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Sami Al Kasab
*Medical University of South Carolina*

Eyad Almallouhi
*Medical University of South Carolina*

Ali Alawieh
*Emory University*

Stacey Wolfe
*Wake Forest School of Medicine*

Kyle M. Fargen
*Wake Forest School of Medicine*

*See next page for additional authors*



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## Authors

Sami Al Kasab, Eyad Almallouhi, Ali Alawieh, Stacey Wolfe, Kyle M. Fargen, Adam S. Arthur, Nitin Goyal, Travis Dumont, Peter Kan, Joon-Tae Kim, Reade De Leacy, Ilko Maier, Joshua Osbun, Ansaar Rai, Pascal Jabbour, Jonathan A. Grossberg, Min S. Park, Robert M. Starke, Roberto Crosa, and Alejandro M. Spiotta

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ORIGINAL RESEARCH

# Outcomes of Rescue Endovascular Treatment of Emergent Large Vessel Occlusion in Patients With Underlying Intracranial Atherosclerosis: Insights From STAR

Sami Al Kasab, MD*; Eyad Almallouhi, MD*; Ali Alawieh, MD, PhD; Stacey Wolfe, MD; Kyle M. Fargen, MD; Adam S. Arthur, MD; Nitin Goyal, MD; Travis Dumont, MD; Peter Kan, MD; Joon-Tae Kim, MD; Reade De Leacy, MD; Ilko Maier, MD; Joshua Osbun, MD; Ansaar Rai, MD; Pascal Jabbour, MD; Jonathan A. Grossberg, MD; Min S. Park, MD; Robert M. Starke, MD; Roberto Crosa, MD; Alejandro M. Spiotta, MD; on behalf of STAR collaborators†



**BACKGROUND:** Some emergent large vessel occlusions (ELVOs) are refractory to reperfusion because of underlying intracranial atherosclerosis (ICAS), often requiring rescue therapy (RT) with balloon angioplasty, stenting, or both. In this study, we investigate the safety, efficacy, and long-term outcomes of RT in the setting of mechanical thrombectomy for ICAS-related ELVO.

**METHODS AND RESULTS:** We queried the databases of 10 thrombectomy-capable centers in North America and Europe included in STAR (Stroke Thrombectomy and Aneurysm Registry). Patients with ELVO who underwent ICAS-related RT were included. A matched sample was produced for variables of age, admission National Institute of Health Stroke Scale, Alberta Stroke Program Early CT Score, onset to groin puncture time, occlusion site, and final recanalization. Out of 3025 patients with MT, 182 (6%) patients required RT because of underlying ICAS. Balloon angioplasty was performed on 122 patients, and 117 patients had intracranial stenting. In the matched analysis, 141 patients who received RT matched to a similar number of controls. The number of thrombectomy passes was higher (3 versus 1, $P<0.001$), and procedural time was longer in the RT group (52 minutes versus 36 minutes, $P=0.004$). There was a higher rate of symptomatic hemorrhagic transformation in the RT group (7.8% versus 4.3%, $P=0.211$), however, the difference was not significant. There was no difference in 90-day modified Rankin scale of 0 to 2 (44% versus 47.5%, $P=0.543$) between patients in the RT and control groups.

**CONCLUSIONS:** In patients with ELVO with underlying ICAS requiring RT, despite longer procedure time and a more thrombectomy passes, the 90 days favorable outcomes were comparable with patients with embolic ELVO.

**Key Words:** acute stroke ■ balloon angioplasty ■ intracranial atherosclerosis ■ mechanical thrombectomy ■ rescue therapy ■ stenting

Mechanical thrombectomy (MT) is the standard of care for patients with emergent large vessel occlusion (ELVO) and salvageable brain tissue.[1] Outcomes following MT depend primarily on achieving fast and successful revascularization.[2,3] Approximately 10% to 20% of patients undergoing MT, however, fail

Correspondence to: Sami Al Kasab, MD, Department of Neurology and Neurosurgery, Medical University of South Carolina, 96 Jonathan Lucas St, MSC 606, Charleston, SC 29425. E-mail: alkasab@musc.edu

*S. Al Kasab and E. Almallouhi contributed equally as co-first authors.

†A complete list of the STAR collaborators can be found in the Appendix at the end of the article.

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## CLINICAL PERSPECTIVE

### What Is New?

- In our observational multicenter study, ≈6% of patients with intracranial atherosclerosis (ICAS) who had mechanical thrombectomy underwent also rescue therapy with angioplasty/stenting.
- Compared with patients with non-ICAS, patients with ICAS rescue therapy required longer procedure time and more thrombectomy passes compared with patients with mechanical thrombectomy who did not require rescue therapy; however, there was no statistically significant difference in symptomatic hemorrhagic transformation or 90-day outcome after matching for key characteristics including final reperfusion status.

### What Are the Clinical Implications?

- Our observational study suggests a benefit for rescue therapy with angioplasty/stenting in patients with underlying ICAS evident during mechanical thrombectomy.
- Further randomized studies are needed to more definitively answer whether angioplasty/stenting in patients with ICAS is beneficial.

### Nonstandard Abbreviations and Acronyms

| | |
|---|---|
| **ASPECTS** | Alberta Stroke Program Early CT Score |
| **ELVO** | emergent large vessel occlusion |
| **ICAS** | intracranial atherosclerosis |
| **MT** | mechanical thrombectomy |
| **NIHSS** | National Institute of Health Stroke Scale |
| **RT** | rescue therapy |
| **sICH** | symptomatic hemorrhagic transformation |



to achieve successful revascularization.[4–6] Etiology for unsuccessful revascularization can be divided into either failure to access the intracranial vasculature or inability to achieve successful revascularization despite successful access to the intracranial vasculature. In the latter, the most common reason for revascularization failure following successful intracranial access is underlying intracranial atherosclerosis (ICAS), rendering the vessel with fixed severe residual stenosis or in-situ thrombosis with instant reocclusion despite multiple attempts, with other causes including intracranial dissection, or iatrogenic perforation being much less common.[7,8] While management of patients with ICAS presenting with a transient ischemic attack or stroke within 30 days has been established with evidence from large, randomized controlled trials showing that medical management is superior to angioplasty and/or stenting,[9,10] acute management of ICAS-related ELVO is unclear and poses a major challenge. Patients with ICAS-related ELVO often require rescue therapy (RT) with angioplasty, stenting, or both to achieve successful revascularization. Few previous studies have evaluated the safety of RT in patients with ELVO with failed reperfusion because of underlying ICAS. Most of these studies had small sample size and were mostly performed in Asia, which limits their applicability to the Western patient population given that outcomes of ICAS in patients with transient ischemic attack and ischemic stroke are different between Asian and Western countries.[10–12] The aim of this study is to investigate the frequency of ICAS in the setting of mechanical thrombectomy and assess the safety, efficacy, and long-term outcomes associated with RT with angioplasty and/or stenting following failed reperfusion in a large multicenter cohort in the United States and Europe.

## METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request. We used data from the prospectively maintained databases of 10 thrombectomy-capable stroke centers in North America, and Europe included in STAR (Stroke Thrombectomy and Aneurysm Registry). Informed consent was waived. In this analysis, we included patients who underwent mechanical thrombectomy using approved second-generation thrombectomy devices from June 2013 through December 2019.

We evaluated the rate of RT with angioplasty and/or stenting secondary to presumed ICAS (ICAS RT group) during mechanical thrombectomy for ELVO. Initial angiographic images showed complete occlusion in the included patients with thrombectomy. Following thrombectomy, patients who had fixed residual stenosis (50%–99%) or instant intraoperative reocclusion requiring RT were considered as patients with ICAS RT. This definition has been validated in multiple previous studies.[8,13,14] Patients who received RT for reasons other than presumed ICAS were excluded from our analyses. Collected data included baseline demographics, vascular risk factors, and admission National Institute of Health Stroke Scale (NIHSS), whether or not patients received intravenous alteplase (tPA), time from symptom onset to groin puncture, procedural times in minutes, thrombectomy techniques, number of attempts, whether angioplasty and/or stenting was performed, type of stent used, complication rates, and rate of symptomatic hemorrhage.

Successful revascularization was defined as modified thrombolysis in cerebral infarction of 2b-3. Symptomatic hemorrhagic transformation (sICH) was defined using ECAS III (European Cooperative Acute Stroke Study) definition (worsening of ≥4 points in NIHSS attributed to hemorrhagic transformation),[15] and favorable long-term functional outcome was defined as modified Rankin scale of 0 to 2 at 90 days.

## Statistical Analysis

Descriptive statistics were used to report patient demographic and clinical characteristics using median and interquartile range (IQR) for continuous variables and percentages for categorical variables. Characteristics of groups were compared using the Wilcoxon rank-sum (Mann-Whitney) test and Chi-square (or Fisher exact test for cells <5) as appropriate. An alpha level of 0.05 was used as the level of statistical significance. We assessed the predictors of receiving RT during MT using a logistic regression model controlling for age, sex, race, stroke risk factors (diabetes mellitus, hypertension, atrial fibrillation, hyperlipidemia), Alberta Stroke Program Early Computerized Tomography (CT) Score (ASPECTS) on admission, baseline NIHSS, location of occlusion, and onset to groin time. To determine predictors of favorable outcomes in patients in the ICAS RT group, we used a logistic regression model controlling for age, sex, race, and baseline NIHSS, location of occlusion, rescue technique used, and final recanalization score.

To evaluate outcomes of patients with ICAS RT, a control group sample of patients with MT with embolic ELVO was produced by matching the following variables: age, onset to groin time, admission NIHSS, location of the occlusion, and final modified thrombolysis in cerebral infarction score. The center that procedure was done at was used in addition to the previously mentioned variables to match another control group (Table S1). We used Wilcoxon rank-sum (Mann-Whitney) test and Chi-square (or Fisher exact test for cells <5) to compare baseline features (age, sex, race, stroke risk factors, admission NIHSS, use of IV-tPA, ASPECTS on admission and location of occlusion), procedural variables (time from symptom onset to groin puncture, procedure duration, final modified thrombolysis in cerebral infarction score, number of passes and complications) and outcomes, sICH, 90-day mortality and 90-day modified Rankin scale between matched ICAS RT patients and the control groups.

To ensure the robustness of our results, we performed sensitivity analysis using a binary logistic regression model to assess: (1) the association between RT and favorable 90-day outcome in patients who achieved successful recanalization, (2) the relationship between RT and 90-day mortality in patients who had unsuccessful recanalization. Our sensitivity model was derived with inverse probability of treatment weight using propensity scores. The propensity scores were calculated using a binary logistic regression model for ICAS RT adjusting for age, sex, race, stroke risk factors, ASPECTS on admission, baseline NIHSS, location of occlusion, and onset to groin time. Covariates in the propensity score model that have a <0.20 standardized difference before and after weighting were considered well-matched. Finally, we introduced the center variable to both regression models.

All final models were tested for collinearity. The analysis was conducted using SPSS v25 (IBM Corporation, New York, NY) with Fuzzy extension v1.

## Institutional Review Board Approval

The study was approved by the Institutional Review Board at each of the included centers.

# RESULTS

## RT Group

Total of 3025 patients underwent mechanical thrombectomy in the included centers. Of those, 189 patients received intracranial rescue angioplasty, stenting, or both during MT for ELVO. Seven patients were excluded because of dissection being the reason for RT, leaving 182 who met ICAS-related ELVO criteria. Table 1 summarizes the baseline features of patients included in the study. Compared with patients with embolic ELVO, patients in the ICAS RT group were younger (age 67 versus 71 years, $P$=0.004), more likely to have diabetes mellitus (36.8% versus 28.5%), more likely to have hyperlipidemia (51.1% versus 37%), and less likely to have atrial fibrillation (16.5% versus 35.3%) compared with other patients with MT. Median NIHSS on admission was 14 (IQR, 9–20), and median ASPECTS was 9 (IQR, 7–10) in the ICAS RT group. On multivariate analyses after adjusting for potential confounders, predictors for RT secondary to ICAS were diabetes mellitus (odds ratio [OR], 1.49; 95% CI, 1.03–2.17; $P$=0.035), hyperlipidemia (OR, 1.92; 95% CI, 1.33–2.78; $P$=0.001), and onset to groin time (OR, 1.03; 95% CI, 1.01–1.05; $P$=0.003), while atrial fibrillation was associated with lower odds of requiring RT (OR, 0.34; 95% CI, 0.23–0.58; $P$<0.001).

In terms of thrombectomy technique before RT, aspiration only was used in 107 patients; stent retriever in 37 patients, "Solumbra" (combined stent-retriever and aspiration) in 13 patients, and the remaining 25 patients had other techniques used. The median number

**Table 1. Baseline Features and Outcomes of Patients Who Underwent Rescue Therapy for Presumed Intracranial Atherosclerotic Disease**

| | Rescue Therapy Group (n=182) | Non-Rescue Therapy Group (n=2843) | *P* Value* |
|---|---|---|---|
| Age, median (IQR) | 67 (59–76) | 71 (60–80) | 0.004† |
| Women, n (%) | 82 (45.1) | 1410 (49.6) | 0.235 |
| White, n (%)‡ | 106 (58.2) | 1442 (61.8) | 0.341 |
| Hypertension, n (%) | 140 (76.9) | 2074 (73) | 0.241 |
| DM, n (%) | 67 (36.8) | 811 (28.5) | 0.017† |
| AF, n (%) | 30 (16.5) | 1004 (35.3) | <0.001† |
| Hyperlipidemia , n (%) | 93 (51.1) | 1053 (37) | <0.001† |
| Prior stroke, n (%) | 28 (15.4) | 243 (8.5) | 0.002† |
| Admission NIHSS, median (IQR) | 14 (9–20) | 15 (10–20) | 0.432 |
| IV-tPA, n (%) | 63 (34.6) | 1409 (49.6) | <0.001† |
| ASPECTS, median (IQR) | 9 (7–10) | 9 (7–10) | 0.731 |
| Posterior circulation, n (%) | 29 (15.9) | 324 (11.4) | 0.064 |
| Onset to groin in min, median (IQR) | 341 (215–626) | 240 (150–381) | <0.001† |
| No. of passes, median (IQR) | 3 (2–4) | 2 (1–3) | <0.001† |
| mTICI ≥2b, n (%) | 151 (83) | 2199 (77.3) | 0.078 |
| Procedure duration in min, median (IQR) | 52 (29–94) | 42 (23–73) | 0.003† |
| Peri-procedural complications, n (%) | 13 (7.1) | 190 (6.7) | 0.81 |

AF indicates atrial fibrillation; ASPECTS, Alberta Stroke Program Early Computerized Tomography (CT) Score; DM, diabetes mellitus; IQR, interquartile range; IV-tPA, intravenous tissue plasminogen activator; mTICI, modified thrombolysis in cerebral infarction; and NIHSS, National Institute of Health Stroke Scale.

*Calculated using $\chi^2$ for categorical variables and Wilcoxon test for the continuous variables.

†Indicates statistical significant value.

‡Missing 510.

of thrombectomy passes before RT was 3 (IQR, 2–4). In terms of type of RT used, 65 patients required angioplasty alone, 60 patients required stenting alone, and 57 patients required both. Intra-arterial tPA before RT was used in 19 (10.4%) of the 182 patients. The approach to RT was dependent on the interventionist, angioplasty was first attempted in cases with residual, fixed stenosis, and a stent was placed if re-stenosis occurred. In cases of in-situ thrombosis, a follow up angiography was typically performed at 3 to 10 minutes interval and if reocclusion occurred, a stent was placed. Patients who received intravenous tPA were less likely to get stented (*P*=0.015). In the tPA group, stenting was performed in 33 patients (52.4%) versus 84 (70.6%) in the non-tPA group. The specific stent type was available for 69 of 117 patients. Neuroform Atlas (Stryker Neurovascular, Fremont, USA) stent was used in 41, Wingspan stent was used (Stryker) in 12 cases, balloon mounted stents were used in 10, of those 7 were resolute integrity stents (Medtronic Inc. Santa Rosa, CA, USA) and 3 were multilink stents (Multilink Duet, Guidant Corporation, Inc.), and 6 cases were LVIS Jr (Microvention, CA, USA) stents. The antiplatelet regimen used was available for 99 of 117 who underwent stenting; 97 patients received weight based tirofiban, eptifibatide, or abciximab loading dose depending on local institution protocol followed by continuous infusion for 6 hours, and loading doses of 650 mg aspirin and 600 mg clopidogrel (no loading dose was used for patients already on aspirin and/or clopidogrel before presentation), followed by daily dose of aspirin 325 mg and clopidogrel 75 mg. Two patients received heparin infusion followed by aspirin and clopidogrel loading and daily maintenance doses.

The sICH occurred in 15 (8.2%) patients, and 69 (37.9%) patients achieved favorable long-term functional outcome at 90 days (modified Rankin scale, 0–2). Among patients who received a stent, 9 of 117 (7.7%) patients had sICH (2 received intravenous tPA and 7 did not receive tPA, *P*=0.678). On multivariate analysis, rescue technique was not an independent predictor for favorable 90 days outcomes (OR, 0.72; 95% CI, 0.47–1.09; *P*=0.120) after controlling for age, sex, race, location of occlusion, NIHSS on admission, and final recanalization score.

## Matched Analysis

We matched 141 patients from the ICAS RT group with the same number of patients with MT who have similar age, admission NIHSS, location of the occlusion, onset to groin time, and revascularization status. Table 2 presents baseline features, procedural metrics, and outcomes in the 2 treatment groups.

**Table 2. Baseline Features, Procedural Metrics, and Outcomes in the 2 Groups (Rescue Therapy Versus Matched Control)**

| Variable | Rescue Therapy Group (N=141) | Control Group (n=141) | *P* Value* |
|---|---|---|---|
| Age, median (IQR) | 67 (60–76) | 68 (59–78) | 0.522 |
| Women, n (%) | 65 (46.1) | 67 (47.5) | 0.811 |
| White, n (%) | 101 (71.6) | 108 (76) | 0.341 |
| Hypertension, n (%) | 109 (77.3) | 115 (81.6) | 0.377 |
| DM, n (%) | 54 (38.3) | 43 (30.5) | 0.168 |
| AF, n (%) | 20 (14.2) | 50 (35.5) | <0.001† |
| Hyperlipidemia, n (%) | 71 (50.4) | 66 (46.8) | 0.551 |
| Prior stroke, n (%) | 20 (14.2) | 10 (7.1) | 0.053 |
| Admission NIHSS, median (IQR) | 14 (9–20) | 14 (10–19) | 0.838 |
| IV-tPA, n (%) | 56 (39.7) | 67 (47.5) | 0.187 |
| ASPECTS, median (IQR) | 8 (7–9) | 8 (7–9) | 0.731 |
| Posterior circulation stroke, n (%) | 16 (11.3) | 16 (11.3) | >0.999 |
| Onset to groin in min, median (IQR) | 310 (206–525) | 303 (207–542) | 0.804 |
| No. of passes, median (IQR) | 3 (2–4) | 1 (1–2) | <0.001† |
| mTICI ≥2b, n (%) | 124 (87.9) | 124 (87.9) | 1 |
| Procedure duration in min, median (IQR) | 52 (28–92) | 36 (25–59) | 0.004† |
| Peri-procedural complications, n (%) | 12 (8.5) | 10 (7.1) | 0.227 |
| sICH, n (%) | 11 (7.8) | 6 (4.3) | 0.211 |
| 90-d mRS, median (IQR) | 3 (1–5) | 3 (1–6) | 0.543 |
| Favorable 90-d outcomes, n (%) | 62 (44) | 67 (47.5) | 0.55 |
| 90-d mortality | 32 (22.7%) | 41 (29.1%) | 0.221 |

AF indicates atrial fibrillation; ASPECTS, Alberta Stroke Program Early Computerized Tomography (CT) Score; DM, diabetes mellitus; IQR, interquartile range; IV-tPA, intravenous tissue plasminogen activator; mRS, modified Rankin scale; mTICI, modified thrombolysis in cerebral infarction; NIHSS, National Institute of Health stroke scale; and sICH, symptomatic hemorrhagic transformation.

*Calculated using $\chi^2$ test for categorical variables and Wilcoxon test for the continuous variables.

†Indicates statistical significant value.

There was no difference in age, race, or sex between the 2 groups. More patients in the control group had atrial fibrillation (70 [43.5%] versus 20 [12.4%], *P*<0.001). Other stroke risk factors (diabetes mellitus, hypertension, hyperlipidemia, and prior stroke) were balanced between both groups. There was no difference in admission NIHSS, ASPECT score on admission, location of occlusion, or time from symptom onset to groin puncture (Table 2). Patients in the control group had a lower number of thrombectomy passes (1 [IQR, 1–2] versus 3 [IQR, 2–4], *P*<0.001). Of the 141 patients, balloon angioplasty was performed in 49 patients, stenting was performed in 46 patients, and 46 patients underwent both angioplasty and stenting. Patients in the ICAS RT group had longer procedure duration (52 [IQR, 28–92] versus 36 [25–59] minutes, *P*=0.004). There was no difference in the rate of sICH between the 2 groups (11 [7.8%] in the ICAS RT group versus 5 [4.3%] in the control group, *P*=0.211) (Table S1 compares the rate of sICH in anterior versus posterior circulation). Finally, no statistically significant difference was found in the rate of favorable 90-day functional outcome (62 [44%] versus 67 [47.5%], *P*=0.55), and 90-day mortality (32 [22.7%] versus 41 [29.1%], *P*=0.221) in the ICAS RT group compared with the control group. Figure shows the distribution of 90-day modified Rankin scale in the patients in the matched analysis.

## Sensitivity Analysis

On the logistic regression analysis with inverse probability of treatment weight and propensity score, receiving RT secondary to ICAS was not an independent predictor of favorable 90-day outcomes (OR, 0.82; 95% CI, 0.55–1.24; *P*=0.351) in patients who achieved successful recanalization. In addition, receiving RT secondary to ICAS was not an independent predictor of 90-day mortality (OR, 1.54; 95% CI, 0.86–7.53, *P*=0.094) in patients who had failed recanalization. After introducing the center variable, it was not a statistically significant predictor in either of the models (*P*>0.999).

# DISCUSSION

To our knowledge, our multicenter study is the largest to date to provide safety and long-term outcome data on patients undergoing mechanical thrombectomy for ELVO because of underlying ICAS requiring rescue angioplasty, stenting, or both. Our study shows that ≈6% of patients undergoing MT have underlying ICAS and require RT with angioplasty and/or stenting. In terms of procedural metrics, our study shows that patients with ICAS-related ELVO require longer procedural times and a higher number of thrombectomy passes compared with patients with embolic ELVO. Also, compared with patients with embolic ELVO, patients receiving RT had numerically higher rates of sICH, though this was not statistically significant. Nevertheless, there was no difference in 90-day functional outcomes in the RT group.

Intracranial atherosclerosis-related emergent large vessel occlusion poses a major challenge to endovascular thrombectomy. The major challenge of ICAS-related ELVO is the tendency of intra-procedural in-situ reocclusion or cause a residual, fixed severe

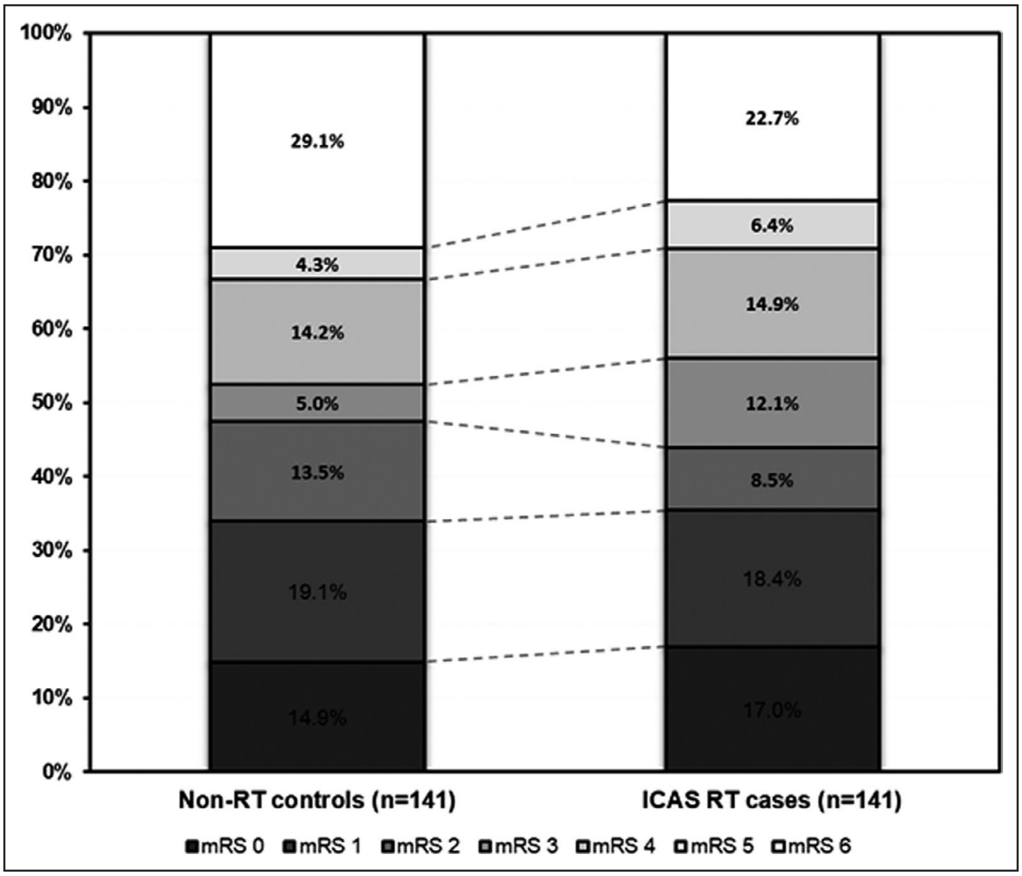


**Figure 1. The distribution of 90-day modified Rankin scale in the rescue therapy secondary to intracranial atherosclerosis group compared with the control group.**
ICAS indicates intracranial atherosclerosis mRS, modified Rankin scale; and RT, rescue therapy.



stenosis rendering the vessel with suboptimal revascularization.[16] It is estimated that reocclusion occurs in approximately one third of patients with ICAS-related ELVO, compared with 2.7% in patients with embolic ELVO.[14] The exact pathophysiology behind this is unclear; however, postmortem studies suggest fibrous cap disruption and sub-intimal dissection and in-situ thrombosis of the involved vessel as the potential reason for reocclusion.[17] A study by Kang et al, evaluated the rate of instant reocclusion during MT, in their study, 40 of 132 (30%) had in situ thrombosis with reocclusion, and all of those patients had underlying ICAS on follow-up imaging.[8] Given the known risks associated with intracranial angioplasty and stenting in patients with ischemic stroke, the interventionist is often left with a dilemma of either leaving the affected vessel occluded which often results in disabling stroke or acutely perform angioplasty and/or stenting. The risk-benefit profile however is different when managing patients with ICAS with ELVO compared with those without ELVO for whom the benefit of angioplasty with/without stenting doesn't outweigh the associated risks.[9,10] Our study shows that patients with ICAS-related ELVO requiring rescue angioplasty and/or stenting were able to achieve comparable long-term outcomes compared with patients with embolic ELVO with similar safety profile even after requiring RT. A possible explanation to the good outcome in this group is that patients with ICAS have better collateral circulation compared with patients with embolic ELVO, therefore lower baseline infarct volume.[18] Moreover, a study by Suh et al found that baseline infarct volume was lower in patients with ICAS-related ELVO compared with embolic ELVO (14 versus 54 mL, $P<0.001$).[19]

A number of studies have evaluated the safety and efficacy of angioplasty, stenting, or both stenting as a rescue technique in the setting of ELVO and underlying ICAS. Most of these studies were limited by small sample size. Furthermore; the vast majority of these studies were performed in Asia with only few studies coming from the United States and Europe.[10,20] Aside from ICAS being more common in Asian patient population, similar to ICAS in the non-emergent setting, studies coming from the United States and Europe have shown different results compared with those coming from Asia.[10–12] While it remains unclear why there are such stark differences in treatment effects between Asian and Western patient populations with ICAS, studies have suggested genetic, socioeconomic, and dietary differences as contributing factors.[21,22] A study done in Korea by Yoon et al evaluated the safety of emergent angioplasty with or without stenting in patients with ICAS-related ELVO, the authors reported more favorable outcomes in the ICAS group compared with the control group with no difference in symptomatic intracranial hemorrhage, or mortality.[23] Conversely, a study from Spain by Matias-Guiu reported longer procedural times; higher mortality and lower rates of good functional outcomes in ICAS-related ELVO requiring RT with angioplasty with or without stenting.[24] This study, however, only had 15 patients with ICAS.[25,26] Other studies reporting on comparably small sample sizes performed in the United States and Europe have reported conflicting results with regards to rates of successful revascularization, complication rates, and long-term outcomes.[16] The small sample size in those studies is likely attributable to the fact that ICAS is less prevalent in Western compared with Asian population.[27]

Our findings support a 2019 systematic review and meta-analysis conducted by Chun On Tsang et al that reported higher prevalence of hypertension, hyperlipidemia, and diabetes mellitus and lower atrial fibrillation in patients with ICAS-related ELVO.[16] In our study, hyperlipidemia and diabetes mellitus were independent predictors of requiring RT for ICAS. Similarly, our study supports the findings of this meta-analysis demonstrating longer procedural times and similar rates of final successful revascularization and sICH. Our study, however, only included patients in the United States and Europe, and therefore provides evidence supporting the safety and efficacy of rescue angioplasty and/or stenting in patients with ICAS-related ELVO in non-Asian patient population.

It is important to point out that while our study shows that rescue angioplasty and/or stenting in the setting of ICAS-related ELVO, the optimal rescue technique is patients with failed MT secondary to reocclusion or fixed stenosis remains uncertain, and the approach to such patients varies by center. In our study, we found that angioplasty alone can be effective in up to one third of patients, it is important, however, to keep in mind that among the 122 patients who underwent angioplasty, 57 patients (47%) eventually required stenting. Importantly, the type of stent used varied by center, and the most commonly used stents were self-expandable stents. A recent study by Gross et al suggests the use of balloon-mounted stents given higher radial force, in this study however, patients undergoing stenting with balloon-mounted stents had higher rates of sICH and mortality.[28] Of note, our study did not show a correlation between stenting and sICH in patients who have already received intravenous tPA.

In this study, we presented the outcomes of using stenting, angioplasty, or both as an RT but other rescue techniques have become available recently including intra-arterial infusion of antiplatelet, such as Tirofiban or Abxicimab. A recent study performed in Korea compared the outcomes of using intra-arterial glycoprotein IIb/IIIa inhibitor infusion and emergent angioplasty found that both techniques resulted in a successful revascularization rate of about 95% with similar rates of symptomatic hemorrhage, 3-month functional independence and mortality.[29] However, the study was limited by major differences in baseline and procedural characteristics which could have influenced the results. Nevertheless, such new treatments appear less invasive and need to be compared with rescue angioplasty/stenting.

### Strength and Limitations

The main strength of our study is the inclusion of large cohort derived from the real-world daily practice in different countries in North America and Europe. On the other hand, some limitations of our work must be acknowledged. First, the retrospective design, the lack of randomization, and potential residual confounders should be kept in mind when interpreting the results of our study. In addition, given lack of follow-up imaging data, we couldn't comment on stent patency and whether or not some of those patients had residual in stent stenosis. Furthermore, the specific devices, reperfusion approaches, stents used, intraprocedural sedation, and post-procedural blood pressure targets were heterogeneous and were selected according to the treating physicians' preference. Also, data about collateral score are not available, and the safety and efficacy outcomes in different centers were self-reported without central adjudication.

## CONCLUSIONS

Our multicenter study reports that there was no statistically significant difference in the 90-day outcomes in patients with ICAS RT who were treated with acute stenting, angioplasty, or both compared with a control group of patients with MT with embolic ELVO. Patients who require RT, however, had longer procedural times, and higher number of thrombectomy passes. Future randomized clinical trials are required to definitely evaluate the potential efficacy of RT with angioplasty and/or stenting in patients with ICAS-related ELVO undergoing MT.

## APPENDIX

### STAR Contributors

Medical University of South Carolina, Charleston, SC, USA: [Kimberly Kicielinski, Jonathan R. Lena, Reda Chalhoub]. University of Arizona, Tucson, AZ, USA:

[Mohammad El-Ghanem]. University of Miami Health System, Miami, FL, USA: [Dileep R. Yavagal, Eric C. Peterson]. Baylor College of Medicine, Houston, TX, USA: [Daniel Raper]. Wake Forest Baptist Health, Winston-Salem, NC, USA: [Patrick A. Brown]. University of Washington, Seattle, WA, USA: [Louis J. Kim, Melanie Walker]. The University of Tennessee Health Science Center, Memphis, TN, USA: [Daniel Alan Hoit, Violiza Inoa-Acosta, Christopher Nickele, Lucas Elijovich]. Médica Uruguaya, Montevideo, Uruguay: [Fernanda Rodriguez-Erazú]. Universitätsmedizin Göttingen, Göttingen, Germany: [Jan Lima]. University of Basel, Basel, Switzerland: [Alex Brehm].

## ARTICLE INFORMATION

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### Affiliations

Department of Neurology (S.A.K., E.A.) and Department of Neurosurgery (S.A.K., E.A., A.M.S.), Medical University of South Carolina, Charleston, SC; Department of Neurosurgery, Emory University School of Medicine, Atlanta, GA (A.A., J.A.G.); Department of Neurosurgery, Wake Forest School of Medicine, Winston Salem, NC (S.W., K.M.F.); Department of Neurosurgery, Semmes-Murphey Neurologic and Spine Clinic (A.S.A., N.G.) and Department of Neurology (N.G.), University of Tennessee Health Science Center, Memphis, TN; Department of Neurosurgery, University of Arizona Health Sciences, Tucson, AZ (T.D.); Department of Neurosurgery, Baylor School of Medicine, Houston, TX (P.K.); Department of Neurology, Chonnam National University Hospital, Seoul, South Korea (J.-T.K.); Department of Neurosurgery, Mount Sinai Health System, New York, NY (R.D.L.); Department of Neurology, University Medical Center Göttingen, Göttingen, Germany (I.M.); Department of Neurosurgery, Washington University of School of Medicine, St. Louis, MO (J.O.); Department of Radiology, West Virginia School of Medicine, Morgantown, WV (A.R.); Department of Neurosurgery, Thomas Jefferson University Hospitals, Philadelphia, PA (P.J.); Department of Neurosurgery, University of Virginia, Charlottesville, VA (M.S.P.); Department of Neurosurgery, University of Miami Health System, Miami, FL (R.M.S.); and Department of Neurosurgery, Endovascular Neurological Center, Médica Uruguaya, Montevideo, Uruguay (R.C.).

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### Disclosures

None.

### Supplementary Material

Table S1

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# SUPPLEMENTAL MATERIAL

**Table S1. Baseline features, procedural metrics and outcomes in the 2 groups (rescue therapy vs. matched control) after matching for age, onset to groin time, admission NIHSS, location of the occlusion, final mTICI score, and the center that the procedure was done at.**

| Variable | Rescue therapy group (N=85) | Control group (n=85) | P-value |
|---|---|---|---|
| **Age, median (IQR)** | 68 (61-75) | 68 (60-76) | 0.976 |
| **Females, n (%)** | 36 (42.4%) | 34 (40%) | 0.755 |
| **White, n (%)** | 49 (57.6%) | 55 (64.7%) | 0.345 |
| **HTN, n (%)** | 62 (72.9%) | 59 (69.4%) | 0.611 |
| **DM, n (%)** | 29 (34.1%) | 25 (29.4%) | 0.51 |
| **Afib, n (%)** | 12 (14.1%) | 29 (34.1%) | **0.002** |
| **HLD, n (%)** | 37 (43.5%) | 34 (40%) | 0.641 |
| **Prior stroke, n (%)** | 8 (9.4%) | 4 (4.7%) | 0.231 |
| **Admission NIHSS, median (IQR)** | 15 (10-20) | 16 (11-20) | 0.687 |
| **IV-tPA, n (%)** | 43 (50.6%) | 43 (50.6%) | >0.999 |
| **ASPECTS, median (IQR)** | 9 (7-10) | 8 (7-10) | 0.534 |
| **Posterior circulation stroke, n (%)** | 4 (4.7%) | 4 (4.7%) | >0.999 |
| **Onset to groin in minutes, median (IQR)** | 288 (187-451) | 291 (200-445) | 0.924 |
| **Number of passes, median (IQR)** | 3 (2-5) | 2 (1-4) | 0.09 |
| **mTICI≥2b, n (%)** | 77 (90.6%) | 77 (90.6%) | >0.999 |
| **Procedure duration in** | 42 (26-87) | 32 (16-60) | **0.007** |

| | | | |
|---|---|---|---|
| **minutes, median (IQR)** | | | |
| **Peri-procedural complications, n (%)** | 1 (1.2%) | 1 (1.2%) | >0.999 |
| **sICH, n (%)** | 6 (7.1%) | 9 (10.6%) | 0.417 |
| **90-day mRS, median (IQR)** | 2 (1-4) | 2 (1-4) | 0.825 |
| **Favorable 90-day outcomes, n (%)** | 44 (51.8%) | 48 (56.5%) | 0.538 |
| **90-day mortality** | 17 (20%) | 11 (12.9%) | 0.215 |

Afib: atrial fibrillation, ASPECT: Alberta Stroke Program Early CT, DM: Diabetes, HLD: hyperlipidemia, HTN: hypertension, IV-tPA: intravenous tissue plasminogen activator, mRS: modified Rankin scale, mTICI: modified Thrombolysis in Cerebral Infarction, NIHSS: National Institute of Health stroke scale, sICH: symptomatic intracerebral hematoma.