JVIN Journal of Vascular and Interventional Neurology

OFFICIAL JOURNAL OF ZEENAT QURESHI STROKE INSTITUTE

Rescue Intracranial Stenting during Endovascular Thrombectomy in Patients with Large Vessel Occlusion Stroke

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Abstract

Introduction— Rescue treatment for failed thrombectomy in patients with acute ischemic stroke (AIS) from large vessel occlusion (LVO) remains controversial. We report our institutional experience with using intracranial stenting of occlusion refractory to aspiration and stent retriever thrombectomy.

Methods— We performed a retrospective review of our prospectively maintained thrombectomy database to identify the LVO AIS patients who underwent intracranial stenting during endovascular thrombectomy between 1/2015-7/2021. Modified Rankin scale (mRS) at 90 days was used as primary outcome. Secondary outcomes included symptomatic intracerebral hemorrhage (sICH), and mortality at 90 days.

Results— We identified 47 acute ischemic stroke patients who underwent intracranial stenting acutely. Median age was 66 years (Interquartile range (IQR 58-75), median baseline mRS was 0 (IQR 0-1), median NIHSS score was 13.5 (IQR 7-18), and median ASPECTS was 9 (IQR 8-10). The median number of thrombectomy passes prior to stenting was 3 (IQR 2-4). In 48% of patients, a combination of aspiration and stent retriever techniques were used prior to intracranial stenting. Majority of the patients (93%) were loaded with anti-thrombotics intraoperatively. Successful recanalization (TICI 2 B or better) was achieved in 96% of the patients. Fourty nine percent of our cohort had good outcome at 90 days. A total of 4 patients (8.5%) developed a sICH, with a 90 day mortality of rate of 17.0% (8/47).

Conclusion— Rescue intracranial stenting is a safe and effective approach in patients with emergent large vessel occlusion refractory to aspiration and stent retriever thrombectomy.

Keywords— acute ischemic stroke, rescue intracranial stenting, mechanical thrombectomy.

INTRODUCTION

Endovascular thrombectomy (EVT) has been established as the standard of care for patients with large vessel occlusion (LVO) strokes.[1] Failed recanalization during EVT, although rare, but represents a particular challenge in stroke management.

Recent work suggests that rescue intracranial stenting (RS) can be a safe and effective bail out technique for patients who have failed thrombectomy and can be associated with better clinical outcomes and higher reperfusion rates when compared to patients in which recanalization attempts were abandoned without RS.[2,3]

However, most studies evaluated RS mainly in the intracranial internal carotid artery (ICA) and the M1 segment of the middle cerebral artery (MCA), typically in patients with pre-morbid modified Rankin Scale (mRS) ≤1 who presented within 6 hours of symptoms onset. Additionally, guidelines have not been established when it comes to bail out techniques in patients with failed EVT or re-occlusion.

Therefore, the indications and clinical context for performing RS after failed thrombectomy need to be validated in large prospective studies. Most specifically, inclusion criteria including location of occlusion and time of presentation need to be better delineated for patients undergoing RS. This need is especially emerging, when considering that thrombectomy eligibility has exxpanded to include patients presenting in the 6-24 window since last known well and to middle/distal vessel occlusions.[4,5]

Herein, the authors aim to evaluate the safety and efficacy of RS after failed thrombectomy in one of the largest (to date) single-institution consecutive cohorts. Contrary to previously published work, we aimed for broad inclusion criteria, to strengthen the external validity of our results.

Vol.14, No. 1, pp. 16-20, Published March, 2023.

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TABLE 1: Baseline demographic and radiographic characteristics of LVO patients who underwent rescue stenting.

Baseline demographics	Patients with good neurologic outcome at 90 days (24/47)	Patients with poor neurologic outcome at 90 days (23/47)	p-value
Age	66 (56-72)	67 (58.5-78.5)	0.51
Gender			
Female	10 (43.5%)	9 (37.5%)	
Male	13 (56.5%)	15 (62.5%)	0.68
Hypertension	14 (60.9%)	18 (75.0%)	0.30
Hyperlipidemia	8 (34.8%)	10 (41.7%)	0.57
Diabetes	7 (30.4%)	10 (41.7%)	0.42
Atrial Fibrillation	3 (11.5%)	4 (15.4%)	0.69
History of stroke	1 (4.4%)	7 (29.2%)	0.02
History of prior TIA	0 (0.0%)	3 (12.5%)	0.08
Aspirin	16 (69.6%)	18 (75.0%)	0.68
Plavix	2 (8.7%)	6 (25.0%)	0.14
Stroke etiology			
Cardioembolic	8 (34.8%)	11 (45.8%)	
Extracranial large vessel disease	3 (13.1%)	1 (4.2%)	
ICAD	5 (21.8%)	3 (12.5%)	0.57
Others	3 (13.1%)	2 (8.3%)	
Unknown	4 (17.4%)	7 (29.2%)	
Baseline mRS			
0	16 (69.6%)	14 (63.6%)	
1	6 (26.1%)	4 (18.2%)	
2	1 (4.5%)	0 (0.0%)	0.24
3	0 (0.0%)	3 (13.6%)	
4	0 (0.0%)	1 (4.6%)	
ASPECTS score	9 (8-10)	10 (8-10)	0.21
Baseline NIHSS	10.5 (6-17)	14 (10.5-18.5)	0.09
LKW to puncture time (minutes)	539 (333-943)	695 (277-1406)	0.74
Site of occlusion			
ICA	2 (8.7%)	2 (8.3%)	
M1	6 (26.1%)	9 (37.5%)	
M2	7 (30.4%)	0 (0.0%)	0.11
Vertebro-basilar	6 (26.1%)	10 (41.7%)	
PCA	1 (4.4%)	1 (4.2%)	
ACA	1 (4.4%)	2 (8.3%)	

METHODS

We performed a retrospective review of our prospectively maintained thrombectomy database to identify the LVO AIS patients >18 years old who underwent intracranial stenting during endovascular thrombectomy at our comprehensive stroke center between January 2015 and July 2021. The Institutional Review Board of the Mount Sinai Hospital approved our protocol. For all LVO patients who underwent mechanical thrombectomy we collected baseline demographics and clinical characteristics and initial National Institutes of Health Stroke Scale (NIHSS) score. Baseline functional status was identified using the modified Rankin Scale (mRS). Baseline Alberta Stroke Program Early CT Score (ASPECTS) were determined by the neuroradiologist reading the study prior to EVT.

We also collected stroke time metrics including last known well to arterial access time and procedural time in minutes. Other procedural details including mode of anesthesia, stent type, use and type of antiplatelet agents used, final reperfusion score, first pass technique, and number of passes before stenting were also collected.

Primary endpoint was good neurologic outcome defined as mRS 0-3 at 90 days, while mRS of 4-5 at 90 days was defined as poor neurologic outcome. Secondary outcomes included hemorrhagic conversion, parenchymal hematoma type I, parenchymal hematoma type II per ECASS criteria, symptomatic intracerebral hemorrhage (sICH), and mortality at 90 days.

Mann-Whitney U test was used for continuous variables because data was not normally distributed. Pearson's Chi square test was used for categorical variables. Baseline variables with a predetermined $p<0.1$ for the outcome of interest were entered into the linear regression model and a backward elimination strategy was used to develop the multivariable model optimizing area under the receiver operating characteristic (ROC) curve. Multicollinearity evaluation was performed for each model. All analyses were carried out in STATA 15 (College Station, TX, USA). A p value <0.05 was considered statistically significant.

RESULTS

We identified 47 patients who underwent rescue intracranial stenting during EVT for an acute ischemic stroke from LVO. At total of 48.9% of the patients (23/47) achieved a good neurologic outcome at 90 days. Patients who achieved a good neurologic outcome were less likely to have a history of stroke (4.4% vs 29.2%, p=0.02). Cardioembolic stroke was the most common stroke etiology (40.4%), however there was no significant difference in etiologies between patients with a good or poor neurologic outcome at 90 days, (p=0.57). The remaining demographic baseline characteristics were otherwise similar and are outlined in Table 1.

Notably, baseline mRS scores were similar between both groups (p=0.33). Median ASPECTS score was also comparable between both groups (9 vs 10, p=0.09). The most common site of occlusion was vertebrobasilar (16/47= 34.1%), however site of occlusion did not significantly correlate with neurologic outcome at 90 days in univariate analyses (p=0.11).

Patients who achieved a poor neurologic outcome at 90 days had longer procedural time (122 minutes vs 71 minutes, p=0.05), were less likely to achieve a TICI2C or better (45.8% vs 73.9%, p=0.05, and had a higher NIHSS scale 24 hours post procedure (14.5 vs 7, p=0.001). The most common inta-operative thrombotic regimen used was aspirin and integrilin (78.7%), though this was not significantly different between the two groups.

TABLE 2: Procedural details of LVO patients who underwent rescue stenting.

Procedural Details	Patients with good neurologic outcome at 90 days	Patients with poor neurologic outcome at 90 days	p-value
General anesthesia	11 (47.8%)	10 (41.7%)	0.67
Procedure time (minutes)	71 (55-103)	122 (85-160)	0.05
Combined antiplatelet regimen			
ASA+Integrilin	21 (91.3%)	16 (66.7%)	0.12
ASA+Plavix	0 (0.0%)	2 (8.3%)	
ASA+Plavix+integrilin	2 (8.7%)	3 (12.5%)	
ASA+Cangrelor drip	0 (0.0%)	3 (12.5%)	
Stent type			
Enterprise	11 (47.8%)	12 (50.0%)	0.65
Neuroform	7 (30.4%)	4 (16.7%)	
Wingspan	1 (4.4%)	1 (4.2%)	
Wingspan+enterprise	4 (17.4%)	7 (29.2%)	
Use of intravenous antithrombotic agent	23 (100.0%)	22 (91.7%)	0.16
Balloon angioplasty (before or after stenting)	8 (34.8%)	11 (45.8%)	0.44
First pass technique			
Stentreiver	10 (43.5%)	9 (37.5%)	0.68
Direct aspiration	13 (56.5%)	15 (62.5%)	
Number of passes before stenting	2 (1-3)	3 (1-4)	0.33
Final TICI score			
2B or better	22 (95.7%)	23 (95.8%)	0.98
2C or better	17 (73.9%)	11 (45.8%)	0.05
3	15 (65.2%)	9 (37.5%)	0.06
24-hour NIHSS scale	7 (3-12)	14.5 (8.5-17.5)	0.001

The most commonly used intracranial stent was the Enterprise intracranial stent (Codman & Shurtleff Inc., Raynham, MA) 27/52 (51.9%), followed by the Neuroform Atlas stent (Stryker Neurovascular, Fermont, CA) 11/47 (23.4%), and the Wingspan stent (Stryker Neurovascular, Fermont, CA) 2/47 (4.3%). Eleven out of 47 patients required more than one stent (Wingspan and Enterprise). The type of stent utilized did not significantly correlate with neurologic outcomes at 3 months in univariate analyses (p=0.65) (Figure 1). The most commonly used first pass thrombectomy technique was direct aspiration 28/47 (59.6%) (Figure 2), and most patients had a median of 3 passes prior to resolving to intracranial stenting. Balloon angioplasty was preformed pre or post stenting in 18/47 patients (40.4%). Other procedural details including mode of anesthesia, and first pass technique before stenting were comparable between both groups (Table 2).

Based on the results of univariate analyses and biologically plausible variables that could influence outcomes, we conducted a linear regression model adjusting for baseline NIHSS, age, procedural time in minutes, use of intravenous antithrombotic agents, site of occlusion, and reperfusion grade. In a linear regression model adjusting for above confounders, younger age [Correlation Coefficient (Coeff)=00.01, 95% Confidence Interval (CI)=0.02- -0.02, p=0.02], Use of an intravenous antithrombotic agent intraoperatively [Coeff=0.82, 95%CI=0.18-1.46, p=0.01], and achieving a TICI2C or higher reperfusion [Coeff=0.49, 95%CI=0.14-0.84, p=0.007], were significantly associated with a better neurologic outcome at 90 days (Table 3).

Mortality data were available for all but one patient who was lost to follow up. A total of 8 (17.1%) patients had died at 90 days. Five out of 8 patients had a baseline mRS of 0, one patient had a baseline mRS of 1, and one patient had a mRS of 3. Baseline characteristics and procedural data were comparable with patients who survived at 90 days.

Six patients developed hemorrhagic transformation in 24-hour post EVT CT scan. Two patients developed parenchymal hematoma type 1 (PH1), and 5 developed parenchymal hematoma type II (PHII). 1 out of 2 patients with PH1 had a poor neurologic outcome at 90 days, and both were alive at 90 days. 5 out of 4 patients with PHII had a poor neurologic outcome at 90 days and 3/4 of these patients had died at 90 days. Of note, all patients who developed a PHII received intravenous antithrombotics intraoperatively.

Four out of 47 patients (8.5%) developed symptomatic ICH (sICH). All four patients had poor neurologic outcome at 90 days, and 3 out of 4 patients (75%) had died at 90 days. Patients with sICH had a lower median ASPECTS (8 vs 9) and a higher baseline median NIHSS (14.5 vs 13) though neither were statistically significant findings (p=0.16, and p=0.6).

DISCUSSION

In this cohort of patients who underwent EVT and required intracranial stenting, approximately half of the patients had good clinical outcome at 90 days. Younger age, shorter procedural time, and achieving a TICI 2C or higher reperfusion significantly correlated with good neurologic outcome at 90 days. The rate of sICH was 8.5%. The majority of our cohort received intravenous antithrombotics (bolus dose followed by continuous drip of either Inegrilin or Cangrelor) intraoperatively (95.7%), which was continued postoperatively until the patient was able to receive oral dual antiplatelet therapy (Aspirin plus Plavix or Brilinta).

We observed successful reperfusion in 95.7% and a good neurologic outcome at 90 days in 49% patients, this is significantly higher than the reported good neurologic outcome if patients were not recanalized (TICI 0 or 1) or were to experience re-occlusion.[6,7] Our results are comparable with recent retrospective studies investigating rescue intracranial stenting in patients undergoing mechanical thrombectomy.[3] A recent meta-analysis including 8 studies, showed that good neurologic outcome can be achieved in 43% of patients with failed thrombectomy after intracranial stenting with a successful reperfusion rate of 71%.[8] Stracke et al similarly described a 44% good neurologic function rate in patients who underwent RS after failed mechanical thrombectomy,[3] and 39.6% patients were reported to have a good neurologic outcome after RS after a failed M1 thrombectomy.[2]

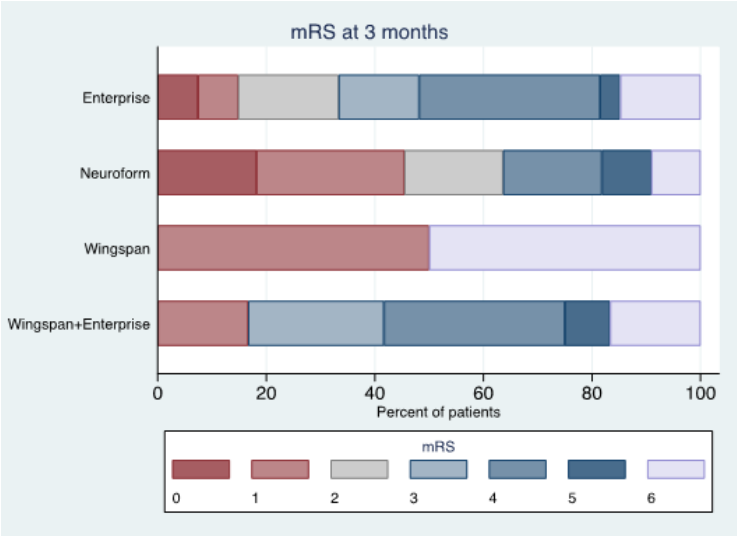

FIGURE 1: Stent type and neurologic outcome at 90 days.

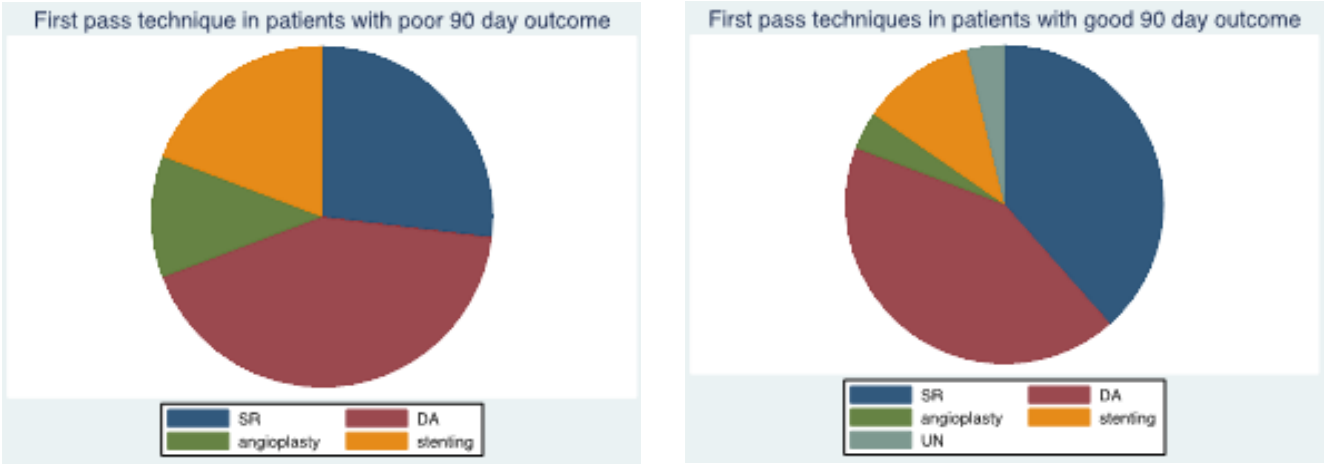

FIGURE 2: First pass mechanism in patients with acute intracranial stenting in patients with good and poor neurologic outcome at 90 days.

Good neurologic outcome at 90 days	Correlation Coefficient	Std. Err.	P>|z|	[95% Conf. Interval]
Baseline NIHSS scale	-0.01	0.01	0.24	-0.037-0.01
Age	-0.01	0.01	0.02	-0.02 - -0.01
Procedure time in minutes	-0.01	0.01	0.38	-0.01- -0.01
Use of intravenous Antithrombotic agent	0.82	0.32	0.01	0.18-1.46
Anterior circulation occlusion	0.21	0.14	0.14	-0.08-0.51
TICI 2C or better	0.49	0.18	0.007	0.14-0.84

TABLE 3: Linear regression model for good neurologic outcome at 90 days while adjusting for baseline NIHSS, age, procedural time, use of antithrombotic intravenous agent, Site of occlusion (Anterior vs posterior), and achieving a TICI2C or higher result

Despite the lack of randomized clinical trials investigating the efficacy of rescue intracranial stenting for LVOs, rescue strategies with angioplasty and/or stenting have been recently described in retrospective studies with encouraging results when it comes to the safety profile. However, one of the main safety concerns that arises during rescue intracranial stenting is the lack of a standardized antithrombotic therapy and the increased risk of symptomatic ICH as a result of dual antiplatelet use acutely. A total of 95.7% of our patients received an intravenous antithrombotic agent intraoperatively, which is comparable to reported antiplatelet regiments in RS studies, with GPIIb/IIIa antagonist use ranging between 82% and 89%.[3,8]

A total of 8.5% of our patients experienced a sICH, this rate is slightly higher when compared to the sICH rate reported in MRCLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands) of 7.7%, and the aggregated rate reported from the major endovascular intervention trials of 4.4%.[1,9] However, this rate is comparable with recent rescue intracranial studies including 11% (Stacke et al) and 12% (Wareham et al).[3,8] Interestingly, 7/47 (14.9%) of our cohort had a medium vessel (M2) occlusion, which is a much larger percentage of medium vessel occlusions when compared to prior studies. All patients with medium vessel occlusions had a good neurologic outcome at 90 days, and none experienced a sICH. This is likely reflective of recent advances in the field, with a higher number of medium vessel occlusions being the primary target of EVT. It is important to mention that our cohort included patients with small infarct core with median baseline ASPECTS score >7. Safety and efficacy of SR in failed thrombectomy in patients with lower ASPECTS score needs to be investigated in a separate study.

Longer procedural time, reflected in a higher number of passes, significantly correlated with poor neurologic outcome at 90 days. This is suggestive that better neurologic outcome can be achieved by resorting to rescue intracranial stenting earlier during the procedure in patients who demonstrate characteristics of underlying intracranial atherosclerotic disease and reocclusion after initial successful recanalization, while considering size of core infarct and time from ictus. This is supported by previous data indicating that clinical outcome did not significantly improve beyond 3 retrieval attempts.[10]

Another consideration that may influence outcomes is the stent choice. Approximately half of our patient cohort received an Enterprise (closed cell design) stent. Although Enterprise stents were hypothesized to have a lower radial force than other open cell design intracranial stents,[11] our reperfusion rates were comparable to prior RS in LVO studies. Further studies are warranted to compare safety and efficacy of self-expanding stents versus balloon mounted stents (BMS) as recent studies have demonstrated promising results in using BMS in intracranial lesions.[12]

We acknowledge the limitations of our study. First, given our small sample size and the retrospective nature of this study, the risk of inherent bias is high. Second, the decision to stent and the choice of the antiplatelet therapy was up to the neurointerventionalist which can create a bias given the heterogenous nature of the data. Lastly, some confounders that are known to affect neurologic outcome including collateral quality and exact baseline core size are not available which may limit the generalization of our results.

CONCLUSION

Rescue intracranial stenting appears safe and effective in patients with large vessel occlusion and failed EVT. Good neurologic outcomes were significantly higher in this retrospective study when compared to patients who were not successfully recanalized in prior endovascular thrombectomy studies. Large, prospective studies are needed to confirm our finding and further delineate the patient population that could benefit the most from rescue intracranial stenting during mechanical thrombectomy.

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