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Endovascular recanalization for symptomatic intracranial internal carotid and middle cerebral artery occlusion lasting longer than 72 h: Experience in a single center

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Abstract:

OBJECTIVE: The objective of this study was to assess the safety, feasibility, and outcomes of endovascular recanalization for symptomatic intracranial internal carotid and middle cerebral artery occlusion lasting longer than 72 h.

METHODS: Thirty-nine consecutive patients with symptomatic occlusion of the anterior circulation and failure of medical therapy underwent endovascular recanalization and were included in this retrospective study. Patient characteristics, atherosclerotic risk factors, successful recanalization rates, and angiographic data were collected.

RESULTS: Recanalization was successful in 37 cases (94.9%). The average residual stenosis immediately after intervention was $11.6 \pm 4.3\%$. The patients who underwent balloon angioplasty alone had similar residual stenosis to those who also underwent stent placement ($15.6 \pm 7.3\%$ vs. $9.0 \pm 6.4\%$, $P = 0.184$). Intra- and perioperative complications occurred in three cases (7.69%). One patient (2.7%) developed severe in-stent restenosis with transient ischemic attack symptoms at 1-year follow-up.

CONCLUSIONS: Endovascular recanalization is feasible for symptomatic occlusion of the anterior circulation lasting longer than 72 h. Recanalization provides a higher success rate when performed within 6 months of the qualifying event.

Keywords:

Endovascular, intracranial, occlusion, recanalization

Introduction

Intracranial arterial occlusion has emerged as a specific subtype of vascular insult and is the main cause of ischemic stroke in Asia.^[1] A previous study revealed that endovascular recanalization has a clinical benefit when performed within 24 h after intracranial arterial occlusion.^[2,3] Furthermore, the Wingspan Stent System Post Market Surveillance

Study (WEAVE trial) demonstrated a low periprocedural complication rate and excellent safety for patients with intracranial atherosclerotic stenosis treated with a stent.^[4] However, the feasibility and efficacy of recanalization for symptomatic intracranial occlusion more than 24 h after the event remain undefined.

Intracranial arterial occlusion is associated with a high risk of death, poor outcomes, and recurrent stroke.^[5,6] Atherosclerosis is the most common cause of intracranial

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arterial stenosis and occlusion.^[7,8] Antiplatelet therapy and risk factor control have been used to prevent the most severe consequences of intracranial atherosclerotic disease.^[9] However, the WASID study showed that the 2-year recurrent ischemic stroke rate was 19.7% in patients with intracranial arterial stenosis treated with aspirin.^[10] Recently, endovascular recanalization has been attempted in these patients. Aghaebrahim *et al.* reported that endovascular recanalization is feasible for strictly selected patients with intracranial atherosclerotic occlusion.^[11] However, most studies have focused on vertebrobasilar artery recanalization in small numbers of patients, so the general efficacy and risk of this procedure remain poorly understood.

Most intracranial arterial occlusions are located in the anterior circulation.^[12] We herein report a single-center experience of endovascular recanalization of intracranial atherosclerotic occlusions of the anterior circulation lasting longer than 72 h to investigate its feasibility and risks.

Methods

Study design

We examined our center's results of endovascular recanalization of intracranial atherosclerotic occlusions of the anterior circulation, lasting longer than 72 h, from October 2016 to April 2020. Due to the nature of this noninterventional retrospective study, the requirement for informed consent was waived by the institutional review board, which also approved this study protocol.

Patient selection

The inclusion criteria for patient selection were as follows: absent or minimal antegrade flow through the occlusion, as defined by a Thrombolysis in Cerebral Infarction (TICI) score of 0 or 1;^[11,13] preintervention ischemic stroke symptoms, including recurrent transient ischemic attack (TIA) and progressive neurological impairment refractory to aggressive antiplatelet treatment; occlusion lasting longer than 72 h; brain computed tomography angiography (CTA) or digital subtraction angiography (DSA) confirming the presence of an arterial bed at the distal end of the occlusion; diameter of the occluded artery ≥ 2.0 mm, length ≤ 15 mm, and location in the intracranial internal carotid or middle cerebral artery (MCA); a collateral flow score, according to the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology, <3 on DSA or a cerebral blood flow decrease of $\geq 30\%$ in the hypoperfusion area compared to the contralateral side on perfusion CT; and presence of at least two vascular risk factors (hypertension, diabetes, dyslipidemia, age >60 years, and smoking).

The exclusion criteria were large infarcts within 3 weeks; a nonatherosclerotic occlusion; excessive proximal vessel tortuosity or severe calcification of the vascular wall at the occluded segment; known allergy, contraindication, or resistance to aspirin and clopidogrel; intolerance of general anesthesia; and life expectancy lower than 2 years due to other medical conditions.

Endovascular treatment

All patients received aspirin (100 mg/d) and clopidogrel (75 mg/d) for at least 3 days preoperatively. The procedure was performed under general anesthesia. Intravenous heparin was administered at the beginning of the operation, and a 6F guiding catheter was advanced into the internal carotid artery (ICA) as far as the vessel tortuosity allowed. A microcatheter and micro-guidewire were conducted through the occluded portion to the distal vessel. Balloon angioplasty, alone or followed by stent implantation, was performed, with the treatment choice based on the measurement of the proximal and distal arterial diameters, occlusion length, vascular tortuosity, and antegrade flow after balloon dilation. In general, if high-grade stenosis persisted after balloon dilation, the Wingspan self-expanding stent (Boston Scientific, America) or Apollo balloon-mounted stent (MicroPort NeuroTech, China) was implanted. The balloon-mounted stent was used in patients with smooth arterial access and a Mori A lesion; the self-expanding stent was used in patients with tortuous arterial access or a Mori C lesion. Control angiography was performed to confirm the patency of the target artery, and the microwire and guiding catheter were removed. Technical success was defined as residual stenosis $<30\%$ and modified TICI score $\geq 2b$ of the recanalized portion on postprocedural angiography.

All patients were treated with aspirin and clopidogrel for a minimum of 3 months after discharge, followed by lifelong monotherapy with aspirin (100 mg/day). Functional outcomes were followed up by clinic visits or telephone calls, and modified Rankin Scale (mRS) scores were evaluated by two physicians. In case of unavailable postoperative outcomes due to loss to follow-up, mRS at discharge was considered. At follow-up, brain CT or magnetic resonance imaging examinations were performed in patients who had neurological deterioration.

Statistical analysis

Statistical analysis was performed using SPSS (version 17.0; IBM, Armonk, NY, USA). Patient characteristics are presented as median and interquartile ranges (IQRs) and frequencies or percentages for continuous and categorical variables, respectively. Statistical comparisons of categorical data between two groups were performed using the Kruskal–Wallis

test. The Chi-square test (or Fisher's exact test for frequencies <5) was used for categorical variables. $P < 0.05$ was considered statistically significant.

Results

Baseline characteristics

From October 2016 to April 2020, 39 patients (25 males; median age: 62 years, IQR: 51–70 years) with symptomatic arterial occlusion of the anterior circulation lasting longer than 72 h were treated with endovascular recanalization. The clinical and treatment characteristics of the patients are summarized in Table 1. The median pretreatment National Institutes of Health Stroke Scale (NIHSS) score was 2.2 (IQR: 0–5). The most common risk factor was hypertension (79.5% of patients). The median intervals from qualifying event to endovascular procedure and from radiographic documentation to the procedure were 23 and 19 days, respectively. Nineteen patients had recurrent TIA, and twenty patients had a recurrent stroke or worsening neurological impairment at the time of presentation. Occlusion sites included the ICA terminus ($n = 19$) and the M1 segment of the MCA ($n = 20$).

Primary procedural results

Recanalization was technically successful in 37/39 cases (94.9%). The procedure was interrupted in two cases: one because of failure of the micro-guidewire to penetrate the occluded portion and the other due to subarachnoid hemorrhage (SAH) caused by the micro-guidewire perforating the blood vessel. The interval from the first qualifying event to endovascular treatment in these two patients was longer than 6 months.

The number of patients who underwent balloon dilation alone, balloon predilation plus self-expanding stent implantation, and balloon predilation followed by balloon-mounted stent implantation for successful recanalization was 10, 22, and 5, respectively. The average residual stenosis was $11.6 \pm 4.3\%$ immediately after the intervention. The patients treated with balloon dilation alone had residual stenosis not significantly different than patients also treated with stenting ($15.6 \pm 7.3\%$ vs. $9.0 \pm 6.4\%$; $P = 0.184$) [Figures 1 and 2].

Intra- and perioperative complications occurred in three cases (7.69%). The first patient, as mentioned above, had SAH caused by the micro-guidewire perforating the blood vessel during the procedure; however, the clinical symptoms remained stable postoperatively. The second patient had a symptomatic perforator stroke, and the third patient experienced hematoma in the basal ganglia within 3 days postoperatively. All clinical symptoms improved after treatment in these three patients. Among the successfully recanalized patients, immediate postprocedural improvement (NIHSS decrease of more

than 4 points 1 week postoperatively) occurred in twenty patients. Moreover, we noticed that the patient's clinical symptoms remained stable in case the micro-guidewire failed to penetrate the occluded segment [Table 2].

Follow-up outcome

Transcranial Doppler ultrasound demonstrated that all the target arteries were patent within 1 week after the procedure. All recanalized patients were followed

Table 1: Baseline patient demographics (n=39)

Variables	n (%)	Median (IQR)
Age		62 (51-70)
Pretreatment NIHSS		2.2 (0-5)
Pretreatment mRS		1.1 (0-1)
Interval from symptom onset to procedure (days)		23 (6-90)
Males	25 (64.1)	
Hypertension	31 (79.5)	
Diabetes mellitus	19 (48.7)	
Hyperlipidemia	17 (43.6)	
Smoking	10 (25.6)	
Occluded artery		
ICA terminus	19 (48.7)	
MCA	20 (51.3)	
mTICI score		
0	31 (79.5)	
1	8 (20.5)	
Angioplasty strategy		
Self-expanding stent	22 (59.5)	
Balloon dilation alone	10 (27.0)	
Balloon-mounted stent	5 (13.5)	

mRS: Modified Rankin Scale, NIHSS: National Institutes of Health Stroke Scale, ICA: internal carotid artery, MCA: Middle cerebral artery, mTICI: Modified Thrombolysis in Cerebral Infarction score, IQR: Interquartile range

Table 2: Complications and clinical outcome of patients

Variables	n (%)
Complications	4 (10.3)
Subarachnoid hemorrhage	1 (2.56)
Hematoma	1 (2.56)
Perforator infarction	1 (2.56)
Seizure	1 (2.56)
Postoperative mTICI	
0 or 1	2 (5.13)
3	37 (94.8)
Postprocedure symptoms (n=37)	
Stable	15 (40.5)
Improved	20 (54.1)
Worsened	2 (5.4)
1-year restenosis	1 (2.7)
1-year recurrent symptoms	1 (2.7)
1-year mRS	
0-1	32 (86.5)
2	5 (13.5)
3-4	0

mRS: Modified Rankin Scale, mTICI: Modified Thrombolysis in Cerebral Infarction score

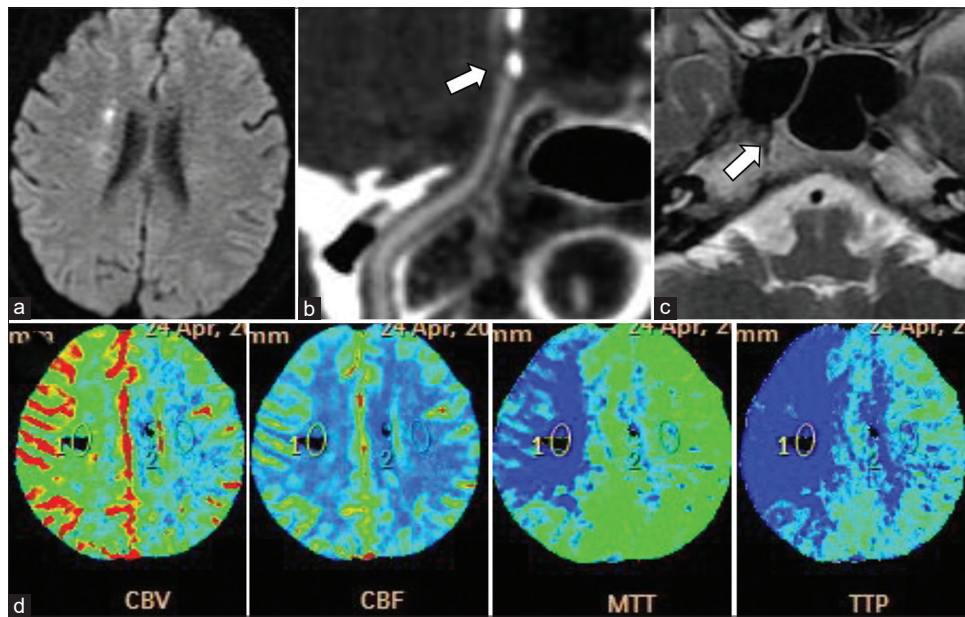


Figure 1: Magnetic resonance imaging, computed tomography angiography, and computed tomography perfusion on admission of one representative patient. (a) Diffusion-weighted imaging revealed infarction in the internal boundary area of the right corona radiata. (b and c) Computed tomography angiography and magnetic resonance imaging revealed occlusion of the C7 segment of the right internal carotid artery (white arrow). (d) Computed tomography perfusion showed hypoperfusion in the right hemisphere

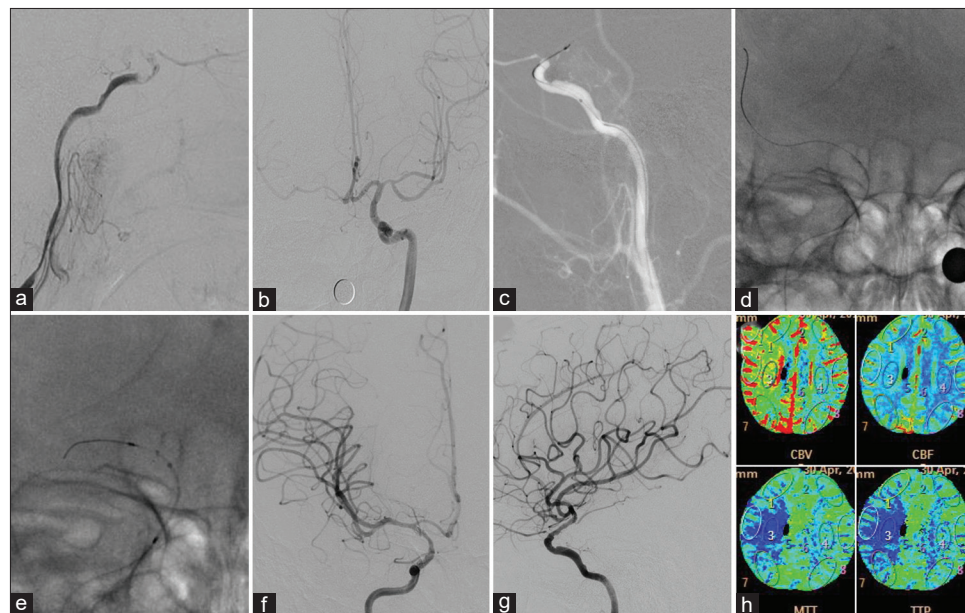


Figure 2: Endovascular procedure. (a) Right carotid angiography showed an occlusion of the C7 internal carotid artery segment; (b) left carotid angiography showed that the anterior communicating arteries were patent, though the arterial collateral circulation grade in the right middle cerebral artery territory was 1. (c) The occluded portion was traversed with a coaxial assembly of a soft micro guidewire and microcatheter. (d) The occluded portion was predilated with a 2.0 mm × 12 mm balloon; (e) A stent of 3.0 mm × 20 mm was placed on the lesion and released. (f and g) Postoperative angiography confirmed the in stent patency and a Thrombolysis in Cerebral Infarction score of 3. (h) Computed tomography perfusion 3 days after endovascular recanalization showed improved perfusion of the right hemisphere

up 1 year postoperatively. The median mRS score was 1 (range: 0–4). Thirty-one patients underwent DSA or CTA 1 year after the treatment [Figure 3]. One patient treated with a self-expanding stent (4.17%) had a TIA due to severe in-stent restenosis (>70%), and the symptoms were relieved by repeated balloon dilation. No patient died [Table 2].

Discussion

Our study showed that rates of recanalization, perioperative complications, and recurrent ischemic events at 1-year follow-up were 94.9%, 7.69%, and 2.7%, respectively, in patients treated for intracranial arterial atherosclerotic occlusion. In addition, the recanalization

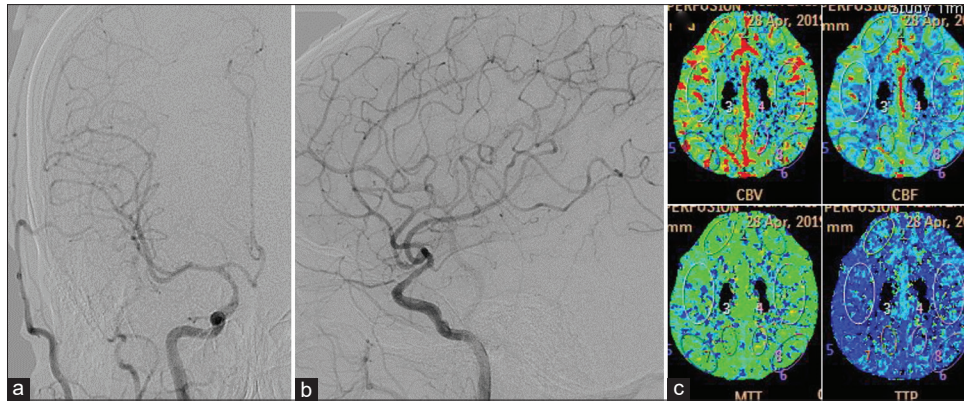


Figure 3: One-year follow-up. (a and b) Angiography showed no stenosis of the right internal carotid artery and adequate antegrade perfusion to the internal carotid artery territory. (c) Computed tomography perfusion showed no side difference in perfusion

was more challenging if the arterial occlusion occurred more than 6 months before treatment.

The treatment for intracranial atherosclerotic occlusion aims to restore cerebral blood flow with a low risk of complications. In general, the brain region perfused by the occluded artery receives a reduced blood flow, and the clinical symptoms and prognosis vary depending on the extent of this hypoperfused area. A subset of patients with hypoperfusion may experience recurrent ischemic events and progressive disability despite receiving aggressive medical therapy.^[13] Therefore, revascularization is considered the treatment of choice for these patients. The WEAVE trial demonstrated the excellent safety of stenting for patients with intracranial atherosclerotic disease.^[4] Numerous studies also reported the high success rates of recanalization for intracranial arterial atherosclerotic occlusion. Our results were consistent with these reports, with a successful recanalization rate of 94.9%. However, the main technical challenge was penetrating the occluded segment with the guidewire. The occlusive material in chronic occlusions consists of fibrous-calcific components that are difficult to penetrate with a micro-guidewire and microcatheter. Longer durations of vascular occlusion indicated more extensive fibrous-calcific elements in the occluded segment and thus more challenging recanalization.^[13] The interval from the qualifying event to the endovascular procedure of the two patients not recanalized was longer than 6 months. Experience with coronary angioplasty showed that chronic total occlusions longer than 3 months can often be successfully dilated.^[14] Therefore, we believe that the longer occlusion duration may have precluded the recanalization.

However, the rate of perioperative complications needs to be reduced. Major complications include ischemic and hemorrhagic events. In our study, one patient suffered a perforator infarction, and the interval from occlusion to endovascular treatment

was 3 days. A previous study revealed that timing is crucial in minimizing perioperative complications and long-term cerebral vascular events in intracranial arterial stenotic and occlusive disease.^[4,15] Our previous study found that early stent placement (within 14 days) in the setting of ischemic stroke caused by intracranial atherosclerotic artery occlusion may result in a higher stroke recurrence rate and higher risk of restenosis.^[16] Similar results were also found in patients with ischemic stroke or TIA treated with extracranial-intracranial bypass within 7 days had a higher perioperative stroke rate than those having late surgery.^[17] The occluding plaques are unstable in acute poststroke stages, and the “snowplowing” effect of stenting could lead to distal embolism or periprocedural perforator stroke.^[18] In contrast, performing a delayed recanalization allows fragile plaques to stabilize, reducing the rate of perforator occlusion and artery-to-artery embolism.^[18] Another complication reported is cerebral hemorrhage in the basal ganglia induced by hyperperfusion. Previous studies revealed that the incidence of hemorrhagic transformation and hyperperfusion syndrome was 29.0% after recanalization in patients with symptomatic cerebral artery occlusion,^[19] possibly because the blood–brain barrier is altered after the brain tissue suffers an ischemic injury; therefore, the risk of hyperperfusion and cerebral hemorrhage is increased.^[20,21]

The current study also found that balloon angioplasty alone had similar efficacy to stent placement following dilation. We believe that the anatomical features of the ICA and MCA are more suitable for balloon angioplasty. Unfavorable vascular anatomy, such as severe tortuosity of the occluded segment in the terminal ICA and proximal MCA, presents technical challenges to stent placement, resulting in a high risk of in-stent thrombosis and in-stent restenosis.^[22,23] In addition, multiple perforator arteries originate from the M1 segment of the MCA, leading to a high perforator stroke risk after stent placement.^[24] Furthermore, balloon angioplasty alone avoids the need

for long-term dual antiplatelet drugs, reducing the risk of bleeding complications. Finally, patients undergoing balloon dilation had similar residual stenosis percentages and no ischemic events during follow-up, indicating that balloon dilation alone is also an effective treatment.

A major strength of our study was the high number of patients with intracranial arterial occlusion. However, there were some limitations. First, the study was a retrospective case series; hence, there is a lack of a control arm. Second, all patients were Chinese, so the results might not be generalized to other ethnic groups.

Conclusion

We found that endovascular recanalization is feasible for anterior circulation occlusions lasting longer than 72 h, reducing the long-term recurrence rate of TIA or stroke. In addition, recanalization is more successful when performed within 6 months after the first qualifying event. However, further large-scale studies are needed to determine the feasibility and long-term outcomes associated with this treatment.

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Conflicts of interest

There are no conflicts of interest.

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