LETTER TO THE EDITOR

Safety and Efficacy of Stent-Supported Thrombolysis in Acute Ischemic StrokeJing-Cheng Li,¹ Chuan-Qin Fang,¹ Chang-Yue Gao,¹ Jian-Hong Wang,¹ Bing-Hu Li,¹ Hong Yang² & Li-Li Zhang¹¹ Department of Neurology, Institute of Surgery Research, Daping Hospital, Third Military Medical University, Chongqing, China² Department of Nursing, Chongqing Medical and Pharmaceutical College, Chongqing, China**Correspondence**

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Stroke is the primary cause of disability and death worldwide, of which ischemic stroke accounts for 70–85% of stroke events [1]. Acute arterial stenosis or occlusion is responsible for 70% of ischemic stroke. Thrombolysis in ultra-early stage can get recanalization and improve outcome. Besides the traditional intravenous thrombolysis, novel techniques for recanalization of occluded arteries, including mechanical opening techniques [2, 3] have developed in recent years. This study compared the safety and efficacy of pharmacologic thrombolysis and stent-supported thrombolysis in acute ischemic stroke, in an aim to identify an optimal strategy for treatment of ischemic stroke.

Thirty-four patients with acute cerebral infarction due to occlusion or $\geq 50\%$ stenosis in middle cerebral artery (MCA) or intracranial internal carotid artery were retrospectively studied. Nineteen patients underwent pharmacologic thrombolysis (group P) and 15 patients underwent stent implantation thrombolysis (group S).

Endovascular treatment was performed with Digital subtraction angiography. In brief, microcatheter was placed in the proximity of thrombus through 6-French guide catheter. Urokinase (100,000 U) was infused via microcatheter with additional injection (10,000 U/min) until the artery got recanalization or the total amount of urokinase reached 800,000 U [3, 4]. Stent implantation was directly performed if the microguidewire could get across the lesion. Sometimes urokinase was administered in advance of stenting [4]. Aspirin and Clopidogrel were applied for 3–6 months and low molecular weight heparin was applied for 5 days after stenting.

Satisfied recanalization was accepted when the intervened arteries got residual stenosis less than 30%, or TIMI (thrombolysis in myocardial ischemia) score ≥ 2 level after thrombolysis [5]. Re-

occlusion was defined when the recanalized arteries got $\geq 50\%$ stenosis 24 h after operation. National Institutes of Health Stroke Scale (NIHSS) scores were assessed immediately after operation, at discharge, 1 and 3 months postoperation. NIHSS improving ≥ 4 points was considered as good clinical outcome [3].

For statistical analysis, the SPSS statistical package was used. Means and frequencies were compared using nonpaired *t*-test and Fisher's exact test. The $P < 0.05$ was considered as significantly different.

Baseline characteristics are presented in Table 1. The most common location of occlusion was MCA in both groups. The average time of hospitalization in group S was much shorter than that in group P ($P = 0.03$).

Compared with group P, patients in group S got better recanalization with low average residual stenosis (18% vs. 44.2% $P = 0.004$). There were 73% patients in group S, whereas 37% in group P, got acceptable residual stenosis ($\leq 30\%$) ($P = 0.02$), and 100% patients in group S acquired a ≥ 2 TIMI score compared to the 68% in group P ($P = 0.02$). Unsatisfied recanalization (residual stenosis $> 50\%$) was found in 13% patients in group S but in 32% patients in group P. (Figure 1, Table 1).

The ratio of patients who displayed ≥ 4 increase of NIHSS score was 73% at discharge and 87% at 1 and 3 months after operation in group S, whereas in group P, this ratio was 37%, 47%, and 53% respectively. ($P < 0.05$ at discharge and 1 month postoperation) (Table 1).

Intracranial hemorrhage occurred in two patients in group P and one patient in group S. The patient in group S died of cerebral hernia 3 days later. Two patients in group P survived with poor outcomes. Three of 7 patients (43%) in group P and 1 of 12

Table 1 Baseline characteristics, surgery-related characteristics and perioperation clinical results of patients

Parameters	Total (n = 34)	Group P (n = 19)	Group S (n = 15)	P value
Age (years)	66.7 ± 1.0	67.6 ± 1.3	65.7 ± 1.6	0.35
Male/female	18/16	11/8	7/8	0.73
Location of occlusion				
Internal carotid artery, intracranial part	15 (44%)	9 (47%)	6 (40%)	0.74
Cerebral middle artery, M1/M2 parts	19 (56%)	10 (53%)	9 (60%)	0.74
Preoperation average TIMI (level)	0.76 ± 0.13	0.68 ± 0.15	0.87 ± 0.22	0.48
NIHSS score at admission	17.1 ± 0.9	16.1 ± 1.2	18.3 ± 1.3	0.20
Time from onset to operation (min)	225 ± 6.1	220 ± 9.4	231 ± 7.1	0.43
Hospitalization time (days)	16.0 ± 0.9	17.7 ± 1.2	13.8 ± 1.1 ^a	0.03
Average stenosis, (%)				
Preoperation	90 ± 2.0	89 ± 3.0	91 ± 2.5	0.67
Postoperation	32.7 ± 4.7	44.2 ± 6.4	18.0 ± 4.9 ^a	0.004
Residual stenosis ≤30%, n (%)	19 (56%)	7 (37%)	12 (73%) ^a	0.02
Residual stenosis >50%, n (%)	8 (24%)	6 (32%)	2 (13%)	0.25
Postoperation TIMI ≥2 grade, n (%)	28 (82%)	13 (68%)	15 (100%) ^a	0.02
NIHSS increase ≥4 points, n (%)				
Immediately after recanalization	3 (8.8%)	1 (5.3%)	2 (13%)	0.57
At discharge	18 (53%)	7 (37%)	11 (73%) ^a	0.045
1 month postoperation	21 (62%)	9 (47%)	13 (87%) ^a	0.029
3 months postoperation	23 (68%)	10 (53%)	13 (87%)	0.064
Symptomatic intracranial haemorrhage/death, n (%)	3 (9%)	2 (11%)	1 (7%)	1.0
Reocclusion within 24 h after operation, n (%)	4 (12%)	3 (43%)	1 (8%)	0.29

Continuous variables were presented as means ± SD.

^a*P* < 0.05 versus group P.

patients (8%) in group S got reocclusion more than 50% within 24 h postoperation, although no significant difference (*P* = 0.29) was observed (Table 1).

To date, the recommended standard method for recanalization is intravenous thrombolysis using t-PA (tissue-plasminogen activator), expanded to 4.5 h after clinical onset [6]. However, this strategy was only in limited used due to very short therapeutic window and uncertain efficacy [7]. Recently, intraarterial thrombolysis has been reported to provide a better recanalization rate in anterior circulation within 6 h of onset. In PROACT and PROACT II trial, the recanalization rate of intraarterial pharmacologic thrombolysis reached 57% and 66%. However, this approach also displayed high reocclusion and hemorrhage incidence and unsatisfied clinical prognosis [8,9]. In the present study, the recanalization rate of intraarterial thrombolysis using urokinase alone was 37%. The ratio of patients with good outcome was 37%, 47% and 53% respectively at discharge, 1 and 3 months after operation. The reocclusion rate was 43% and intracranial hemorrhage rate was 11% in these patients. These results indicated low recanalization and unsatisfied outcome in patients underwent pharmacologic intraarterial thrombolysis.

Stent-supported thrombolysis combined with or without urokinase has rapidly developing in recent years and was accepted as

an alternative strategy for recanalization of occluded arteries, although the efficacy and safety need to be further investigated. In this study, the recanalization rate of stent-supported thrombolysis was 73%. Besides, 100% patients acquired a ≥2 TIMI score after stenting. Recanalization of occluded intracranial arteries within 6 h of symptom onset has been demonstrated to be effective in improving long-term outcome in patients with acute ischemic stroke [10]. Not surprisingly, we found that stent-supported thrombolysis gave better clinical outcome than pharmacologic thrombolysis at discharge and 1 month postoperation.

One patient in group S got intracranial hemorrhage and died of cerebral hernia, indicating that stenting should be used very cautiously in patients with bleeding tendency or intensely curved pathway.

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Figure 1 Recanalization of occluded arteries after thrombolysis detected by DSA. (A, B) Occluded MCA was partially recanalized after pharmacologic thrombolysis by urokinase, with incomplete and slow filling of the vascular territory (TIMI score =2). (C, D) Occluded MCA got optimal recanalization after stent-supported thrombolysis (TIMI score =3).

References

1. Yu JG, Zhou RR, Cai GJ. From hypertension to stroke: Mechanisms and potential prevention strategies. *CNS Neurosci Ther* 2011;**17**:577–584.
2. Choi JH, Bateman BT, Mangla S, et al. Endovascular recanalization therapy in acute ischemic stroke. *Stroke* 2006;**37**:419–424.
3. Seifert M, Ahlbrecht A, Dohmen C, Spuentrup E, Moeller-Hartmann W. Combined interventional stroke therapy using intracranial stent and local intraarterial thrombolysis (LIT). *Neuroradiology* 2011;**53**:273–282.
4. Gupta R, Schumacher HC, Mangla S, et al. Urgent endovascular revascularization for symptomatic intracranial atherosclerotic stenosis. *Neurology* 2003;**61**:1729–1735.
5. Higashida RT, Furlan AJ, Roberts H, et al. Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke. *Stroke* 2003;**34**:e109–e137.
6. Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *N Engl J Med* 2008;**359**:1317–1329.
7. Qureshi AI, Siddiqui AM, Kim SH, et al. Reocclusion of recanalized arteries during intra-arterial thrombolysis for acute ischemic stroke. *AJNR Am J Neuroradiol* 2004;**25**:322–328.
8. del Zoppo GJ, Higashida RT, Furlan AJ, Pessin MS, Rowley HA, Gent M. PROACT: A phase II randomized trial of recombinant pro-urokinase by direct arterial delivery in acute middle cerebral artery stroke. PROACT Investigators. *Stroke* 1998;**29**:4–11.
9. Furlan A, Higashida R, Wechsler L, et al. Intra-arterial prourokinase for acute ischemic stroke. The PROACT II study: A randomized controlled trial. *Stroke* 1999;**30**:2003–2011.
10. Pulsinelli WA, Waldman S, Rawlinson D, Plum F. Moderate hyperglycemia augments ischemic brain damage: A neuropathologic study in rats. *Neurology* 1982;**32**:1239–1246.