

# Emergency Angioplasty or Stenting for Stroke Patients with Intracranial Atherosclerotic Large Vessel Occlusion

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**Aim:** Mechanical thrombectomy (MT) has become the gold standard for the treatment of large vessel occlusion (LVO) in acute ischemic stroke. However, it remains controversial whether emergency angioplasty or stenting in patients with intracranial atherosclerotic stenosis (ICAS) should be adopted. Thus, we performed a retrospective analysis of clinical data to determine whether emergency angioplasty or stenting is necessary.

**Methods:** We retrospectively analyzed data from patients undergoing MT with ICAS-related LVO of the acute anterior circulation between 2017 and 2019. Eligible patients were divided into two treatment groups: those who received rescue angioplasty or stenting [Patients treated with rescue angioplasty or stenting (PTAS) group] and those who received thrombectomy alone (non-PTAS group). The primary outcomes were good prognosis at 90 days (mRS: 0–2). Mortality, symptomatic intracranial hemorrhage, and reocclusion rate were evaluated as secondary outcomes.

**Results:** A total of 184 patients with severe stenosis after MT were enrolled, including 64 patients receiving rescue angioplasty or stenting and 120 patients without rescue angioplasty or stenting. Compared with the non-PTAS group, a better functional outcome (mRS0–2) (51.6% vs. 35.0%, adjusted odds ratio: 2.11, 95% confidence interval [CI]: 1.22–4.29;  $P=0.02$ ), lower 7-day National Institutes of Health Stroke Scale [6 (3–12.75) vs. 10 (4–16);  $P=0.04$ ], lower 24-h neurological deterioration rate (7.8% vs. 21.7%,  $P=0.02$ ), and lower 24-h reocclusion rate were observed in the PTAS group (6.3% vs. 17.5%,  $P=0.03$ ). There were no significant differences in mortality or incidence of symptomatic intracerebral hemorrhage.

**Conclusion:** Emergency angioplasty or stenting could be a safe and feasible therapeutic option with better outcomes for stroke patients with ICAS-related LVO.

**Key words:** Stroke, Stenting, Mechanical thrombectomy, Endovascular therapy, Intracranial atherosclerotic stenosis, Large vessel occlusion

## Introduction

Intracranial atherosclerotic stenosis (ICAS) is one of the most common causes of stroke worldwide and

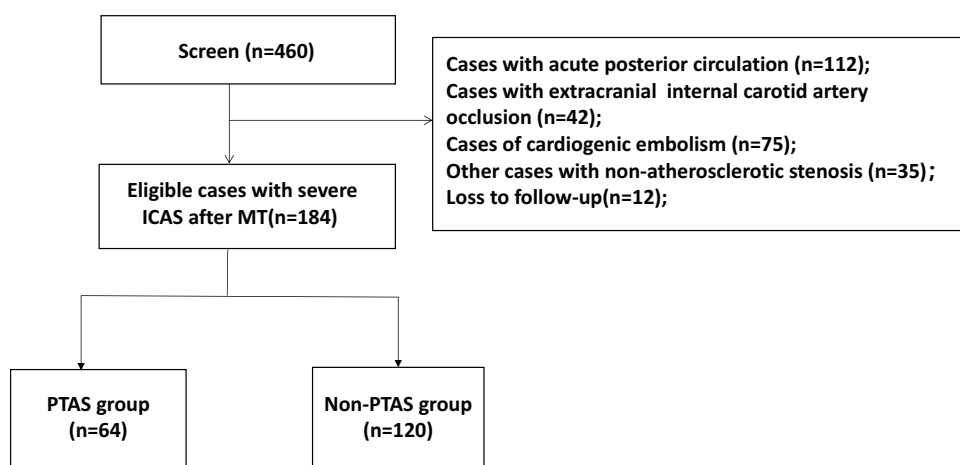
is highly prevalent in Asian population, especially among Chinese<sup>1, 2</sup>. Moreover, acute stroke patients with ICAS tend to have higher recurrence rates than other subtypes (about 4.9%–12.1%)<sup>3</sup>, making it

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**Fig. 1.** Patient screening flowchart. Four hundred and sixty patients with AIS underwent mechanical thrombectomy

Excluding acute posterior circulation occlusion ( $n=112$ ), extracranial ICA occlusion ( $n=42$ ), cardiogenic embolism ( $n=75$ ), and other nonatherosclerotic occlusions ( $n=35$ ). A total of 184 eligible patients were included in this study; 64 in the PTAS group and 120 in the non-PTAS group.

important to choose the optimal treatment strategy for such patients. Mechanical thrombectomy (MT) has been recommended as a standard of care in clinical practice for stroke patients with emergent large vessel occlusion (LVO)<sup>4, 5</sup>, because of advantages related to treatment time (within 24 h after stroke onset) and the successful reperfusion rate (greater than 80%). This approach could effectively improve the clinical outcomes of patients with LVO<sup>6</sup>. The success of MT lies in the use of stent retrievers to remove clots<sup>7</sup>.

The use of MT alone is very suitable for patients with embolic stroke. However, this approach may not be an ideal therapy for patients with emergent LVO due to underlying severe ICAS<sup>7, 8</sup>. Moreover, successful reperfusion in ICAS patients usually requires increased numbers of thrombus removals. More importantly, even if reperfusion is achieved by MT, early reocclusion frequently occurs at the ICAS site, which leads to early neurological deterioration and affects long-term prognosis<sup>9, 10</sup>. Thus, rescue therapy, such as emergency angioplasty or stenting is often required.

Acute extracranial carotid stenting is commonly performed, but emergency intracranial arterial stenosis stenting or angioplasty is controversial and is only recommended as class II b and grade C evidence<sup>4, 11</sup>. Furthermore, no randomized controlled trial has so far assessed the efficacy and safety of emergency intracranial arterial stenosis stenting or angioplasty<sup>12</sup>. Currently, only a few retrospective studies focus on the comparison of the efficacy and safety of emergency intracranial angioplasty or stenting versus no rescue angioplasty or stenting<sup>13, 14</sup>. The optimal treatment

strategy for patients with emergent LVO due to underlying ICAS is still unclear.

Accordingly, this study aimed to investigate the efficacy and safety of emergency angioplasty or stenting in patients with ICAS-related occlusion in the Asian population through a single-center retrospective study.

## Methods

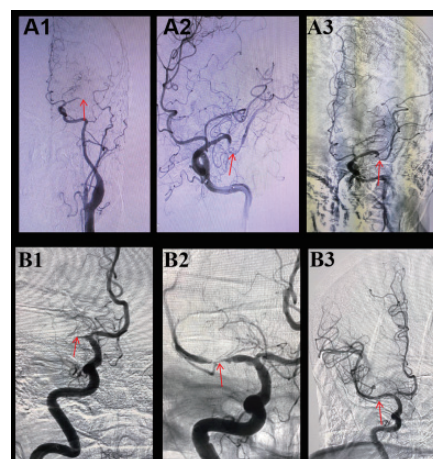
### Patient Selection

We retrospectively analyzed 460 patients who underwent MT for LVO at Xuanwu Hospital of Capital Medical University from January 2017 to November 2019. Patients with acute posterior circulation stroke were excluded. We included 184 patients with 70% or more ICAS following MT and excluded those with embolic occlusion from all causes, arterial dissection, other nonatherosclerotic stenosis, and loss of follow-up. LVO related to underlying ICAS was first screened by cerebral computed tomography angiography (CTA) or magnetic resonance angiography (MRA), with digital subtraction angiography (DSA) used to then confirm that the occlusion was at the same site. The screening process is presented in **Fig. 1**. In addition, computed tomography perfusion (CTP) imaging was used by our center to determine whether there was a significant ischemic penumbra for wake-up stroke patients. If CTP imaging showed a significant cerebral blood flow/cerebral blood volume mismatch, the neurointerventionist would give the patient endovascular treatment. The patient inclusion/

exclusion criteria were as follows: (1) Age: 18–80 years; (2) Clinically confirmed acute ischemic stroke (AIS); (3) Baseline National Institutes of Health Stroke Scale (NIHSS)  $\geq 6$  points; (4) Intracranial hemorrhage excluded by computed tomography (CT) or magnetic resonance imaging (MRI) scans; (5) DSA confirmation of LVO related to underlying severe ICAS ( $>70\%$  stenosis), including intracranial segment of internal carotid artery (ICA) or middle cerebral artery (MCA)-M1; (6) Time from onset to the beginning of MT of within 24 h; (7) Patient or his/her family signed the informed consent.

### Endovascular Therapy

We divided the patients into the following two groups: patients treated with rescue angioplasty or stenting (PTAS) group and the non-PTAS group, depending on whether the patient had been given rescue intracranial angioplasty or stenting following MT. Before MT, we first verified whether there was a microcatheter first-pass effect, which was helpful to identify ICAS<sup>15</sup>. Subsequently, MT would be attempted. A stent retriever like the Solitaire FR stent (Medtronic Neurovascular, Irvine, CA, USA) and direct aspiration of the thrombus using the ADAPT (A Direct Aspiration First-Pass Thrombectomy) technique through a large-bore aspiration catheter are the first-line treatment options for MT. Since not all ICAS patients had the microcatheter first-pass effect<sup>15</sup>, the time of the immediate recanalization after the passage of the microcatheter or the time to successful recanalization on the first image after MT was defined as the time of recanalization. ICAS was defined as significant fixed focal stenosis at the occlusion site, which was evident on the final angiographic assessment or observed during MT. Significant stenosis was defined as degree of fixed stenosis  $>70\%$ , or any degree of fixed stenosis with either flow and perfusion impairment on angiography or an evident tendency toward reocclusion after treatment and stent retrieval<sup>7</sup>. For patients with occlusion caused by significant stenosis, we observed blood flow after MT for 30 min. If the reocclusion did not recur, no stent was implanted, and the patient received standard antiplatelet therapy after the operation. If the blood flow was not maintained after 30 min of observation, angioplasty or stenting was given. For the PTAS group patients, balloon angioplasty was first attempted. If the stenosis rate after balloon angioplasty was still  $>70\%$  or blood flow could not be maintained, stenting was performed<sup>12</sup>. For stenting, Solitaire (Ev3 Inc., USA) or Apollo stent (MicroPort®, China) was used for intracranial arteries. The Solitaire AB/FR device is a



**Fig. 2.** Preoperative and postoperative angiography between the PTAS and the non-PTAS groups

A and B indicate stenting and nonstenting of the intracranial artery, respectively; Both A1 and B1 indicate preoperative angiography (all show vascular occlusion). A2 and B2 indicate the presence of ICAS after thrombectomy. A3 demonstrates mild focal stenosis in the non-PTAS group. B3 indicates no obvious stenosis after angioplasty or stenting.

laser-cut, self-expanding, split-design, closed-cell nitinol stent device. As a detachable version, it is available with a diameter of 4 mm (length, 15 or 20 mm) or 6 mm (length, 20 or 30 mm) and is delivered through a 0.021- or 0.027-in microcatheter. The Apollo stent is a balloon-expandable stent delivered through a sprinter rapid exchange balloon dilatation catheter. The stent is delivered to the occlusion site together with the balloon. After the balloon is pressurized, the stent is released to unblock the occluded vessel. DSA images before and after vascular recanalization in patients in the PTAS and non-PTAS groups are presented in **Fig. 2**. Recanalization was evaluated with the modified Thrombolysis in Cerebral Infarction (mTICI) grade, which was defined as successful vascular recanalization in grade 2b/3<sup>16</sup>. Patients in the two groups were treated with tirofiban. When using tirofiban, a loading dose of 0.4  $\mu\text{g}/(\text{kg}\cdot\text{min})$  was intravenously administered for 30 min, and then 0.1  $\mu\text{g}/(\text{kg}\cdot\text{min})$  was intravenously infused for 24 h<sup>17, 18</sup>. To prevent the occurrence of hyperperfusion syndrome in patients with successful reperfusion following MT, postoperative blood pressure should be controlled below 180/105 mmHg according to the guideline recommendations. When intracranial hemorrhage was ruled out by brain CT examination 24 h after operation, clopidogrel (75 mg/d) and aspirin (100 mg/d) were given for 90 days to patients with stenting. Patients without stenting were treated with aspirin (100 mg/d) or clopidogrel (75

mg/d) alone for non-cardiac embolism. Furthermore, dual antiplatelet therapy was used to overlap with tirofiban therapy for 4 h. Transcranial Doppler (TCD) or cerebral CTA/MRA examinations were routinely performed 24–48 h after surgery to determine whether there was reocclusion.

## Outcome Assessment

### Primary Outcome

The primary outcome was good functional outcome at 90 days (mRS0-2). Outcome data were obtained by telephone interviews conducted by local trained neurologists. The mRS score of 0–2 was defined as good prognosis<sup>19)</sup>.

### Secondary Outcomes

Secondary outcomes were as follows: 90-day mRS score; 7-day NIHSS score; any intracranial hemorrhage at 24 h, symptomatic intracranial hemorrhage (sICH); reocclusion; and early neurological deterioration 24 h after surgery as well as 90-day mortality. Intracranial hemorrhage was measured by dual-energy CT, and postoperative occlusion was evaluated by TCD. If the TCD detecting blood flow was poor, we chose CTA or MRA to confirm the vascular occlusion. Intracranial hemorrhage was regarded as symptomatic (sICH) if the patient's NIHSS increased to  $\geq 4$  and there were no other evident causes for the increased NIHSS. The CT scan time was 22–36 h after treatment<sup>20)</sup>. Early neurological deterioration (END) was defined as NIHSS at 24 h increased by more than 4 points from baseline<sup>21)</sup>. The main causes of END include ICH, reocclusion, infarct expansion, or undetermined causes.

### Statistical Analysis

We used SPSS 23.0 for the statistical analysis of the datasets. Data were expressed as mean  $\pm$  standard deviation (SD) or median (interquartile range, IQR). Student's *t*-test or the Mann–Whitney *U* test was used for continuous variables data and  $\chi^2$  test or Fisher's exact test for categorical variable data. Multivariate regression analysis was used to eliminate the influence of confounding factors. For continuous data, such as NIHSS, we used multiple linear regression to obtain the effect value. For categorical data, such as the rate of good outcome at 90 days (mRS0-2) and the rate of neurological improvement at 24 h, we used logistic regression to obtain the odds ratio (OR) values following adjustment for age, gender, initial NIHSS, occluded artery, anesthesia, treatment with intravenous alteplase, and postoperative application of tirofiban. In addition, for 90-day mRS scores, a

multivariable ordinal logistic regression was employed to obtain common OR value. Variables with  $P < 0.2$  in the univariate analysis were included in the regression model to determine the risk factors for the 90-day prognosis.

## Results

### Baseline Characteristics

A total of 184 eligible patients were enrolled in this study; 64 patients in the PTAS group, with an average age of 61.1 years, and 120 patients in the non-PTAS group, with an average age of 62.5 years. The NIHSSs were 15 (12–18) in the PTAS group and 15.5 (11–19) in the non-PTAS group. In addition, the ASPECT scores were 9 (8–10) in the PTAS group and 9 (7–10) in the non-PTAS group. The percentages of patients who received IVT were 45.3% (29/64) and 38.3% (46/120), respectively. The onset times of puncture were 314 and 328 min in the two respective groups, whereas the onset times of recanalization were 421 and 420 min. The proportion of wake-up stroke accounted for 15.6% and 22.5% in the PTAS and the non-PTAS groups, respectively. The proportion of the PTAS group receiving general anesthesia accounted for 48.4%, whereas that of the non-PTAS group was 35.8%. The proportions of postoperative use of tirofiban antiplatelet therapy were 82.8% and 46.7% in the PTAS group and the non-PTAS group, respectively; the difference was statistically significant ( $P < 0.01$ ). The average hospital stay was 6 and 7 days in the two groups, respectively. The specific baseline data is presented in [Table 1](#). In addition, all patients with residual stenosis  $> 70\%$  following MT underwent further intervention. Of the 64 patients who were treated with rescue PTAS, 38 cases (59.4%) underwent only balloon angioplasty, and 26 (40.6%) cases in addition needed stenting.

### Primary Outcome

To compare the efficacy of rescue PTAS vs. non-PTAS, we performed statistical analysis on the data from the two groups. It was found that the good prognosis (mRS 0–2) rate at 90 days was significantly higher in the PTAS group than in the non-PTAS group (51.6% vs. 35%, adjusted OR: 2.11, 95% confidence interval [CI]: 1.22–4.29;  $P = 0.02$ ); see [Fig. 3 and Table 2](#).

### Secondary Outcomes

The 90-day mRS scores were 2 (2–4) and 3 (2–5) in the PTAS and non-PTAS groups, respectively (adjusted OR: 1.42, 95% CI: 0.63–2.71;  $P = 0.21$ ). The 7-day NIHSS scores were significantly lower in

**Table 1.** Comparison of baseline data of patients

| Variable  | PTAS group<br>(n=64) | Non-PTAS group<br>(n=120) | P Value         |
|---|----------------------|---------------------------|-----------------|
| Age — yr  | 61.1 ± 10.3          | 62.5 ± 12.3               | 0.44            |
| Male sex — no. (%)                                | 46 (71.9)            | 83 (69.2)                 | 0.70            |
| Smoking — no. (%)                                 | 30 (46.9)            | 50 (41.7)                 | 0.50            |
| Coronary artery disease— no. (%)                  | 8 (12.5)             | 15 (12.5)                 | 1               |
| Diabetes mellitus — no. (%)                       | 14 (21.9)            | 25 (20.8)                 | 0.87            |
| Hypertension — no. (%)                            | 45 (70.3)            | 80 (66.7)                 | 0.61            |
| — no. (%)   | 18 (28.1)            | 23 (19.2)                 | 0.16            |
| Treatment with intravenous alteplase — no. (%)    | 29 (45.3)            | 46 (38.3)                 | 0.36            |
| Median NIHSS score (IQR)                          | 15 (12-18)           | 15.5 (11-19)              | 0.61            |
| Median ASPECTS score (IQR)                        | 9 (8-10)             | 9 (7-10)                  | 0.65            |
| Onset to puncture time— min (IQR)                 | 314 (242-418)        | 328 (256-414)             | 0.55            |
| Onset to the first recanalization time— min (IQR) | 421 (357-512)        | 420 (340-507)             | 0.85            |
| Site of stenosis and occlusion, n (%)             |                      |                           |                 |
| MCA   | 41 (64.1)            | 72 (60)                   | 0.64            |
| ICA   | 23 (35.9)            | 48 (40)                   |                 |
| Type of stroke onset — no. (%)                    |                      |                           |                 |
| On awakening                                      | 10 (15.6)            | 27 (22.5)                 | 0.27            |
| Unwitnessed stroke                                | 3 (4.7)              | 5 (4.2)                   | 0.87            |
| Witnessed stroke                                  | 51 (79.7)            | 88 (73.3)                 | 0.34            |
| General anesthesia                                | 31 (48.4)            | 43 (35.8)                 | 0.10            |
| Treated with tirofiban                            | 53 (82.8)            | 56 (46.7)                 | <i>P</i> < 0.01 |
| Score on mTICI — no. (%)                          |                      |                           |                 |
| 2b  | 35 (54.7)            | 63 (52.5)                 | 0.78            |
| 3   | 29 (45.3)            | 57 (47.5)                 |                 |
| ICU hospitalization days                          | 6 (3-12)             | 7 (2-13)                  | 0.89            |

Abbreviations: IQR=interquartile range; ASPECTS=Alberta Stroke Program Early CT Score; NIHSS=National Institutes of Health Stroke Scale; ICA=Internal Carotid Artery; MCA=Middle Cerebral Artery; mTICI=Modified Thrombolysis in Cerebral Infarction. Data is expressed as number (proportions), mean ± SD, or median (quartiles).

the PTAS group than in the non-PTAS group (6 (3–12.75) vs. 10 (4–16); adjusted OR: 3.26, 95% CI: 1.25–7.87; *P*=0.04); see [Table 2](#).

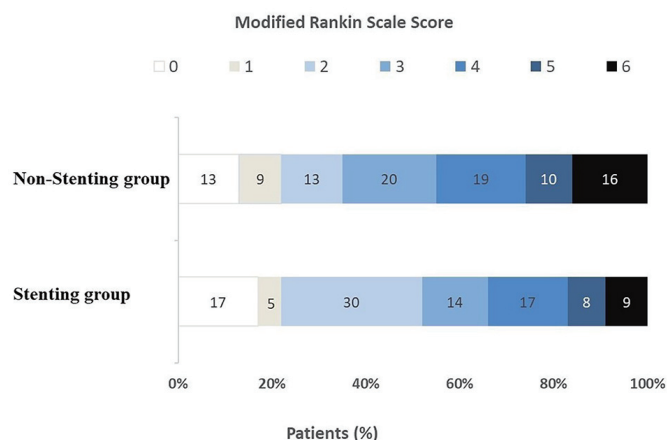
### Safety Outcomes

Safety analysis of data from both study groups revealed that postoperative reocclusion occurred in 4 patients (6.3%) in the PTAS group and 22 patients (17.5%) in the non-PTAS group. These differences were statistically significant (adjusted OR: 0.23, 95% CI: 0.07–0.81; *P*=0.03). In addition, the incidence rates of END in the PTAS and non-PTAS groups were 7.8% and 21.7%, respectively. There were five END cases (5/64) in the PTAS group, including three cases (3/64) with ICH, one case (1/64) with reocclusion, and one case (1/64) with an undetermined cause. In the non-PTAS group, there were 19 END cases (19/120), including 4 cases (4/120) with ICH, 6 cases (6/120) with reocclusion, 5 cases with infarct expansion (5/120), and 4 cases

(4/120) with undetermined causes. This suggested that the incidence of END in the PTAS group was significantly lower than that in the non-PTAS group (adjusted OR: 0.25, 95% CI: 0.05–0.81, *P*=0.02). However, there was no significant difference in the incidence of sICH and any intracranial hemorrhage between the PTAS and non-PTAS groups (*P*>0.05). In addition, a non-significant decrease in mortality in the PTAS group compared with the non-PTAS group was observed (9.4% vs. 15.8%, adjusted OR: 2.75, 95% CI: 0.52–17.28; *P*=0.31); see [Table 2](#).

### Discussion

This study found that rescue intracranial balloon angioplasty or stenting after MT produces a better prognosis at 90 days, including a lower rate of END, lower 7-day NIHSS, and a lower risk of reocclusion following surgery compared with non-PTAS patients. Emergency rescue balloon angioplasty or stenting after



**Fig. 3.** Modified Rankin scale score distribution ratio

The score is divided into 7 grades ranging from 0 to 6. Grade 0: No symptoms; Grade 1: Although there are symptoms, there is no obvious dysfunction (can complete daily work and life); Grade 2: Mild disability, unable to complete all activities before the illness, but able to self-care; Grade 3: Moderately disabled, needs some help, but the patient remains ambulant; Grade 4: Moderately severe disabled, unable to walk independently, unable to meet their own needs without help from others; Grade 5: Severely disabled, requiring continuous care and attention; Grade 6: Death. The results showed the good prognosis (mRS0-2) rate at 90 days was significantly higher in the PTAS group than the non-PTAS group (51.6% vs. 35.0%, adjusted OR: 2.11, 95% CI: 1.22–4.29;  $P=0.02$ ), and 90-day mRS scores were 2 (2–4) and 3 (2–5) in the PTAS and non-PTAS groups, respectively (adjusted OR:1.42, 95% CI: 0.63–2.71;  $P=0.21$ ).

**Table 2.** Primary outcome and Secondary outcomes

| Outcomes                              | PTAS group<br>(n=64) | Non-PTAS group<br>(n=120) | Adjusted OR <sup>a</sup><br>(95%CI) | P Value |
|---------------------------------------|----------------------|---------------------------|-------------------------------------|---------|
| <b>Primary outcome</b>                |                      |                           |                                     |         |
| mRS 0-2 at 90 days — no. (%)          | 33 (51.6)            | 42 (35.0)                 | 2.11 (1.22-4.29)                    | 0.02    |
| <b>Secondary outcomes</b>             |                      |                           |                                     |         |
| mRS score (IQR) at 90 days            | 2 (2-4)              | 3 (2-5)                   | 1.42 (0.63-2.71)                    | 0.21    |
| NIHSS score at 7 day                  | 6 (3-12.75)          | 10 (4-16)                 | 3.26 (1.25-7.87)                    | 0.04    |
| <b>Safety outcomes — no. (%)</b>      |                      |                           |                                     |         |
| Reocclusion at 24 hr                  | 4 (6.3)              | 22 (17.5)                 | 0.36 (0.05-0.77)                    | 0.02    |
| END at 24 hr                          | 5 (7.8)              | 19 (21.7)                 | 0.25 (0.05-0.81)                    | 0.02    |
| sICH at 24 hr                         | 5 (7.8)              | 8 (6.7)                   | 1.51 (0.42-7.18)                    | 0.60    |
| Any intracerebral hemorrhage at 24 hr | 25 (39.1)            | 36 (30)                   | 2.15 (0.80-5.21)                    | 0.21    |
| Death at 90 days                      | 6 (9.4)              | 19 (15.8)                 | 2.89 (0.45-18.55)                   | 0.26    |

Data is expressed as number (proportions), proportions, or median (quartiles).

Abbreviations: mRS=modified Rankin scale; NIHSS=National Institutes of Health Stroke Scale; END=Early neurologic deterioration; sICH=Symptomatic intracranial hemorrhage.

<sup>a</sup>Adjusted for age, gender, initial NIHSS score, occluded artery, anesthesia, treatment with intravenous alteplase, and postoperative application of tirofiban.

MT was an independent protective factor for a good prognosis at 90 days for AIS patients.

Our retrospective study screened a total of 460 patients with LVO, and ultimately, 184 patients with ICAS were included in the analysis. These numbers suggest a very high rate of intracranial artery stenosis, which is significantly more than that reported in other studies. Notably, however, all included patients were Asian, and since ICAS is the most common cause of

ischemic stroke in this population, the differences seem to be likely related to ethnicity<sup>10, 22</sup>. A prospective trial evaluating the use of angioplasty in patients with AIS showed that angioplasty with or without stenting was safe, with a high rate of revascularization and good prognosis<sup>23</sup>. Yang *et al.* reported that primary angioplasty and stenting may be superior to thrombectomy for acute atherosclerotic LVO<sup>24</sup>. In this study, we divided the endovascular

therapy after MT into rescue PTAS and non-PTAS groups and found that the good prognosis ratios at 90 days were 51.6% and 35%, respectively. These findings were similar to the results of a recent meta-analysis of Rescue Intracranial Stenting After Failed Mechanical Haemobectomy for AIS (stents group 48.5% vs. without stents group 19.7%)<sup>25</sup>. However, stenting remains controversial. A recent meta-analysis included a total of 1639 patients, of which 450 were in the ICAS-LVO group treated with intracranial angioplasty and/or stenting and 1189 were in the non-ICAS-LVO group. The results showed that intracranial angioplasty and/or stenting did not improve favorable functional outcome in patients with underlying ICAS-LVO. Different outcomes may be attributed to different inclusion criteria and control settings<sup>26</sup>. Previous studies divided the LVO patients into the ICAS-LVO and non-ICAS-LVO groups according to the disease pathogenesis<sup>27-30</sup>, whereas our study included all severe ICAS patients. Furthermore, the patients were divided into the PTAS and non-PTAS groups, according to whether they received rescue angioplasty or stenting. Therefore, previous studies have only addressed the differences in the prognosis of patients with two different causes of LVO and notably, because the control group is not comparable, cannot answer the question of whether or not rescue angioplasty or stenting is more beneficial for ICAS patients. In addition, Kang in 2016<sup>2</sup> also conducted a similar study to ours involving 140 cases, in which all enrolled patients with LVO were attributed as severe ICAS. However, the key differences were that the two interventions were performed at two different centers (intracranial angioplasty with or without stenting and intra-arterial infusion of a glycoprotein IIb/IIIa inhibitor). And more importantly, Kang's study did not determine statistical differences in symptomatic hemorrhage, 3-month modified Rankin scale of 0–2, and mortality between the two interventions. Given that the patients were from the two centers, it is possible that the baseline differences might have affected the results of this study. In contrast, our study involved patients from a single center with the same screening criteria. More importantly, we did not administer angioplasty or stenting to all patients with severe stenosis. Rescue angioplasty or stenting was only given when blood flow could not be maintained after 30 min of observation during endovascular treatment, which may be more in line with the principles of medical ethics.

END is a common problem after IVT in AIS with an incidence of 14%. This is thought to be related to reocclusion and hemorrhagic transformation<sup>31</sup>. In addition, MT also has the same problem.

Previously, the DAWN and DEFUSE 3 trials reported that the incidence rates of END were 14% and 9% respectively<sup>6, 32</sup>. Goyal's study found that END was closely related to poor prognosis following AIS<sup>33</sup>. Furthermore, our previous study found that 44 of 614 patients with AIS with successful recanalization after MT experienced reocclusion within 24 h, which confirmed that the prognosis of reocclusion after MT was poor<sup>10</sup>. Therefore, prevention of reocclusion and hemorrhagic transformation may be a key to END. In this study, the main causes of END include ICH, reocclusion, infarct expansion, and undetermined causes. Our study found that the END rate after emergency angioplasty or stenting was significantly lower than that of the non-PTAS group (7.8% vs. 21.7%), which strongly suggests that emergency or angioplasty stenting is necessary for stroke patients with LVO of ICAS.

Finally, we must consider the safety concerns associated with angioplasty or stenting procedures. Angioplasty or stenting may cause hyperperfusion or hemorrhagic complications in the distal vascular region. Stenting may require glycoprotein IIb/IIIa antagonist to prevent in-stent thrombosis, but glycoprotein IIb/IIIa antagonists may increase the rate of sICH. A recent meta-analysis of 509 patients that received stenting in 33 studies revealed that the incidence of sICH was 7%<sup>34</sup>. In addition, Baek and Chang's studies also confirmed that sICH did not differ between the stenting and the nonstenting groups<sup>13, 14</sup>. In our study, although the application rate of tirofiban in the PTAS group was significantly higher than that in the non-PTAS group (82.8% vs. 46.7%), no significant difference in the incidence of sICH between the PTAS and non-PTAS groups and no increase in mortality were observed. In addition, Kim *et al.* published a study in 2020 involving local tirofiban infusion for remnant stenosis in LVO. Patients receiving rescue treatment involving tirofiban infusion had higher rates of favorable outcomes and less serious hemorrhagic complications than those who did not receive tirofiban<sup>35</sup>. Therefore, the better clinical results in the PTAS group may be attributed to the synergistic effect of angioplasty or stenting combined with tirofiban treatment. Additionally, we have to consider that not only the lack of tirofiban but also the lack of dual antiplatelet therapy, including loading dose, might affect the clinical outcome in the non-PTAS group.

### Study Limitations

This is a single-center retrospective study with inherent selection and patient population bias. Notably, this study also lacks objective criteria for the

accurate judgment of atherosclerotic stenosis, and only DSA angiography was used to measure vascular stenosis. Furthermore, vascular lumen imaging may underestimate the severity of intracranial atherosclerotic diseases of the vessel wall, especially for non-stenotic lesions. Searching for vascular lesion sites solely based on the degree of stenosis often leads to misdiagnosis or missed diagnosis. In future studies, it may be necessary to use intracranial vessel wall MRI technology to investigate atherosclerotic stenosis and plaque composition at the stenosis site to improve the accuracy of the study results. In addition, the treatment decision (angioplasty and stenting vs. no-PTAS) was left up to the neurointerventionalist, which may be a source of selection bias.

### Conclusions

This retrospective analysis study showed that rescue intracranial angioplasty or stenting following MT significantly improved the patient's clinical outcome at 90 days, improved the neurological function score at 7 days, and reduced the incidence of 24-h reocclusion. We also found that END was reduced for patients with acute anterior circulation atherosclerotic occlusion, and there was no increased incidence of intracranial hemorrhage or mortality. A prospective, multicenter, large sample randomized controlled trial should be conducted to further evaluate the efficacy and safety of emergency rescue intracranial angioplasty or stenting following MT.

### Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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### Conflict of Interest

There are no conflicts to report.

### Ethics Statement

This study was approved by the ethics committee of Xuanwu Hospital, Capital Medical University. The

participants provided their written informed consent to participate in this study.

### References

- 1) Banerjee C, Chimowitz MI. Stroke caused by atherosclerosis of the major intracranial arteries. *Circ Res*, 2017; 120: 502-513
- 2) Kang DH, Yoon W, Kim SK, Baek BH, Lee YY, Kim YW, Kim YS, Hwang YH, Kim JT, Park MS. Endovascular treatment for emergent large vessel occlusion due to severe intracranial atherosclerotic stenosis. *J Neurosurg*, 2018; 1: 1-8
- 3) Lovett J K, Coull A J, Rothwell P M. Early risk of recurrence by subtype of ischemic stroke in population-based incidence studies. *Neurology*, 2014; 62: 569-573
- 4) Powers WJ, Derdeyn CP, Biller J, Coffey CS, Hoh BL, Jauch EC, Johnston KC, Johnston SC, Khalessi AA, Kidwell CS, Meschia JF, Ovbiagele B, Yavagal DR; American Heart Association Stroke Council. 2015 American Heart Association/American Stroke Association Focused Update of the 2013 Guidelines for the Early Management of Patients With Acute Ischemic Stroke Regarding Endovascular Treatment: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke*, 2015; 46: 3020-3035
- 5) Wahlgren N, Moreira T, Michel P, Steiner T, Jansen O, Cognard C, Mattle HP, van Zwam W, Holmin S, Tatlisumak T, Petersson J, Caso V, Hacke W, Mazighi M, Arnold M, Fischer U, Szikora I, Pierot L, Fiehler J, Gralla J, Fazekas F, Lees KR; ESO-KSU, ESO, ESMINT, ESNR and EAN. Mechanical thrombectomy in acute ischemic stroke: Consensus statement by ESO-Karolinska Stroke Update 2014/2015, supported by ESO, ESMINT, ESNR and EAN. *Int J Stroke*, 2016; 11: 134-147
- 6) Nogueira RG, Jadhav AP, Haussen DC, Bonafé A, Budzik RF, Bhuva P, Yavagal DR, Ribo M, Cognard C, Hanel RA, Sila CA, Hassan AE, Millan M, Levy EI, Mitchell P, Chen M, English JD, Shah QA, Silver FL, Pereira VM, Mehta BP, Baxter BW, Abraham MG, Cardona P, Veznedaroglu E, Hellinger FR, Feng L, Kirmani JF, Lopes DK, Jankowitz BT, Frankel MR, Costalat V, Vora NA, Yoo AJ, Malik AM, Furlan AJ, Rubiera M, Aghaebrahim A, Olivot JM, Tekle WG, Shields R, Graves T, Lewis RJ, Smith WS, Liebeskind DS, Saver JL, Jovin TG; DAWN Trial Investigators. Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct. *N Engl J Med*, 2018; 378: 11-21
- 7) Lee JS, Hong JM, Lee KS, Suh HI, Choi JW, Kim SY. Primary stent retrieval for acute intracranial large artery occlusion due to atherosclerotic disease. *J Stroke*, 2016; 18: 96-101
- 8) Tsang ACO, Orru E, Klostranec JM, Yang IH, Lau KK, Tsang FCP, Lui WM, Pereira VM, Krings T. Thrombectomy Outcomes of Intracranial Atherosclerosis-Related Occlusions. *Stroke*, 2019; 50: 1460-1466
- 9) Heo JH, Lee KY, Kim SH, Kim DI. Immediate reocclusion following a successful thrombolysis in acute stroke: a pilot study. *Neurology*, 2014; 60: 1684-1687



- 10) Li W, Ding J, Sui X, Qi Z, Wu L, Sun C, Ji K, Ma Q, Ji X, Liu KJ. Prognosis and risk factors for reocclusion after mechanical thrombectomy. *Ann Clin Transl Neurol*, 2020; 7: 420-428
- 11) Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, Jauch EC, Kidwell CS, Leslie-Mazwi TM, Ovbiagele B, Scott PA, Sheth KN, Southerland AM, Summers DV, Tirschwell DL; American Heart Association Stroke Council. 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *J Vasc Surg*, 2018; 267: 1934-1934
- 12) Li H, Zhang Y, Zhang L, Li Z, Xing P, Zhang Y, Hong B, Yang P, Liu J. Endovascular Treatment of Acute Ischemic Stroke Due to Intracranial Atherosclerotic Large Vessel Occlusion: A Systematic Review. *Clin Neuroradiol*, 2020; 30: 777-787
- 13) Baek JH, Kim BM, Kim DJ, Heo JH, Nam HS, Yoo J. Stenting as a Rescue Treatment After Failure of Mechanical Thrombectomy for Anterior Circulation Large Artery Occlusion. *Stroke*, 2016; 47: 2360-2363
- 14) Chang Y, Kim BM, Bang OY, Baek JH, Heo JH, Nam HS, Kim YD, Yoo J, Kim DJ, Jeon P, Baik SK, Suh SH, Lee KY, Kwak HS, Roh HG, Lee YJ, Kim SH, Ryu CW, Ihn YK, Kim B, Jeon HJ, Kim JW, Byun JS, Suh S, Park JJ, Lee WJ, Roh J, Shin BS, Kim JM. Rescue Stenting for Failed Mechanical Thrombectomy in Acute Ischemic Stroke: A Multicenter Experience. *Stroke*, 2018; 49: 958-964
- 15) Yi TY, Chen WH, Wu YM, Zhang MF, Zhan AL, Chen YH, Wu ZZ, Shi YC, Chen BL. Microcatheter "First-Pass Effect" Predicts Acute Intracranial Artery Atherosclerotic Disease-Related Occlusion. *Neurosurgery*, 2019; 84: 1296-1305
- 16) Zaidat OO, Yoo AJ, Khatri P, Tomsick TA, von Kummer R, Saver JL, Marks MP, Prabhakaran S, Kallmes DF, Fitzsimmons BF, Mocco J, Wardlaw JM, Barnwell SL, Jovin TG, Linfante I, Siddiqui AH, Alexander MJ, Hirsch JA, Wintermark M, Albers G, Woo HH, Heck DV, Lev M, Aviv R, Hacke W, Warach S, Broderick J, Derdeyn CP, Furlan A, Nogueira RG, Yavagal DR, Goyal M, Demchuk AM, Bendzus M, Liebeskind DS; Cerebral Angiographic Revascularization Grading (CARG) Collaborators; STIR Revascularization working group; STIR Thrombolysis in Cerebral Infarction (TICI) Task Force. Recommendations on angiographic revascularization grading standards for acute ischemic stroke: a consensus statement. *Stroke*, 2013; 44: 2650-2663
- 17) Yang M, Huo X, Gao F, Wang A, Ma N, Shi H, Chen W, Wang S, Wang Y, Miao Z. Low-dose rescue tirofiban in mechanical thrombectomy for acute cerebral large-artery occlusion. *Eur J Neurol*, 2020; 27: 1056-1061
- 18) Fu Z, Xu C, Liu X, Wang Z, Gao L. Safety and Efficacy of Tirofiban in Acute Ischemic Stroke Patients Receiving Endovascular Treatment: A Meta-Analysis. *Cerebrovasc Dis*, 2020; 49: 442-450
- 19) Newcommon NJ, Green TL, Haley E, Cooke T, Hill MD. Improving the assessment of outcomes in stroke: use of a structured interview to assign grades on the modified Rankin Scale. *Stroke*, 2003; 34: 377-378
- 20) Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos A, Guidetti D, Larrue V, Lees KR, Medeghri Z, Machnig T, Schneider D, von Kummer R, Wahlgren N, Toni D; ECASS Investigators. (ECASS III)Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *N Engl J Med*, 2008; 359: 1317-1329
- 21) Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, Schonewille WJ, Vos JA, Nederkoorn PJ, Wermer MJ, van Walderveen MA, Staals J, Hofmeijer J, van Oostayen JA, Lycklama à Nijeholt GJ, Boiten J, Brouwer PA, Emmer BJ, de Bruijn SF, van Dijk LC, Kappelle LJ, Lo RH, van Dijk EJ, de Vries J, de Kort PL, van Rooij WJ, van den Berg JS, van Hasselt BA, Arden LA, Dallinga RJ, Visser MC, Bot JC, Vroomen PC, Eshghi O, Schreuder TH, Heijboer RJ, Keizer K, Tielbeek AV, den Hertog HM, Gerrits DG, van den Berg-Vos RM, Karas GB, Steyerberg EW, Flach HZ, Marquering HA, Sprengers ME, Jenniskens SF, Beenen LF, van den Berg R, Koudstaal PJ, van Zwam WH, Roos YB, van der Lugt A, van Oostenbrugge RJ, Majoie CB, Dippel DW; MR CLEAN Investigators. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med*, 2015; 372: 11-20
- 22) Yang W, Zhang Y, Li Z, Zhang L, Li H, Hua W, Zhang H, Feng M, Shen H, Xing P, Chen Q, Zhang Y, Yang P, Liu J. Differences in Safety and Efficacy of Endovascular Treatment for Acute Ischemic Stroke. *Clinical Neuroradiology*, 2021; 31: 457-464
- 23) Yoon W, Kim SK, Park MS, Kim BC, Kang HK. Endovascular treatment and the outcomes of atherosclerotic intracranial stenosis in patients with hyperacute stroke. *Neurosurgery*, 2015; 76: 680-686
- 24) Yang D, Lin M, Wang S, Wang H, Hao Y, Zi W, Lv P, Zheng D, Xiao G, Xu G, Xiong Y, Liu X; ACTUAL Investigators. Primary angioplasty and stenting may be superior to thrombectomy for acute atherosclerotic large-artery occlusion. *Interv Neuroradiol*, 2018; 24: 412-420
- 25) Maingard J, Phan K, Lamanna A, Kok HK, Barras CD, Russell J, Hirsch JA, Chandra RV, Thijs V, Brooks M, Asadi H. Rescue Intracranial Stenting After Failed Mechanical Thrombectomy for Acute Ischemic Stroke: A Systematic Review and Meta-Analysis. *World Neurosurg*, 2019; 132: e235-e245
- 26) Zhang P, Xing Y, Li H, Yao Q, Shen J, Liu Y, Wei Y, Guo Y. Efficacy and safety of rescue angioplasty and/or stenting for acute large artery occlusion with underlying intracranial atherosclerosis: A systematic review and meta-analysis. *Clin Neurol Neurosurg*, 2021; 203: 106538
- 27) Lee JS, Hong JM, Lee KS, Suh HI, Demchuk AM, Hwang YH, Kim BM, Kim JS. Endovascular therapy of cerebral arterial occlusions: intracranial atherosclerosis versus embolism. *J Stroke Cerebrovasc Dis*, 2015; 24: 2074-2080
- 28) Yoon W, Kim SK, Park MS, Kim BC, Kang HK. Endovascular treatment and the outcomes of atherosclerotic intracranial stenosis in patients with hyperacute stroke. *Neurosurgery*, 2015; 76: 680-686;
- 29) Lee JS, Lee SJ, Yoo JS, Hong JH, Kim CH, Kim YW, Kang DH, Kim YS, Hong JM, Choi JW, Ovbiagele B,

- Demchuk AM, Sohn SI, Hwang YH. Prognosis of acute intracranial atherosclerosis-related occlusion after endovascular treatment. *J Stroke*, 2018; 20: 394-403
- 30) Lee YY, Yoon W, Kim SK, Baek BH, Kim GS, Kim JT, Park MS. Acute basilar artery occlusion: differences in characteristics and outcomes after endovascular therapy between patients with and without underlying severe atherosclerotic stenosis. *AJNR Am J Neuroradiol*, 2017; 38: 1600-1604
- 31) Seners P, Turc G, Oppenheim C, Baron JC. Incidence, causes and predictors of neurological deterioration occurring within 24 h following acute ischaemic stroke: a systematic review with pathophysiological implications. *J Neurol Neurosurg Psychiatry*, 2015; 86: 87-94
- 32) Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, McTaggart RA, Torbey MT, Kim-Tenser M, Leslie-Mazwi T, Sarraj A, Kasner SE, Ansari SA, Yeatts SD, Hamilton S, Mlynash M, Heit JJ, Zaharchuk G, Kim S, Carrozzella J, Palesch YY, Demchuk AM, Bammer R, Lavori PW, Broderick JP, Lansberg MG; DEFUSE 3 Investigators. Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging. *N Engl J Med*, 2018; 378: 708-718
- 33) Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, Dávalos A, Majoie CB, van der Lugt A, de Miquel MA, Donnan GA, Roos YB, Bonafé A, Jahan R, Diener HC, van den Berg LA, Levy EI, Berkhemer OA, Pereira VM, Rempel J, Millán M, Davis SM, Roy D, Thornton J, Román LS, Ribó M, Beumer D, Stouch B, Brown S, Campbell BC, van Oostenbrugge RJ, Saver JL, Hill MD, Jovin TG; HERMES collaborators. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*, 2016; 387: 1723-1731
- 34) Wilson MP, Murad MH, Krings T, Pereira VM, O'Kelly C, Rempel J, Hilditch CA, Brinjikji W. Management of tandem occlusions in acute ischemic stroke - intracranial versus extracranial first and extracranial stenting versus angioplasty alone: a systematic review and meta-analysis. *J Neurointerv Surg*, 2018; 10: 721-728
- 35) Kim YW, Sohn SI, Yoo J, Hong JH, Kim CH, Kang DH, Kim YS, Lee SJ, Hong JM, Choi JW, Hwang YH, Lee JS. Local tirofiban infusion for remnant stenosis in large vessel occlusion: tirofiban ASSIST study. *BMC Neurology*, 2020; 20: 284