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Outcomes of late endovascular recanalization for symptomatic non-acute atherosclerotic intracranial large artery occlusion

Yin-Dan Yao[a,b,c], Ao-Fei Liu[b], Han-Cheng Qiu[b], Ji Zhou[b], Chen Li[b], Qi Wang[b], Jin Lv[d], Wei-Jian Jiang[a,b,*]

[a] The PLA Rocket Force Characteristic Medical Center, the Teaching Hospital of Soochow University, Beijing, China
[b] Department of Vascular Neurosurgery, New Era Stroke Care and Research Institute, The PLA Rocket Force Characteristic Medical Center, Beijing, China
[c] Department of Neurology, Hwa Mei Hospital, University of Chinese Academy of Sciences, Ningbo, Zhejiang, China
[d] Department of Central Laboratory, the PLA Rocket Force Characteristic Medical Center, Beijing, China

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ABSTRACT

Objectives: The optimal treatment of symptomatic non-acute atherosclerotic intracranial large artery occlusion (ILAO) beyond 24 h from onset remains uncertain. We investigate the outcomes of late endovascular recanalization for symptomatic non-acute atherosclerotic ILAO.

Patients and methods: From September 2013 to July 2018, with safety as the first principle, late endovascular recanalization for symptomatic non-acute atherosclerotic ILAO beyond 24 h from onset was attempted in 32 consecutive patients. Primary safety outcome was any stroke or death within 30 days. Primary efficacy outcome were functional independence at 90 days.

Results: The median time from imaging-documented occlusion to treatment was 25.5 days (interquartile range: 10.5–36.5) for all patients. Technical success in recanalization was achieved in 17 patients (53.1%, 17/32). The 30-day rate of any stroke or death was 5.9% (1/17) in the recanalized group versus 6.7% (1/15) in the failure group (P = 0.927). The rate of functional independence at 90 days (70.5%, 12/17) was increased significantly as compared with that before operation (23.5%, 4/17) in the recanalized group (P = 0.015). The rate of functional independence at 90 days (66.7%, 10/15) was not different from that before operation (66.7%,10/15) in the failure group (P = 1.00). The median score reduction in mRS from baseline at 90 days was 1.0 (interquartile range: 1.0–2.0) in the recanalized group versus 0 (interquartile range: 0.0-0.0) in the failure group (P < 0.001).

Conclusion: For carefully selected patients with symptomatic non-acute atherosclerotic ILAO beyond 24 h from onset, late endovascular recanalization is technically feasible. The periprocedural safety of late endovascular recanalization is acceptable. Successful recanalization may effectively improve the degree of disability in such patients. However, it should be emphasized that revascularization of non-acute ILAO is a high risk procedure, which should only be performed by experienced operators with safety as the first principle.

1. Introduction

Large artery intracranial occlusive disease has emerged as the most common cause of stroke worldwide and is associated with high risk of stroke recurrence and poor stroke outcome [1,2]. Non-acute atherosclerotic intracranial large artery occlusion (ILAO) is the special type of large artery intracranial occlusive diseases, and remains a common medical dilemma. The Chinese Intracranial Atherosclerosis Study have shown that ischemic stroke patients with ILAO have a high incidence of recurrent stroke, about 7.27 % a year [3]. In particular, non-acute ILAO with hemodynamic compromise or poor collateral flow are at higher risk for subsequent stroke [4,5]. In addition, non-acute ILAO may also affect cognitive function and lead to poor quality of life [6,7]. Currently, the therapeutic time window for the treatment of acute ischemic stroke due to large artery occlusion using endovascular thrombectomy has expanded up to 24 h from time last known well if patients are carefully selected [8,9]. However, The optimal treatment of non-acute atherosclerotic ILAO beyond 24 h from onset remains unclear. There were some small-sample case-series studies have reported endovascular recanalization appeared to be safe and efficient for non-acute ILAO [10–15]. However, conflicting results and heterogeneity of outcome were presented regarding recanalization. The purpose of this study was

* Corresponding author at: The PLA Rocket Force Characteristic Medical Center, the Teaching Hospital of Soochow University, Beijing, China. Department of Vascular Neurosurgery, New Era Stroke Care and Research Institute, the PLA Rocket Force Characteristic Medical Center, Beijing, China.
E-mail address: jiangweijian2018@163.com (W.-J. Jiang).

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to investigate the outcomes of late endovascular recanalization for symptomatic non-acute atherosclerotic ILAO beyond 24 h from onset.

2. Materials and methods

2.1. Patients

In this study, non-acute ILAO was defined as ILAO with a time window of more than 24 h of onset. Inclusion criteria were as follows: age > 18 years; total ILAO were verified by catheter angiography; occlusion sites included: intracranial vertebral artery (ICVA), intracranial internal carotid artery (ICICA), basilar artery (BA), first segment of middle cerebral artery (M1); time from the last qualifying event to endovascular treatment was beyond 24 h, qualifying event was defined as transient ischemic attack (TIA) or ischemic stroke attributable to ILAO; computed tomography (CT) or magnetic resonance (MR) diffusion-weighted imaging (DWI) was performed to identify patients with a small infarct core, small infarct core was defined as an Alberta Stroke Program Early Computed Tomography Score (ASPECTS) or posterior circulation ASPECTS based on CT/DWI of 6 to 10 [16,17]; the collateral flow, which was grade according to the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology Collateral Flow Grading System was ≤ 2 on angiogram [18]; symptoms still progressed or relapsed despite aggressive medical treatment (dual antiplatelet aggregation, lipid lowering therapy, and management of risk factors according to the American Heart Association guidelines [19]); and at least 1 atherosclerotic risk factor (arterial hypertension, diabetes mellitus, hyperlipidemia, and cigarette smoking).

Exclusion criteria included non-atherosclerotic diseases: suspected cerebral vasculitis, arterial dissection, moyamoya disease, and potential source of cardiac embolism; concomitant with intracranial aneurysms proximal or distal to the occlusive artery; any bleeding disorder; known contraindication to heparin, aspirin, clopidogrel, anesthesia, or contrast media; life expectancy < 1 year due to other medical conditions. Between September 2013 and July 2018, 32 consecutive patients with symptomatic non-acute atherosclerotic ILAO underwent selective late endovascular recanalization therapy at our institute. Baseline data and follow-up information of patients were prospectively collected. Written informed consent was obtained from all patients, including for the off-label use of Enterprise stents (Codman & Shurtleff, Raynham, Massachusetts, USA). The study was approved by the institutional ethics committee of the PLA Rocket Force Characteristic Medical Center (KY2013031).

2.2. Endovascular recanalization procedures

All procedures were performed under general anesthesia by an experienced interventional neuroradiologist (W-JJ). Intravenous heparin bolus was given intraoperatively to maintain activated clotting time between 200 s and 250 s. A 6 F guiding catheter (Envoy, Cordis, USA) was then advanced into the distal cervical vertebral or internal carotid artery. Under high-magnification roadmap guidance, with safety as the first principle, an assembly of a microcatheter (Excelsior SL-10, Stryker Neurovascular, Fremont, California, USA) and a microwire (Synchro, Stryker Neurovascular, Fremont, California, USA) was attempted to cross the occluded segment with safety as the first principle. The microwire was shaped by about 30 °, and the assembly was repeatedly tried to search for the true cavity at the occlusion stump. The operation needed to be terminated, if the following conditions occurred: (1) the tip of the microwire entered the subintima, and the microcatheter angiography confirmed vascular dissection; (2) the procedure time exceeded half an hour, and the microwire still failed to pass the occluded segment. If the microwire successfully steered through the occluded segment, then, microcatheter injection confirmed the position distal to occlusion in the distal true lumen. After the microcatheter was removed, an angioplasty balloon catheter (Gateway, Boston Scientific, Natick, Massachusetts, USA) was advanced over the microwire, centered across the lesion, and inflated slowly from the distal to proximal. Based on measurement of the proximal and distal diameters of target vessel as well as the length of the occluded segment after balloon dilation, a self-expandable stent (Enterprise, Codman & Shurtleff, Raynham, Massachusetts, USA) was introduced and deployed. If two or more stents were needed, they were deployed from the distal to proximal. Control angiography was performed to confirm patency and followed by removal of the microwire and guiding catheter. Technical success was determined by recanalization with an Thrombolysis in Cerebral Infarction (TICI) [18] grade of 2b or 3 on postprocedural angiography.

2.3. Periprocedural management and follow-up

Brain DWI/MR perfusion-weighted imaging or CT/CT perfusion, and catheter angiography were performed to evaluate infarct core and collateral compensation. Patients were pretreated with 300 mg aspirin plus 75 mg clopidogrel daily for at least 5 days before the operation. Patients who were not taking clopidogrel at a dose of 75 mg each day for at least 5 days before recanalization treatment were given a 300-mg loading dose of clopidogrel before recanalization treatment. Thromboelastography was used to evaluate platelet reactivity. If the inhibition ratio of either arachidonic acid or ADP was < 50%, indicating a relative resistance to aspirin or clopidogrel, then cilostazol (Zhejiang Otsuka Pharmaceutical Co, Ltd, Shanghai, China) 100 mg twice a day was added for 4 weeks [20]. All patients were maintained on aspirin and clopidogrel for at least 3 months after stenting and then either aspirin or clopidogrel for life. After operation, a patient's blood pressure was maintained at about 80% of baseline level for 3 days to prevent hyperperfusion syndrome with an intravenous ß blocker, calcium channel blocker, or both. Edaravone (Simcere Pharmaceutical Group, Nanjing, China), an oxygen free radical scavenger, was also used intravenously for 3 days. Brain CT immediately after the operation was performed to rule out intracranial hemorrhage. Patients were given 5000 IU Fragmin (Vetter Pharma-Ferrtigung GmbH, Germany) every 12 h subcutaneously for 3 days and monitored until discharge. Atherosclerotic risk factors were managed according to the American Heart Association guidelines [19].

After discharge, they had follow-up visits at 30 and 90 days. Subsequent follow-ups were completed by clinic visits or by telephone until the end of November 2018. Follow-up angiography was scheduled after 6, 12 and 24 months on a voluntary basis or when restenosis was suspected clinically. In-stent restenosis was defined as an angiographically verified > 50 % stenosis and > 20 % absolute luminal loss within the stent or at the edge of the stent in the range of 3 mm. National Institutes of Health Stroke Scale (NIHSS) score and modified Rankin Scale (mRS) score and end point events were independently assessed by stroke neurologists, who assessed daily during hospitalization, and followed up in clinic or by telephone after discharge, discrepancies were settled through consensus.

2.4. Outcome measures

Primary safety outcome was any stroke or death within 30 days. Primary efficacy outcome was functional independence (defined as a score on the mRS of 0–2) at 90 days. Stroke was defined as a focal neurologic deficit persisting longer than 24 h.

2.5. Statistical analysis

All continuous variables were expressed as mean ± SD or median with interquartile range (IQR) each for normal or skewed distribution data. Categorical variables were expressed as numbers and percentages. Independent groups Student t tests, Fisher's Exact tests or Mann-

Table 1
Comparison of baseline characteristics between recanalized and failure groups.

Variable	Recanalized group (N = 17)	Failure group (N = 15)	P value
Age, mean (SD), years	52.9 (10.0)	53.3 (10.4)	0.589
Male, No. (%)	14 (82.4)	10 (66.7)	0.306
Time from image-documented occlusion to treatment, median (IQR), days	17.0 (7.5-28.0)	33.0 (16.0-60.0)	0.033
Preoperative NIHSS, median (IQR)	4.0 (2.0-10.5)	1.0 (0-3.0)	0.016
Preoperative mRS, median (IQR)	3.0 (2.5-4.0)	2.0 (2.0-3.0)	0.006
Preoperative ASPECTS/pc-ASPECTS, median (IQR)	7.0 (6.0-8.0)	8.0 (8.0-10.0)	0.001
Baseline medical history, No. (%)			
Hypertension	12 (70.6)	12 (80.0)	0.539
Diabetes mellitus	4 (23.5)	4 (26.7)	0.838
Hyperlipidemia	8 (47.1)	8 (53.3)	0.723
Smoke	9 (52.9)	6 (40.0)	0.464
Coronary artery disease	2 (11.8)	1 (6.7)	0.621
Previous stroke	3 (17.6)	4 (26.7)	0.538
Occlusion location, No. (%)			0.045
ICICA	4 (12.5)	2 (6.3)	
M1	1 (3.1)	5 (15.6)	
ICVA	7 (21.9)	1 (3.1)	
BA	5 (15.6)	7 (21.9)	

Abbreviations: ASPECTSAlberta Stroke Program Early Computed Tomography Score; BAbasilar artery; IQRinterquartile range; ICICAintracranial internal carotid artery; ICVAintracranial vertebral artery; mRSmodified Rankin scale; M1first segment of the middle cerebral artery; NIHSSNational Institutes of Health Stroke Scale; pc-ASPECTSposterior circulation Acute Stroke Prognosis Early CT score; SDstandard deviation.

Whitney U tests were used according to the studied variables characteristics. Reported probability values were 2-sided, and p values < 0.05 were considered to be statistically significant. All statistical analyses were performed with SPSS 17.0 software (IBM, Armonk, NY, USA).

3. Results

3.1. Patient characteristics

From September 2013 to July 2018, endovascular recanalization was attempted in 32 consecutive non-acute atherosclerotic ILAO patients (24 men; mean age: 52.9 ± 10.1 years). The characteristics and clinical summary of patients in the recanalized and failure group are listed in the Tables 1–2. There were no significant differences in age, gender, and baseline medical history between the two groups. There were a significantly higher preoperative NIHSS, higher preoprerative mRS, lower ASPECTS/pc-ASPECTS, shorter time from image-documented occlusion to treatment, and higher rates of ICVA and ICICA occlusion in the recanalized group as compared to the failure group.

3.2. Periprocedural outcome

Technical success in recanalization was achieved in 17 patients (53.1 %, 17/32). Post-recanalization angiography demonstrated TICI 3 in 16 cases and TICI 2b in 1 case. According to the classification of occlusion sites, the success rate, in descending order, was 87.5 % (7/8) for ICVA, 66.7 % (4/6) for ICICA, 41.7 % (5/12) for BA, and 16.7 % (1/6) for M1. In the recanalized group, two stents or more were used in 3 patients. The average postoperative residual stenosis was 47.8 ± 11.5%. The representative cases are illustrated in Figs. 1–2.

The 30-day rate of any stroke or death was 5.9% (1/17) in the recanalized group as compared with 6.7% (1/15) in the failure group (P = 0.927, Fisher's Exact test) (Table 3). There were one stroke-related death in the recanalized group, and one ischemic stroke in the failure group. Periprocedural operation-related complications included one case of perforation, which resulted in death from subarachnoid hemorrhage in the recanalized group, and one case of acute thrombosis, resulting in asymptomatic reocclusion; and one case of asymptomatic dissection in the failure group.

The median score reduction in mRS from baseline at discharge was 1.0 (IQR: 1.0–2.0) in the recanalized group as compared with 0 (IQR: 0.0-0.0) in the failure group (P = 0.011, Mann-Whitney U test) (Table 3).

3.3. Follow-up outcome

Median duration of clinical follow-up was 39.4 months (IQR, 30.4–45.7) in 32 patients, and median duration of angiographic follow-up was 11.0 months (IQR:7.0–13.5) in 10 patients. The rate of functional independence at 90 days (70.5%, 12/17) was increased significantly as compared with that before operation (23.5%, 4/17) in the recanalized group (P = 0.015, Fisher's Exact test) (Fig. 3). The rate of functional independence at 90 days (66.7%, 10/15) was not different from that before operation (66.7%,10/15) in the failure group (P = 1.00, Fisher's Exact test). The median score reduction in mRS at 90 days was 1.0 (IQR: 1.0–2.0) in the recanalized group versus 0 (IQR: 0.0-0.0) in the failure group (P < 0.001, Mann-Whitney U test) (Tables 2).

During the follow-up period, there was one patient in the failure group had recurrent TIA, while no TIA or ischemic stroke recurrence in the recanalized group. In the recanalized group, one patient developed asymptomatic in-stent restenosis at 4 months after operation, and two patients developed asymptomatic in-stent reocclusion at 6 months after operation.

4. Discussion

This study showed that, with safety as the first principle, selective late endovascular recanalization for symptomatic non-acute atherosclerotic ILAO was feasible, especially for ICVA and ICICA occlusion. The periprocedural operation-related complication rate and safety of late endovascular recanalization were acceptable. Moreover, our results suggested that successful endovascular recanalization might effectively improve the degree of disability of symptomatic non-acute atherosclerotic ILAO patients.

In this cohort, technical success in endovascular recanalization was finally achieved in 53.1% patients. Similar to previous studies, our study showed that the technical success rates of recanalization for ICVA and ICICA were high (12/14 in Gao's report [15], 10/12 in Wang's [14]). Nevertheless, the technical success rates for BA and M1 in our study were much lower than that reported by previous studies (8/9 in Dashti's [10], 10/13 in Chen's [13]). The low technical success rate was related to the concept of safety as the first principle. In order to ensure the safety, we choosed microwires with soft tips instead of harder tips. During the endovascular recanalization, we paid close attention to the morphological change of the microwire tip, which should not be too bent. The operation needed to be terminated once suspicious vascular dissection occurred. There are factors such as occlusion site, occlusion stump morphology, duration of occlusion, and length and tortuosity of occlusion segment that may affect recanalization [21–24]. In our study, the technical success rates of recanalization for ICVA and ICICA were higher than BA and M1. It is empirically speculated that non-acute atherosclerotic ILAO with fewer perforators is more likely to be recanalized. In addition, the occlusion duration might play a role in recanalization as well. This is evidenced by the significantly shorter median time from imaging-documented occlusion to treatment in the recanalized group.

Perioperative operation-related complications can be divided into two aspects: hemorrhagic complications including perforation; ischemic complications including dissection, acute thrombosis, thromboembolism and perforator stroke. The operation-related complications

Table 2
Clinical summary of 32 patients undergoing endovascular recanalization.

No.	Sex/age (yr)	Qualified events	Mechanism of stroke or TIA	Occlusion location	Time from IDO to ER (days)	Technical success	Stent* number	Post-op residual stenosis (%)	Complication	Pre-op mRS	Discharge mRS	90-day mRS	Angiography FU (months) / restenosis or reocclusion
1	F/69	TIA	HC	BA	32	Failure	NA	NA	None	2	2	3	NA
2	M/50	Stroke	HC, AE	M1	7	Failure	NA	NA	None	2	2	2	NA
3	M/47	Stroke	HC, AE	M1	44	Failure	NA	NA	None	3	3	3	NA
4	M/59	TIA	HC	ICICA	27	Success	EP	45.5	None	2	2	1	NA
5	M/54	Stroke	HC, AE	ICVA	34	Success	EP	48.6	None	3	2	2	12/no
6	F/46	TIA	HC	ICICA	26	Success	EP	21.7	None	2	2	0	11/no
7	F/54	Stroke	HC, PO	BA	25	Failure	NA	NA	None	3	3	2	NA
8	M/45	Stroke	HC, PO	ICVA	18	Success	EP*2	53.9	None	5	5	5	NA
9	M/53	Stroke	HC, PO, AE	ICVA	25	Success	EP	54.1	None	3	3	2	18/no
10	M/40	Stroke	HC, PO, AE	ICVA	13	Success	EP	49.6	None	3	2	1	11/no
11	M/55	TIA	HC	ICICA	75	Failure	NA	NA	None	2	2	2	NA
12	M/41	Stroke	HC, AE	ICICA	9	Success	EP	55.3	None	3	3	2	6/no
13	M/39	Stroke	HC, PO, AE	BA	8	Success	EP	47.0	None	3	3	1	4/restenosis
14	F/79	Stroke	HC, PO	BA	12	Failure	NA	NA	None	2	2	2	NA
15	M/54	Stroke	HC, PO, AE	BA	33	Failure	NA	NA	None	3	3	3	NA
16	M/60	Stroke	HC, PO, AE	BA	37	Success	EP	50.6	None	4	3	3	NA
17	M/69	Stroke	HC, PO	BA	5	Success	EP	55.1	None	3	2	2	7/no
18	M/50	TIA	HC	ICVA	20	Failure	EP	NA	Acute thrombosis	3	3	2	NA
19	M/54	Stroke	HC, PO, AE	ICVA	18	Success	EP*2	43.4	None	3	2	1	5/reocclusion
20	M/52	Stroke	HC, AE	BA	99	Failure	NA	NA	None	2	2	2	NA
21	M/37	Stroke	HC, PO, AE	BA	27	Failure	NA	NA	None	2	2	2	NA
22	M/46	Stroke	HC, PO	BA	9	Failure	NA	NA	Dissection	2	2	2	NA
23	F/59	Stroke	HC, AE	ICICA	69	Failure	NA	NA	None	2	2	2	NA
24	M/41	Stroke	HC, PO	M1	30	Success	EP	47.8	None	3	3	2	NA
25	M/40	TIA	HC	M1	6	Failure	NA	NA	None	2	2	2	NA
26	M/69	Stroke	HC, PO, AE	BA	4	Success	EP	51.1	Perforation	5	6	6	NA
27	F/51	Stroke	HC, AE	M1	37	Failure	NA	NA	None	2	2	2	NA
28	F/59	Stroke	HC, PO	ICICA	34	Success	EP	60.3	None	4	4	3	NA
29	M/65	Stroke	HC, PO, AE	ICVA	11	Success	EP	53.7	None	2	1	1	11/no
30	M/45	Stroke	HC, AE	ICVA	5	Success	EP*2	55.0	None	3	2	0	7/reocclusion
31	F/55	Stroke	HC, PO	BA	10	Success	EP	19.2	None	5	4	4	NA
32	M/57	Stroke	HC, PO	M1	6	Failure	NA	NA	None	3	3	3	NA

Abbreviations: AE, artery-to-artery embolization; BA, basilar artery; EP: Enterprise stent, ER: endovascular recanalization; F, female; FU, follow-up; HC, hemodynamic compromise; ICVA, intracranial vertebral artery; ICICA, intracranial internal carotid artery; IDO, imaging-documented occlusion; M, male; M1, first segment of the middle cerebral artery; mRS, modified Rankin scale; NA, not available; PO, perforating artery occlusion; TIA, transient ischemic attack.

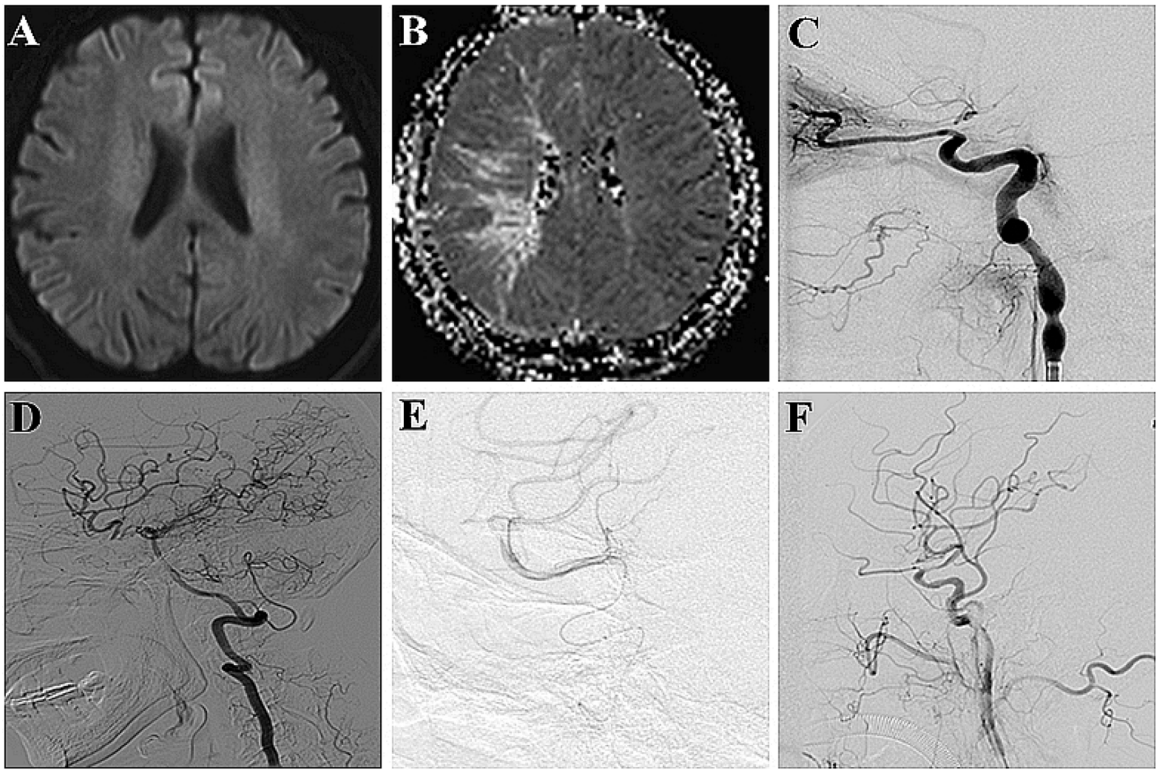

Fig. 1. Case example. Case 4 presented with recurrent numbness and weakness in the left limb for 28 days, diffusion-weighted imaging was normal (A). Perfusion-weighted imaging revealed that there were large areas of hypoperfusion in the right middle cerebral artery territory (B). Preoperative angiography confirmed the occlusion of C6 segment of right ICA, with right anterior communicating artery collateral (C–D). The lesion was traversed with a microwire, and angiogram through the microcatheter demonstrated distal artery was patency (E). After angioplasty and stenting, right ICA was successfully recanalized with Thrombolysis in Cerebral Ischemia grade 3 (F). Abbreviation: ICA, internal carotid artery.

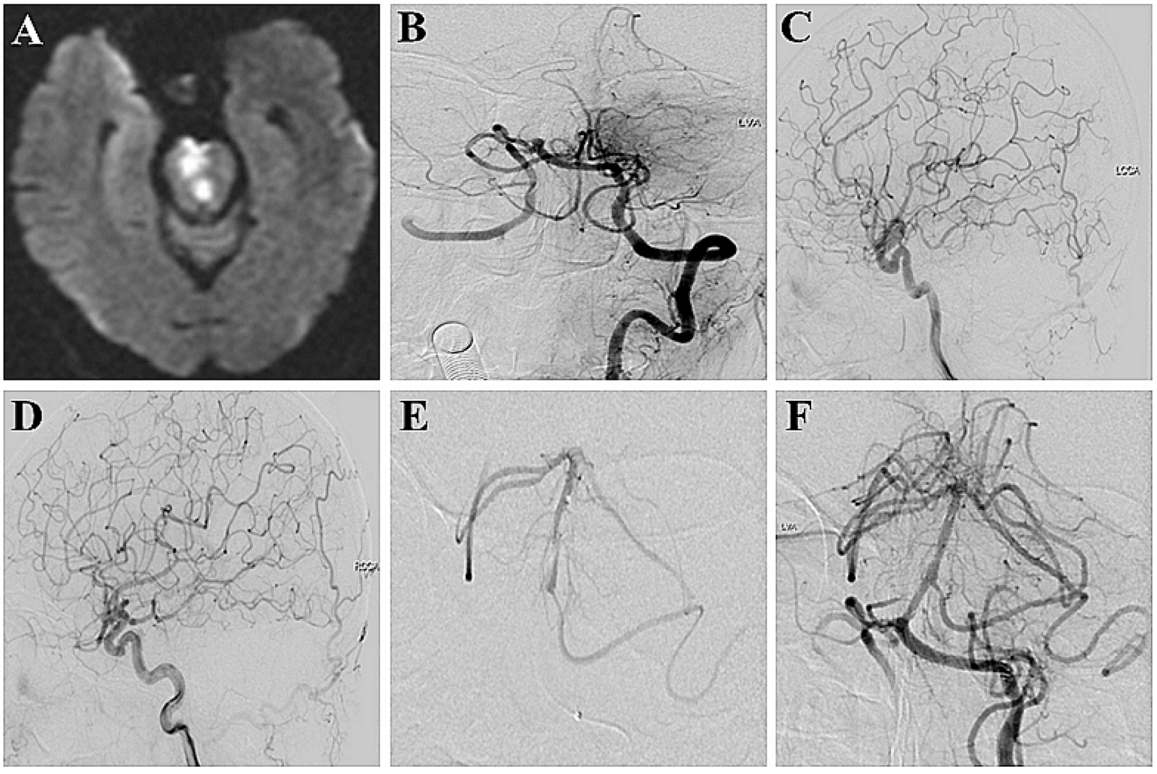

Fig. 2. Case example. Case 31 presented with left limb weakness, vertigo, slurred speech and dysphagia for 10 days, diffusion-weighted imaging showed multiple infarcts in the pons (A). Preoperative angiography confirmed the proximal basilar artery occlusion and bilateral embryonic posterior cerebral arteries (B–D). The lesion was traversed with a microwire, and angiogram through the microcatheter demonstrated distal artery was patency (E). After angioplasty and stenting, the basilar artery was successfully recanalized with Thrombolysis in Cerebral Ischemia grade 3 (F).

Table 3
30-days periprocedural and 90-days follow-up outcomes.

Variable	Recanalized group (N = 17)	Failure group (N = 15)	P value
Any stroke or death within 30 days, No. (%)	1 (5.9)	1 (6.7)	0.927
Ischemic stroke within 30 days	0 (0)	1 (6.7)	
Hemorrhagic stroke within 30 days	1 (5.9)	0 (0)	
Death within 30 days	1 (5.9)	0 (0)	
Score on mRS at discharge, median (IQR)	3.0 (2.0-3.5)	2.0 (2.0-3.0)	0.211
Reduction from baseline in mRS score at discharge, median (IQR)	1.0 (0-1.0)	0 (0-0)	0.011
Score on mRS at 90 days, median (IQR)	2.0 (1.0-3.0)	2.0 (2.0-3.0)	0.192
Reduction from baseline in mRS at 90 days, median (IQR)	1.0 (1.0-2.0)	0 (0-0)	< 0.001
Functional independence at 90 days, No. (%)	12 (70.6)	10 (66.7)	0.811

Abbreviations: IQR, interquartile range; mRS, modified Rankin scale.

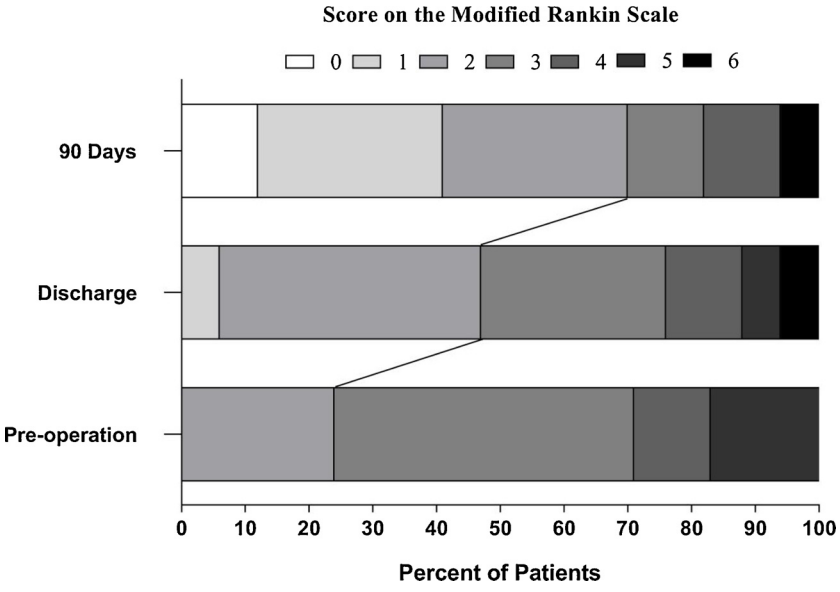

Fig. 3. The modified Rankin Scale distribution at pre-operation, discharge and 90 Days in the recanalization group. Shown is the distribution of scores on the modified Rankin scale (which ranges from 0 to 6, with higher scores indicating more severe disability) among patients in the recanalization group. The numbers in the bars are percentages of patients who had each score; the percentages may not sum to 100 because of rounding. The black line indicate shift in the rate of functional independence at pre-operation, discharge and 90-days.

in this study were similar to that in other studies [10,11,25,26]. Four out of nine patients had complications in Dashti's report [10], one was a perforation, one was an in-stent thrombosis, and two were dissections. Five out of twenty-seven patients had complications in He's study [26], one was an in-stent thrombosis, one was an acute reocclusion, one was thrombus translocation, and two were dissections. Five out of twenty-four patients had complications in Aghaebrahim's report [11], one was a perforation, one was an intracranial hemorrhage, and three were dissections. The previous studies and our results suggest that the most severe complication seems to be perforation, and the most common complication seems to be dissection. In our experience, under current technical conditions, the operator cannot force a successful recanalization. If arterial perforation and severe perforating stroke occur, it may lead to disability or death. Therefore, it should be emphasized that revascularization of non-acute ILAO is a high risk procedure, which should be performed by experienced operators with safety as the first principle.

Besides, there was no hemorrhagic transformation after recanalization in our recanalized group. It is possible that our study restricted enrollment to patients with infarcts of a small core, our results may be concordant with the previous study that the infarct size is a determinant of the risk of parenchymal hematoma after endovascular therapy [27].

Our study showed that compared with their respective preoperative mRS scores, the mRS scores at 90 days were reduced significantly in the recanalized group, while there was no significant difference in the failure group. It suggested that successful endovascular recanalization may effectively improve the degree of disability. Our result was similar to that of previous studies [11–14]. There exists a proportion of patients with ILAO who have enough collateral support to sustain a penumbra and harbor small ischemic cores beyond conventional time window and may benefit from late recanalization [9,28]. We speculated that due to poor collaterals in our patients, the distal perfusion of occluded vessels was poor. When the occluded vessels were recanalized, the hypoperfusion was restored and the clinical outcomes of the patients were improved in the recanalized group. However, some patients' symptoms did not improve after recanalization in our study, which may be due to different mechanisms of stroke. We found that the mechanism of stroke in patients with non-acute ILAO was multifaceted. In addition to hemodynamic compromise, artery-to-artery embolization and perforating artery occlusion were common. Patients with clinical symptoms due to hypoperfusion may benefit from recanalization. However, recanalization was not effective in patients with clinical symptoms due to embolization or perforation occlusion alone.

During the follow-up period, one patients in the failure group had recurrent TIAs, and there was no TIA or ischemic stroke recurrence in the recanalized group. It suggested that successful recanalization may be effective in reducing cerebral ischemia recurrence. In addition, the incidence of in-stent restenosis and reocclusion in our study is similar to other studies [10,12], which may be associated with high postoperative residual stenosis. How to reduce postoperative residual stenosis deserves further study.

Our study has some limitations. First, it was a single-centre study with small sample size and a lack of medical control arm. Whether endovascular recanalization compares favorably with best medical therapy for non-acute ILAO is unknown. Second, there was heterogeneity of the occlusions in this cohort. It is believed that there are differences in difficulty and risk of endovascular recanalization in

different sites of atherosclerotic ILAO. Finally, We did not use perfusion parameters to screen patients in our study because it was difficult to evaluate hypoperfusion in posterior circulation occlusion cases. Instead, our study used the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology Collateral Flow Grading System was ≤ 2 on angiogram to select patients with hemodynamic compromise. Our findings require further large sample, multicenter, randomized controlled trials to validate.

In conclusion, for carefully selected patients with symptomatic non-acute atherosclerotic ILAO beyond 24 h from onset, late endovascular recanalization is technically feasible. The periprocedural safety of late endovascular recanalization is acceptable. Successful recanalization may effectively improve the degree of disability in such patients. However, it should be emphasized that revascularization of non-acute ILAO is a high risk procedure, which should only be performed by experienced operators with safety as the first principle.

Contributors

W-JJ contributed the conception, design, data analysis, and manuscript revision. Y-DY and A-FL collected the data and drafted the manuscript. JZ and CL: analyzed data and revised the manuscript. JL, QW and H-CQ: reviewed and edited the manuscript.

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