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in Acute Symptomatic Cervical Internal
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ORIGINAL RESEARCH

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Microcatheter Navigation and Thrombolysis in Acute Symptomatic Cervical Internal Carotid Occlusion

BACKGROUND AND PURPOSE: The treatment of acute stroke distal to an occluded cervical internal carotid artery (ICA) presents a challenge. We report our results of endovascular therapy in 7 patients presenting with acute symptomatic cervical ICA occlusion.

PATIENTS AND TECHNIQUES: Among patients presenting with acute stroke at our institution from June 2001 to June 2005, we retrospectively identified 7 patients who underwent endovascular therapy of acute cervical ICA occlusion. The techniques used for vessel recanalization were analyzed. Postprocedure CT scans were reviewed for hemorrhage. The clinical outcomes were assessed by using the modified Rankin scale (mRS) with good outcomes assigned scores of ≤ 2 .

RESULTS: All 7 patients revealed cervical ICA occlusion, with additional intracranial thrombus in 6 of the 7 patients. In all patients, a guiding catheter was placed in the ipsilateral common carotid artery proximal to the occlusion and a microcatheter advanced through the ICA clot to deliver intra-arterial (IA) tissue plasminogen activator (in 6 patients, the microcatheter was also advanced intracranially for thrombolysis). Successful recanalization of the occluded ICA was achieved in 6 patients. In 3 patients, balloon angioplasty and stent placement of the cervical ICA was also performed. Follow-up CT in 6 patients showed small basal ganglia infarcts in 4, patchy parietal infarcts in one, and frontal lobe hematoma in one patient. At 1 month after the procedure, 5 patients had good clinical outcomes (mRS of 0 in 4 patients and 1 in one patient).

CONCLUSION: Performance of IA thrombolysis by passing a microcatheter through an acutely occluded internal carotid artery may be an effective therapy in acute stroke.

The National Institute of Neurological Disorders and Stroke trial showed the benefit of intravenous (IV) tissue plasminogen activator (tPA) in patients presenting within 3 hours of onset of symptoms of acute stroke.¹ Recent studies have revealed promising results for intra-arterial (IA) thrombolysis especially in patients with significant clot burden that may be refractory to IV tPA.²⁻⁵ At our institution, patients presenting with symptoms of acute stroke within 3 to 6 hours of onset who have thrombus in the M1 or M2 segments of the middle cerebral artery (MCA) are considered for IA thrombolysis. A unique subset of patients presenting with acute stroke may have an occluded MCA distal to an occluded internal carotid artery (ICA) just distal to the common carotid artery (CCA) bifurcation. Acute ICA occlusions may be embolic, related to atherosclerotic disease, or caused by dissections. These patients may have a poor response to IV tPA.⁶ The natural history of patients presenting with signs and symptoms of acute stroke distal to an acutely occluded cervical ICA is poor. There is a 16% to 55% likelihood of death from complications of infarction, 40% to 69% will be severely disabled, and only 2% to 12% will make a good recovery.⁷ There are various surgical options in acute symptomatic ICA occlusions, which include carotid endarterectomy (CEA), embolectomy, and surgical bypass. Patients with profound neurologic deficits or large infarcts, however, are at high risk for hemorrhagic transformation after CEA, thus making this a strong exclusion criterion in

recent studies evaluating CEA.^{8,9} In addition, the results of urgent surgical recanalization may not be ideal: 26.5% normal neurologic outcome after emergency CEA in a study by Meyer et al.⁷

Catheter navigation through an acutely occluded ICA for the purpose of performing IA thrombolysis has been considered an obstacle and is an issue of debate.⁸ Several small case series have described successful IA thrombolysis in the territory of an acutely occluded cervical ICA.^{8,10,11} Traversing the acutely occluded ICA segment combined with IA tPA may, however, uncover an underlying severe stenosis at the carotid bulb. The management of this residual stenosis or occlusion at the bulb presents an interesting challenge. Some authors have advocated acute angioplasty and stent placement at the time of thrombolysis.¹⁰ We report our results of urgent IA thrombolysis of acute MCA thrombus by navigating a microcatheter through an acutely occluded ICA and discuss the management of the underlying proximal ICA stenosis or occlusion in 7 patients presenting with acute stroke.

Patients and Methods

All patients presenting with symptoms of acute stroke at our institution within 6 hours of onset have a complete neurologic examination and are evaluated with nonenhanced CT scan of the head to rule out hemorrhage. In the absence of intracranial hemorrhage, CT angiogram (CTA) and CT perfusion (CTP) studies are also routinely performed to look for presence of thrombus in the neck/intracranial vasculature and to evaluate tissue at risk, respectively. On CTA, the arterial system from the aortic arch to the circle of Willis is evaluated by using 100 to 120 mL Iohexol (Omnipaque 300; GE Healthcare, Princeton, NJ) injected at a rate of 3 mL/s and a 20- to 22-second delay. CTP is performed covering a 2-cm-thick area at the level of the

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Table 1: Clinical and imaging features of 7 patients with occluded internal carotid artery and acute stroke

Patient No./Age (y)/Sex	Site of Occlusion (CTA)	Presence of Penumbra (CTP)	NIHSS at Presentation	NIHSS at Follow-up
1/54/M	LICA and LMCA: M1	Yes	22	15 (1 mo)
2/51/M	LICA and LMCA: M1 and M2	Yes	15	1 (14 mo)
3/62/F	RICA and RMCA: M1	Yes	21	0 (6 mo)
4/78/F	LICA and LMCA: M1	Yes	11	0 (5 mo)
5/70/F	RICA*	Yes†	17	1 (14 mo)
6/28/F	LICA and LMCA: M1	No perfusion study‡	17	0 (40 mo)
7/24/M	RICA and RMCA: M1	No perfusion study	12	0 (1 mo)

Note:—CTA indicates computed tomographic angiography; CTP, computed tomographic perfusion; NIHSS, National Institutes of Health Stroke Scale; RICA, right internal carotid artery; LICA, left internal carotid artery; RMCA, right middle cerebral artery; LMCA, left middle cerebral artery.

* Seen on MR angiogram.

† Seen on MR perfusion study.

‡ No perfusion imaging performed since the intervention “pre-dated routine perfusion imaging.”

basal ganglia chosen by the radiologist present on-site and involves administration of 40 to 50 mL of additional contrast. All patients with contrast allergy, known chronic renal failure, or elevated creatinine are routinely excluded from CTA and CTP studies at our institution. All scans in the present study population were acquired on a multi-detector CT (GE Lightspeed Plus, Milwaukee, Wis). The CTP data are analyzed off-line on the GE Advantage Windows workstation and cerebral blood volume (CBV), cerebral blood flow (CBF), and mean transit time (MTT) maps are generated. Areas of significantly low CBV are presumed to represent dead tissue (the color coding is set up to show different color at values <2 mL/100 g). Areas with near normal CBV but low CBF and high MTT are presumed to be salvageable tissue.^{12,13} Major vessel thrombus was defined as thrombus present within the distal intracranial ICA, M1/M2 segments of the MCA or A1 segment of the anterior cerebral artery (ACA) on CTA. IV tPA is the standard of care at our institution for patients presenting within 3 hours of onset of stroke symptoms and showing no hemorrhage on the nonenhanced CT scan. In patients presenting within 3 to 6 hours of the onset of symptoms, endovascular therapy is considered if there is major vessel (terminal ICA, M1, M2) thrombus on CTA and salvageable tissue on CTP. These patients are treated with IA thrombolysis and/or mechanical thrombolysis without any IV tPA administration. Endovascular option is also offered to patients presenting within 3 hours of onset if a significant clot burden (terminal ICA, complete M1) is demonstrated on CTA or for patients presenting with an acutely occluded ICA and associated MCA clot. This is based on the presumption that IV tPA may not be efficacious with a significant clot burden.²⁻⁵ These patients are started on two thirds the normal IV tPA dose in the emergency department. The remaining dose of tPA is then administered intra-arterially or until there is recanalization. CTA and CTP are routinely used at our institution for guiding endovascular therapy, although there are occasions where MR angiography and MR perfusion are performed.

Between June 2001 and June 2005, a total of 2640 patients presented with symptoms of acute stroke within 6 hours of onset at our institution, 42 of whom underwent endovascular pharmaceutical and/or mechanical thrombolysis. Written informed consent for endovascular thrombolysis was obtained from all patients and/or their relatives before their treatment after the risks and benefits of the procedure had been explained. Of these, we retrospectively identified 7 patients with cervical ICA occlusion, with 6 of them demonstrating MCA thrombus on imaging. These 7 patients formed the study sample. All 7 patients were treated by endovascular therapy under biplanar fluoroscopic guidance on an Integris EV 3000 angiographic unit (Philips Medical Systems, Best, The Netherlands). Diagnostic angiograms of both CCAs and one vertebral artery were performed initially

to confirm the presence of occlusion and evaluate collateral flow. IV heparin (2000 U) was administered before advancing a microcatheter through the guiding catheter. In 6 patients, a microcatheter (Excelsior/Renegade; Boston Scientific, Natick, Mass) was advanced through the ICA clot and IA tPA was administered into the face of the clot in the MCA. Care was taken to probe the origin of the occluded ICA gently with a microwire (Transcend; Boston Scientific) first. If there was little or no resistance to microwire probing, it was gently advanced into the high cervical ICA. The microcatheter was then advanced over the wire into the distal ICA where a hand-injection of contrast was performed to confirm position within the true lumen. The microwire was then gently advanced distal to the MCA thrombus followed by the microcatheter. Again, a microcatheter injection of contrast was then performed to confirm its position distal to the clot within a patent distal M1 or M2 branch. The microcatheter was then retracted to the proximal margin of the MCA thrombus and tPA was administered. In one patient, IA tPA was administered into the thrombus of the proximal ICA for acute thrombolysis immediately after CEA. Angioplasty and stent placement (Wallstent, Boston Scientific) of the ICA was also performed in 3 patients after IA thrombolysis. An additional patient was treated with 2 overlapping self-expanding covered stents (Symbiot, Boston Scientific) for recanalization of an acute ICA occlusion from traumatic dissection and management of the associated pseudoaneurysm. All patients who were stented were started on 75 mg clopidogrel (Plavix) for at least 2 months and 325 mg aspirin daily. All patients underwent immediate postprocedure CT scans to evaluate for hemorrhage. They also underwent repeat CT scans before discharge from the hospital. Outcomes were assessed by using the modified Rankin scale (mRS) with good outcomes assigned a $mRS \leq 2$. The mean follow-up was for 11.5 ± 13.7 months (range, 1 month to 40 months).

Results

The clinical characteristics and imaging features of the 7 patients are summarized in Table 1. There were 3 men and 4 women, with a mean age of 52.4 ± 20.2 years (range, 24–78 years). The mean time of presentation to the hospital in 5 of the 7 patients was 117 minutes (range, 75–150 minutes) within onset of symptoms of acute stroke. Two patients were inpatients and were investigated with MR imaging scans within 120 and 160 minutes of onset of acute stroke symptoms. All patients presented with significant hemiplegia (power, 2/5 or less) at the time of the initial imaging. There was occlusion of the cervical ICA in all 7 patients and also presence of ipsilateral MCA thrombus in 6 of the 7 patients. One patient presented with an acute occlusion of the ICA at its origin 2 hours after

Table 2: Intervention and outcomes in the 7 patients with acute stroke due to occluded ICA

Patient No.	IA tPA (mg)	Stenting and angioplasty of ICA	Lysis of MCA Clot through occluded ICA	TIMI Flow after Thrombolysis	Post Rx CT	Outcome (mRS) at 30 days
1	20	Yes	Yes	2	Basal ganglia infarct	4
2	10	Yes	Yes	3	Patchy parietal infarcts	3
3	9	No	Yes	3	Basal ganglia infarct	0
4	0*	Yes	No	3	Basal ganglia infarct	0
5	18	No	Yes	3	Basal ganglia infarct	0
6	10	No	No	3	Evolving frontal bleed	1
7	15	Yes†	Yes	3	Small frontal lobe infarct	0

Note:—ICA indicates internal carotid artery; IA tPA, intra-arterial tissue plasminogen activator; MCA, middle cerebral artery; CT, computed tomography; mRS, modified Rankin Scale.

* This patient received 38 mg intravenous tPA prior to angiography.

† ICA pseudoaneurysm was treated with 2 overlapping covered stents.

CEA. One patient had bilateral posttraumatic cervical ICA pseudoaneurysms with an acute dissection occluding the right cervical ICA and presence of thrombus in the ipsilateral M1 segment. Perfusion studies were performed in 5 of the 7 patients (4 on CTP and one on MR perfusion) and tissue at risk was demonstrated in all 5 scans.

In all patients, a guiding catheter was placed in the ipsilateral CCA proximal to the occlusion and a microcatheter advanced through the clot in the ICA to deliver IA tPA (in 6 patients, the microcatheter was advanced to the face of the intracranial thrombus for intracranial thrombolysis). We were able to achieve successful recanalization of the occluded ICA in 6 of the 7 patients. In one patient, after the microcatheter was advanced through the occluded ICA into the face of the thrombus in the MCA and local tPA was infused, there was successful resolution of the MCA thrombus but persistent ipsilateral ICA occlusion (seen on check angiograms performed through the guiding catheter). It was decided to leave the ICA occluded in this patient because of adequate collateral flow across the anterior communicating artery (AcomA) demonstrated on contralateral carotid angiogram. In 3 patients, balloon angioplasty and stent placement of the cervical ICA was also performed after successful thrombolysis. In the patient who had been treated with CEA a few hours earlier, it was decided to stop after successful ICA thrombolysis alone because of concerns about arterial rupture.

Immediate postprocedural CT scans revealed no hemorrhage in 6 patients and a small frontal lobe hematoma in one patient. In CT scans performed before discharge from the hospital in 6 patients, 4 patients showed small basal ganglia infarcts, one showed patchy parietal infarcts, and one showed evolving frontal lobe hematoma.

At 1 month after the procedure, 5 patients had good outcomes (mRS of 0 in 4 patients and 1 in one patient), one had an mRS of 3, and one had an mRS of 4. There were no deaths. Details of the endovascular treatment and outcomes are summarized in Table 2.

Case Illustration 1

A 62-year-old woman presented to the emergency department 2 hours after onset of left complete hemiplegia (power, 0/5), pronounced left facial droop, and marked dysarthria. Noncontrast CT scan of the head showed subtle hypoattenuation in the right basal ganglia with no hemorrhage. CTA revealed complete occlusion of the right ICA with intracranial thrombus in the distal right M1 segment

of the MCA. CTP demonstrated a small area of decreased CBV in the right basal ganglia and a larger area of CBF and prolonged MTT signifying significant penumbra. En route to angiography, 0.6 mg/kg (two thirds the normal IV dose) of tPA was administered intravenously. Diagnostic angiogram of the left ICA revealed good flow across the AcomA but no M1 filling (Fig 1A). The right ICA was completely occluded on right CCA injection. Through a 6F guiding catheter placed in the right distal CCA, a microcatheter was advanced over a 0.014-in microwire through the occluded proximal ICA. Injection through the microcatheter distal to the bifurcation demonstrated thrombus extending to the petrous ICA, although the supraclinoid ICA and A1 segments were patent. The microcatheter was advanced into the right M1 clot, and a total of 9 mg of tPA (diluted 1:1 with heparinized normal saline) was administered into the thrombus for a period of 20 minutes. Repeat injections revealed complete resolution of thrombus and restoration of antegrade flow in the MCA (Fig 1B). Injection into the left ICA revealed cross-filling through the AcomA into the right MCA branches (Fig 1C). The patient started to improve immediately and regained antigravity strength in her left extremities. Her right ICA was left occluded, because we felt that collateral flow across the AcomA was sufficient to perfuse the right brain. Her postprocedure CT demonstrated a small basal ganglia stroke with no hemorrhage. In a follow-up visit 6 months after thrombolysis, the patient had made a full neurologic recovery.

Case Illustration 2

A 24-year-old man presented to the hospital with significant facial and mandibular injury after a motor vehicle crash. After surgical treatment for the fractured mandible, he complained of persistent dysphagia and hoarseness of voice and underwent an MR imaging examination of the head. Diffusion-weighted imaging revealed no evidence of acute stroke. After completing the MR imaging examination, he became completely hemiplegic on the left side. It was just outside the 3-hour IV tPA window when he was shifted for possible IA thrombolysis to the angiographic suite. Lateral angiogram of the left CCA revealed a pseudoaneurysm in the distal cervical ICA with narrowing of the parent artery (Fig 2A). A left vertebral artery angiogram revealed flow through the right posterior communicating artery to the M1 segment and suggested a focal M1 clot. The right CCA angiogram showed complete occlusion of the right ICA just beyond the bulb (Fig 2B). A

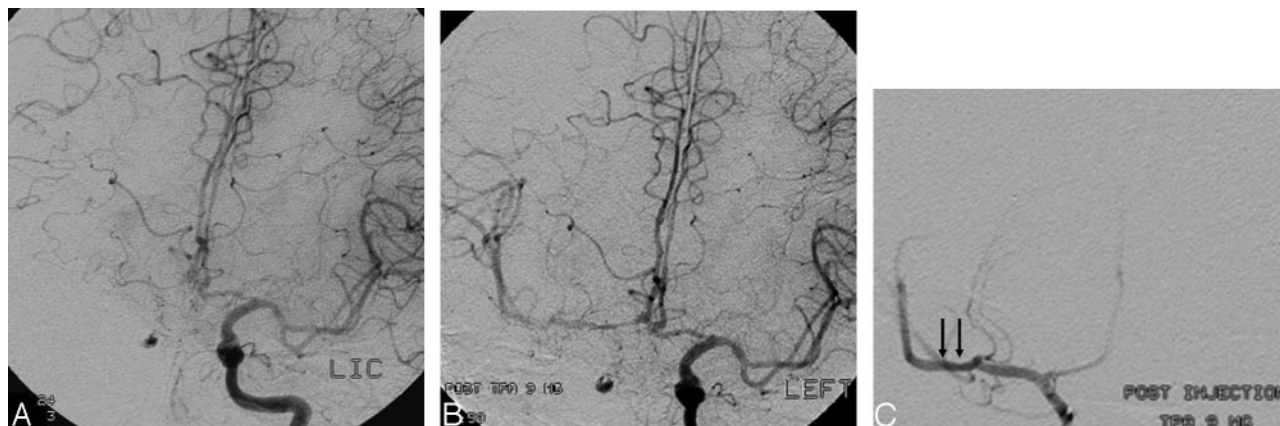


Fig 1. A, Diagnostic angiogram of the left internal carotid artery (ICA) reveals good flow across the anterior communicating artery (AcomA) but poor filling of the right MCA territory because of a thrombus demonstrated on an earlier CT angiogram.

B, Successful recanalization of right MCA is seen after administration of 9 mg of tissue plasminogen activator (tPA) into the middle cerebral artery (MCA).

C, Diagnostic angiogram of the left ICA reveals cross-filling through the AcomA into the right MCA. There is probably dilution of contrast in the MCA by nonopacified blood from the ipsilateral posterior communicating artery because good patency of the MCA was demonstrated on the earlier microcatheter injection.

microcatheter was successfully navigated over a microwire through the occluded cervical ICA into the distal supraclinoid ICA. There was presence of thrombus in the distal M1 segment of the MCA demonstrated on the microcatheter injections (Fig 2C). Then, 7.5 mg of IA tPA was administered through the microcatheter, which was advanced into the face of the thrombus. This resulted in lysis of thrombus and restoration of antegrade flow (Fig 2D). A pseudoaneurysm was also demonstrated in the distal cervical right ICA during the microcatheter injections (Fig 2E). The ICA occlusion and pseudoaneurysm were successfully treated by using 2 overlapping covered stents, and a repeat angiogram through the guiding catheter revealed no filling of the pseudoaneurysm and normal flow in the MCA (Fig 2F, -G). The patient recovered complete power on the left side within minutes of the procedure. Acute management of the contralateral left ICA dissection and pseudoaneurysm was deferred, because there was good distal flow in the ICA and the long-term effects of bilateral ICA covered stents in a young patient are yet unknown. At 2 months postprocedure, the patient had no neurologic deficits.

Discussion

Untreated, the prognosis of patients with acute symptomatic cervical ICA occlusion is poor.⁷ Before endovascular therapy, emergent CEA yielded modest results, with good outcomes in 38%, fair in 29%, and poor in 12% and a surgical mortality rate of 21%.⁷ There were 2 important prognostic factors: the presence of an associated MCA embolus and lack of collateral flow, both of which correlated with poor clinical outcomes. Studies have shown that intravenous thrombolysis is ineffective in recanalizing the occluded cervical ICA.⁶ The poor outcome of less direct thrombolysis in ICA occlusion also involving the MCA is probably due to poor drug delivery to the thrombus and lack of collateral flow from lenticulostriate arteries. The stasis in the ICA proximal to the occlusion delivers little thrombolytic agent to the MCA thrombus.⁸ Several studies have reported successful navigation of an occluded cervical ICA to thrombolize a distal MCA clot.^{8,10,14} The largest series was published by Wang et al¹⁰ and described 6 patients, 5 of

whom had good or excellent outcomes. Favorable clinical outcome at 30 days was also achieved by Mori et al,¹⁵ who performed balloon angioplasty of the MCA and stented the ipsilateral carotid stenosis in a 66-year-old man presenting with acute embolic total occlusion of the left MCA. In our opinion, the primary goal was to address the acute MCA clot first, because this was suspected to be the etiology of the patient's acute symptoms. Once the MCA was recanalized, the attention was then directed to the ICA occlusion. It can be difficult to distinguish angiographically between acute thromboembolic occlusions and dissections causing complete occlusion at the ICA origin. In our limited experience with treatment of acute carotid occlusions, we have encountered mainly presumed atherosclerotic occlusions (except for one young patient with a traumatic dissection) and used similar treatment techniques regardless of its presumed etiology.

Traversing an occluded vascular segment has been described in the coronary arteries, in bypass grafts, and in the extremities. In theory, there is a risk of dislodging more thrombi while crossing the stenosed segment. In our experience, this seems to be a real possibility, although the dislodged thrombi have fortunately responded to IA thrombolysis. The other concern with blindly probing an occluded artery is the risk of entering the false lumen of an ICA dissection. Fortunately, this has not happened in our experience. Thus, we advise gentle probing with a slightly curved microwire and avoidance of advancing the microwire against resistance to prevent iatrogenic dissection of an atherosclerotic lesion or entrance into the false lumen of a dissection. In the one patient presenting with ICA occlusion from a traumatic dissection, the true lumen was easily found by gentle probing with a soft, curved microwire.

After successful intracranial thrombolysis, one is faced with the management dilemma of the proximal ICA occlusion. If traversing the proximal ICA occlusion with the microcatheter and subsequent administration of thrombolytics has resulted in restoration of ICA flow, we have opted to angioplasty and stent the proximal ICA lesion because of concern for future thromboembolic events. The rationale for this approach lies in previously reported macroscopic or histopatho-

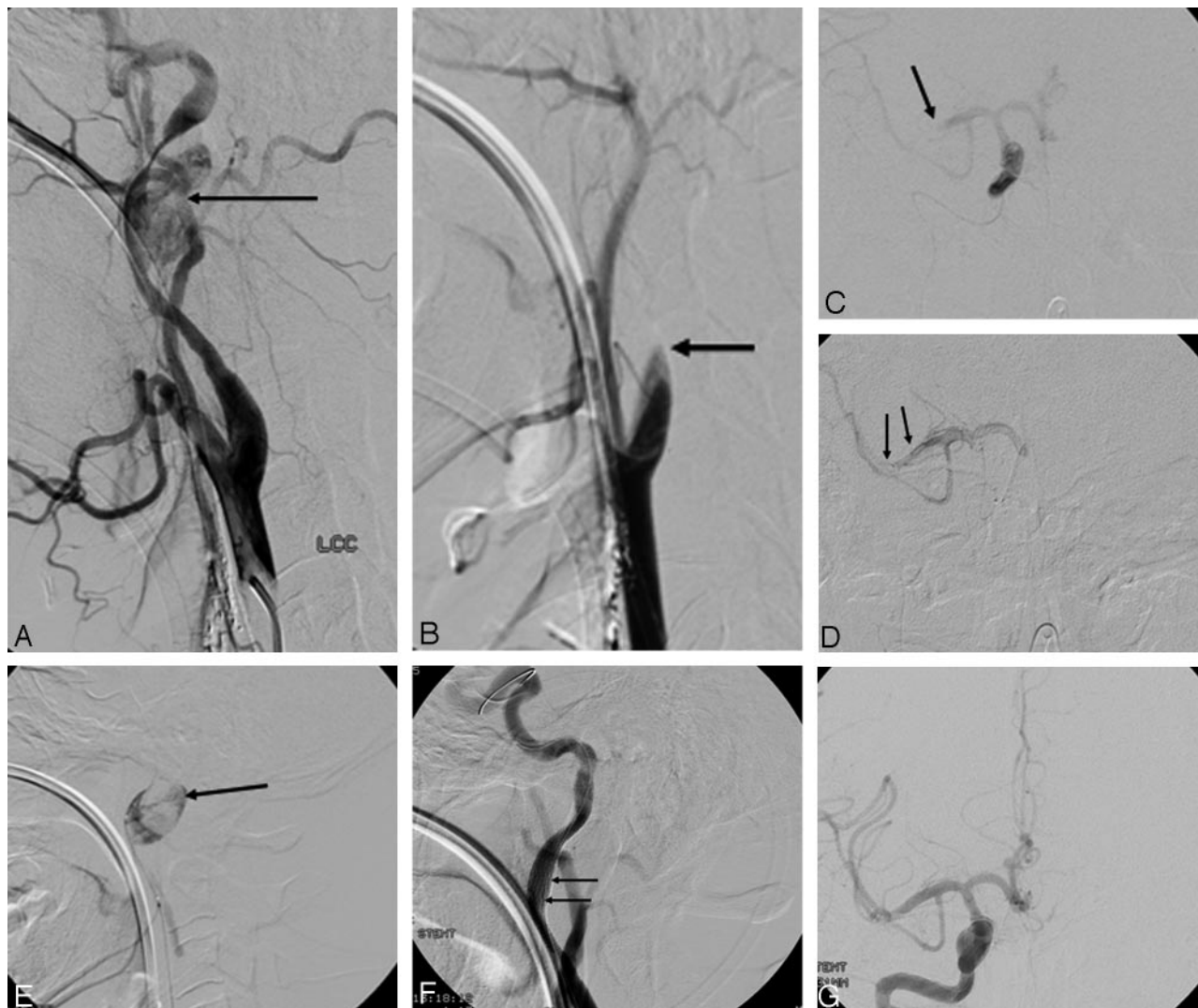


Fig 2. A, Lateral angiogram of the left common carotid artery (CCA) in a 24-year-old man with acute left hemiplegia reveals a pseudoaneurysm (arrow) in the distal cervical internal carotid artery (ICA) with narrowing of the parent artery.

B, The right CCA angiogram shows complete occlusion of the right ICA (arrow) just beyond the bulb.

C, Microcatheter injection demonstrates a thrombus in the distal M1 segment (arrow) of the middle cerebral artery (MCA).

D, Administration of 7.5 mg of intra-arterial tissue plasminogen activator (IA tPA) through the microcatheter, which was advanced into the face of the thrombus, resulted in lysis of thrombus and restoration of antegrade flow.

E, Microcatheter injections demonstrate a pseudoaneurysm in the distal cervical right ICA (arrow).

F and G, Repeat angiogram through the guiding catheter after successful treatment by using 2 overlapping covered stents reveals no filling of the pseudoaneurysm and normal flow in the MCA. The patient recovered complete power on the left side within minutes of the procedure. The left ICA dissection and pseudoaneurysm were managed conservatively and, at 2 months after the procedure, the patient had no neurologic deficits.

logic investigations, which have revealed that lesions of atherothrombotic ICA occlusion often have a thick atheroma plaque associated with fresh thrombus.¹⁶ Some plaques have demonstrated thrombi in areas showing intraplaque hemorrhage.¹⁷ This suggests to us that, if flow is restored in the ICA, the potential for thrombi to develop in areas of plaque hemorrhage exists and may be treated with angioplasty and stent placement. After intracranial thrombolysis, if there is demonstration of good collateral flow to the parenchyma despite a persistent ipsilateral ICA occlusion, we feel it is reasonable to leave the ICA occluded.⁸

In conclusion, performance of IA thrombolysis by passing a microcatheter through an acutely occluded internal carotid artery may be an effective therapy in a setting of acute stroke.

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