, including its retrospective nature, non-randomization, the relatively small sample size in both intervention and control groups, and the lack of standardized protocol for collateral circulation assessment. Nevertheless, it also presents numerous strengths, the most important of which is the application of MT for large-core strokes in a real-life setting.

CONCLUSION

MT is safe and effective for large-core ischemic strokes with significant perfusion mismatch, leading to better functional outcomes without significant complications compared to the best medical treatment.

Ethical approval

The research/study was approved by the Institutional Review Board at North Florida Stroke Patient Registry, number 16-85, dated November 15, 2018.

Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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