Preliminary clinical outcome of mechanical thrombectomy for acute anterior circulation ischemic stroke beyond 8 hour of symptom onset

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ABSTRACT: Objective To explore safety and efficacy of endovascular mechanical recanalization for acute ischemic stroke beyond 8 hour (h) of symptoms onset. **Background** AIS (acute ischemic stroke) therapy is often limited to an 8 h window using mechanical means. However, recent reports have shown delayed recanalization beyond 8 h might be a viable option in a subset of patients. **Methods** A retrospective review was performed of our AIS database for patients who underwent endovascular recanalization beyond 8 h of symptom onset. Clinical and angiographic data were reviewed. Outcome was measured using mRS (modified Rankin Scale) scores at 90 days. **Results** 5 patients (4 men and 1 woman) underwent delayed endovascular treatment for AIS. Mean age was 56.8 years (range 37-73) and mean NIHSS (National Institutes of Health Stroke Scale) was 13.8 (range 8- 24). Mean time from stroke onset to intervention was 10.2h (range 9-12 h). 4 patients presented with successful recanalization (TICI ≥ 2) and the remaining one had a TICI of 1. Recanalized vessels included: MCA M1 segment (n=3), ICA/ MCA (n=2). No patients had intracranial hemorrhage and died. Good outcome (90 day mRS of ≤ 2) was achieved in 3 patients, 2 patients had a 90 day mRS of 3 and 4, respectively. **Conclusion** Endovascular mechanical recanalization may be a safe and feasible approach in a selective group of patients with acute ischemic stroke beyond 8 h of symptom onset. Large cohort study is necessary in the future.
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Key words: mechanical thrombectomy; anterior circulation; ischemic stroke

INTRODUCTION

AIS (acute ischemic strokes) compromise up to 85% of strokes, and timely recanalization of these occlusions often leads to improved neurological outcome. [1-2] Current recommendations for thrombolytic therapy for stroke are limited to 4.5 h for intravenous therapy or 6 h for intra-arterial treatment and the time window of mechanical treatment is 8 h.[3,4] Endovascular mechanical thrombectomy has several theoretic advantages above thrombolytic therapy, such as the ability to deliver site-specific therapy, tailored thrombolytic dosage and delivery, extended treatment time windows, and higher recanalization rates. It also can be used as a rescue therapy in patients who have not responded to IV rtPA or as a combined therapy with other endovascular techniques. Further, all studies have been limited to a time window 8 h from stroke onset. However, it is reasonable in selected subgroups of patients to expect benefit from stent supported revascularization beyond the 8 h window. We here present our center experience in delayed recanalization beyond the 8 h window.

MATERIALS AND METHODS

Approval for collection of interventional and clinical data was given by the institutional review board. We retrospectively analyzed the angiographic and clinical data of 5 patients with ischemic stroke and occlusion in the anterior circulation who were treated with stent-retriever recanalization between May 2010 and October 2012.

All five patients underwent stroke MR imaging, including MRA and diffusion/perfusion imaging to demonstrate vessel occlusion and to assess the extent of salvageable brain tissue.

Inclusion criteria:

1) Severe neurologic deficit (4＜NIHSS＜25); 2) Major-vessel occlusion (ICA/M1/M2) on DSA; 3) Absence of early signs of a major infarction (more than one-third of the MCA territory) with simultaneously reduced perfusion in the territory of the occluded vessel on CT.

Exclusion criteria

Patients were excluded if any of the following was present: CT head showing completed infarct or hemorrhage, NIHSS ≤ 4 or ≥25, absence of diffusione-perfusion mismatch or those with greater than two-thirds middle cerebral artery (MCA) territory infarct.

Follow-up CT imaging was performed 24 h after the intervention or whenever significant neurologic worsening occurred. Symptomatic intracerebral hemorrhage was defined as neurologic

deterioration of at least 4 points on the NIHSS or death, together with blood at any site in the brain. Neurologic status was quantified by NIHSS at admission and discharge, and the modified Rankin Scale was assessed at discharge and at day 90 by a certified neurologist. Good outcome at 90 days was defined as mRS 0–2.

Mechanical modalities included solitare stent retriever, balloon angioplasty or self-expanding stent placement. Successful recanalization was defined as TICI ≥ 2. TICI 0 describes absence of perfusion beyond the occlusion site. TICI 3 is equivalent to complete perfusion.

RESULTS

5 patients (4 men and 1 woman) were included in this study. Mean age was 49 years (37-73). Mean NIHSS was 17 (range 8-24). Mean time from stroke onset to puncture was 66.1 h (range 10-168). The characteristics of clinical and imaging list on table 1.

Cerebral angiography indicated that all patients suffered from acute complete anterior circulation occlusion (TICI score of 0). The location of occlusion was M1 segment (n=3) and ICA/M1 (n=2).

Table 1 characteristics of clinical and imaging

Patient No	*Age (years)*	*Sex*	*Presentation*	*NIHSS*	*MRI (if available)*	**Perfusion MR**
1	37	M	Right hemiplegia and aphasia	8	Left basal ganglia, frontal operculum, insula, temporal and parietal lobe	Restricted perfusion within the MCA distribution beyond areas of diffusion restriction
2	50	M	Right hemiparesis and right hemibody numbness	10	The same as above	the same as above
3	67	M	Left hemiparesis	12	Right basial ganglia	the same as above
4	73	F	Right hemiparesis	24	Left basal ganglia, frontal operculum, insula, temporal and parietal lobe	Restricted perfusion within the ICA distribution beyond areas of diffusion restriction
5	53	M	Right hemiparesis	15	Left frontal, temporal and parietal lobe and basal ganglia	the same as above

Table 2 Angiographic, procedural details and 90 days mRS

Patient No	*Time to femoral puncutre*	*DSA*	*Pre-TICI*	*Mechanical recanalization*	*Post-TICI*	**90 days mRS**
1	9	M1 occlusion	0	solitare stent retriever	3	2
2	10	M1 occlusion	0	the same as above	2	3
3	9	M1 occlusion	0	balloon angioplasty	3	1
4	12	ICA/M1 occlusion	0	Stent placement	1	4
5	11	ICA/M1 occlusion	0	solitare stent retrieve	3	2

Solitare stent retrieval was attempted in 2 patients. Stenting placement and balloon angioplasty alone were done in each patients, no additional post-stent deployment balloon angioplasty was ferformed. Patients who underwent stenting placement and balloon angioplasty received double antiplatelet drugs (aspirin and clopidogrel), others did not received antiplatelet drugs within 24 h after endovascular therapy.

Afer intervention, all five patients presented with successful recanalization (TICI ≥ 2), one patient who presented with TICI scale 1 suffered from long segment ICA/M1 occlusion despite placement of two overlapping long self-expanding stents. Asymptomatic intracranial hemorrhage in the ganglionic region was founded in one patient by CT 24 h after intervention. No patients had symptomatic intracranial hemorrhage and died. At 90 days follow-up, 3 patients had a mRS score of ≤ 2, one patient had mRS score 3; the patient who underwent two stents placement but bad recanalization had progression of stroke in the postoperative period and poor neurological outcome (mRS 4). (table 2)

DISCUSSION

Recently, endovascular mechanical recanalization have been developed and play an increasing role in endovascular recanalization procedures. With these devices, high recanalization rates (89%–100%) and rapid recanalization with a good clinical outcome in a substantial number of patients can be achieved.[5,6] It has been shown that these devices

outperform conventional recanalization devices. The time interval for intravenous rtPA has been shifted from 3 to 4.5 hours after stroke onset.[7,8] However, there is evidence that patients with salvageable brain tissue benefit from thrombolytic treatment up to 9 hours after stroke onset.[9,10]

Diffusion and perfusion MRI (DWI and PWI) have been proposed to increase effectiveness in patient selection for endovascular mechanical recanalization without durg thrombolysis.

Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution (DEFUSE) 2 study[11] demonstrated that a defined target mismatch profile [PWI (time to maximum＞6 seconds) / DWI ≥1.8 and DWI <70 mL and PWI (time to maximum＞ 10 seconds)＜ 100 mL] and a defined time to maximum threshold may predict more accurately the likelihood of cerebral ischemia and clinical outcome. If a patient do not exist target mismatch profile, early reperfusion did not result in a reduction of infarct growth.

Correspondingly, patients with ischemic stroke who have MR imaging– proved diffusion/ perfusion mismatch may be candidates for endovascular mechanical interventions.

There are only a few reports of patients who underwent endovascular acute stroke treatment within an uncertain or extended time window. Natarajan et al[12] performed a retrospective review of 30 patients who underwent endovascular recanalization ＞ 8 hours after stroke onset. In this study, endovascular intervention included various techniques such as intra-arterial thrombolysis, mechanical thrombectomy by using the Merci device or intracranial stents (no stent-retriever devices), and angioplasty, with 20% of patients presenting with mRS 0–2 at 3 months. Findings in our study are similar, with unsatisfactory outcome in most patients despite high recanalization rates. Janjua et al have shown that clinical diffusion-perfusion mismatch can be used to select patients for endovascular therapy beyond 8 h.[13] Seventy-two per cent of their patients showed neurological improvement (NIHSS improvement of ≥ 4) post-recanalization.

Some interesting results were noted for stenting. These include a trend toward significance for extracranial internal carotid stenting, significant association with recanalization for the combination of angioplasty and stenting, significant association with complete recanalization for the combination of IV tPA with intracranial stent placement, and significant association with improvement in NIHSS. Of note, stent placement was only performed if other modalities had failed or for extracranial carotid occlusions. There are several reports in the literature for use of intracranial [14,15] as well as extracranial carotid stenting in acute stroke setting and their effectiveness in achieving recanalization and restoring blood flow.[16] Intracranial stenting is mostly reported as rescue intervention after failure of other pharmacological and mechanical modalities. The results of our study further corroborate the potential of stent placement in the acute ischemic strokes of anterior cerebral circulation.

We acknowledge that there are several limitations of this study. First, the data were reviewed retrospectively; however, we feel that the results are clinically relevant especially given the fact that no prospective studies have yet been published. Second, this study includes patients with acute ischemic stroke in the anterior cerebral circulation only; hence, the results of this study cannot be applied to patients with stroke in the posterior cerebral circulation. Third, the number of patients in each group was small which decreased the power of our study in detecting some significant differences among different groups. However this is also a limiting factor in most published reports on the subject. Fourth, the study lacks long-term follow-up, the fact that is related mainly to the retrospective nature of this study; this precludes any correlation of recanalization rates to long-term outcomes. The limitations of the study indicate the need for a large controlled prospective multicentre trial to determine the best multimodality approach for the treatment of patients with acute ischemic stroke beyond 8 h of symptom onset.

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