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Clinical Article

The Comparison of Outcome between Thromboaspiration and Aggressive Mechanical Clot Disruption in Treating Hyperacute Stroke Patients

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Objective : Stroke is the third leading cause of death in the Republic of Korea. Time is the most important factor in hyperacute stroke. Yet, there had been no protocol for mechanical thrombolysis. We have treated patients with hyperacute stroke by mechanical thrombolysis for 3 years. In current study, we analyzed the outcome of mechanical thrombolysis.

Methods : From March 2008 to February 2011, 36 patients were treated with mechanical thrombolysis. Initially we treated the patients by aggressive mechanical clot disruption (AMCD) who were admitted within 6 hours after the symptom onset. If revascularization was not achieved, balloon angioplasty was performed, followed by stenting or temporary endovascular bypass was performed. The result in 15 cases was not so successful. Since then, we started using the thromboaspiration method as the first line treatment of the mechanical thrombolysis.

Results : After using the thromboaspiration, we had better results in recanalization rate, modified Rankin Score (mRS) and reperfusion injury compared to AMCD. The recanalization rate was 80.85%, mRS is 2.85, and there was only 0.09% hemorrhagic formation.

Conclusion : Even though thromboaspiration is not statistically significant due to the limited numbers of patients enrolled in this study, we think it is a good way in mechanical thronbolysis for hyperacute stroke.

Key Words : Aspiration · Mechanical · Stroke · Acute · Thrombolysis.

INTRODUCTION

The stroke remain as the third most common cause of death in industrialized nations, after myocardial infarction and cancer, and the single most common reason for permanent disability[13]. The primary aim of acute ischemic stroke therapy is to reestablish blood flow to critically ischemic but salvageable brain tissue within the ischemic penumbra[15]. Timely treatment and intervention can minimize the long-term disability by salvaging the at-risk penumbra and, consequently, reducing the associated morbidity and mortality[4].

Currently, the only one known causal drug therapy for ischemic stroke is thrombolysis with recombinant tissue plasminogen activator (rt-PA), which has been proven in many clinical trials to be effective in improving the clinical outcome and reducing subsequent disability[5-7,12,15,16]. Despite treatment with intravenous rt-PA, 58% of the patients still ended up with death or disability as a consequence of the stroke[3]. Intravenous thrombolysis with rt-PA is associated with improved clinical outcomes in patients with acute ischemic strokes, and the approved time window for the application of rt-PA treatment is currently within 3 hours of symptom onset[1]. However, a large proportion of patients are admitted or notified after the 3 hours time window[15]. Only a minority of patients with ischemic stroke actually receive this treatment because of the lack of approval for the use of thrombolytic agent after 3 hours time window[8,11,18].

Endovascular therapy has several theoretic advantages over intravenous rt-PA, it includes site specificity, longer treatment windows, and higher recanalization rates[2,10]. This approach allows a thrombolytic agent to be injected right near any occluded site, and more advanced mechanical and stenting techniques have enabled us to perform successful balloon dilatation or emergency reperfusion. In the beginning, we used a microcatheter and microwire to break up blood clots and injected a thrombolytic agent to guide reperfusion. Recently, however, as the Penumbra device for thrombus aspiration was introduced, we undertook this study on the assumption that good results can

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be obtained by using Penumbra device in the first line treatment of a thrombolysis procedure.

MATERIALS AND METHODS

Patient selection

We conducted a retrospective study of patients who brought at the emergency room between March 2008 and February 2011. For a patient suspected of having acute ischemic stroke from a neurological examination, a stroke team was summoned from the hospital's stroke center to exam the patient.

Diagnostic methods used to determine the presence of cerebral hemorrhage or cerebral infarction included blood testing, electrocardiography, diffusion magnetic resonance imaging (MRI), and brain computerized tomography. If a patient arrived within three hours of symptom onset, a loading dose of intravenous rt-PA was injected to the patient, followed by maintenance dose. In the meantime, perfusion MRI and magnetic resonance angiogram were taken on the patient to see if there was any micro-hemorrhage or a mismatch in the MRI of the brain with diffusion and perfusion imaging. Intra-arterial thrombolysis was performed for patient who showed no improvement in the National Institutes of Health Stroke Scale (NIHSS) score. The intra-arterial thrombolysis was selected as mean treatment when there was a diffusion-perfusion mismatch, large vessel occlusion on cerebral MRI, absence of microbleeding on gradient-echo images, or when no signal change was found on flair images and T2-weighted images. If three hours had passed since symptom onset, the brain MRI was immediately used to determine whether intra-arterial thrombolysis could be performed.

A total of 36 patients were selected for the study, who 15 patients received aggressive mechanical clot disruption (AMCD) and other 21 patients received thromboaspiration. Then, the following categories were compared NIHSS after treatment between patients who received AMCD and thromboaspiration, mechanical thrombolysis approach method, the hours from symptom onset to hospital arrival, the use or non-use of rt-PA, the hours from hospital arrival to reperfusion, and modified Rankin score (mRS).

Statistical analysis was performed using Statistical Product and Service Solutions. A Pearson correlation index was used. Statistical significance was established when $p<0.05$.

Procedures

Most patients underwent intervention under general anesthesia, and 7 Fr. femoral long sheath was used in the procedure. Initial heparinization was performed by intravenous bolus injection of 3,000 units, followed by injecting 1,000 units every hour. Angiography was performed first in three other intact vessels to see if there were any other cerebrovascular lesions and presence of collateral vessels, and finally at occlusion site was detected by cerebral MRI. 6 Fr. guiding catheter which was usually used in anterior circulation was placed into the site of occlusion for angiography, and a buddy wire was used to support unstable guiding catheter during the procedure.

For 15 patients, after placing a microcatheter into the occlusion site with a microwire, we attempted to break up the blood clot by moving the guide wire back and forth. In case this procedure aborted, a thrombolytic agent was injected intra-arterially in a pulsatile manner and the microwire was used to dissolve the clot during the injection. When the method still did not work, we attempted reperfusion through balloon dilatation or stent insertion.

In the other 34 patients, the Penumbra system (Penumbra, Almenda, California) was used as it currently became available in Korea. Thrombolysis was performed using a reperfusion catheter of the Penumbra system, and thrombus aspiration was attempted using a 20 cc syringe instead of the suction device contained in the system. The adopted reperfusion catheter was a 0.026-inch catheter, the smallest one of the reperfusion catheters in the penumbra system. A microwire was used to place the catheter properly beyond the site of occlusion. After that, a contrast medium was injected at the same time through the guiding catheter and the reperfusion catheter (double angiogram), so that the shape and the area of occlusion were identifiable. If the occlusion site was involved in distal segments, and not a large vessel, thrombolysis was performed with the microcatheter and microwire, but if the site was associated with a large vessel or multiple segments, the reperfusion catheter was positioned into the distal portion of the clot and held in place with a sufficient negative pressure produced by a 20 cc syringe. The next action was to move the catheter slowly into the proximal portion. Once the catheter passed by the clot region, blood regurgitated fast into the syringe. After that, the catheter was completely removed so that angiography can be performed again. If reperfusion occurred in any form or if there

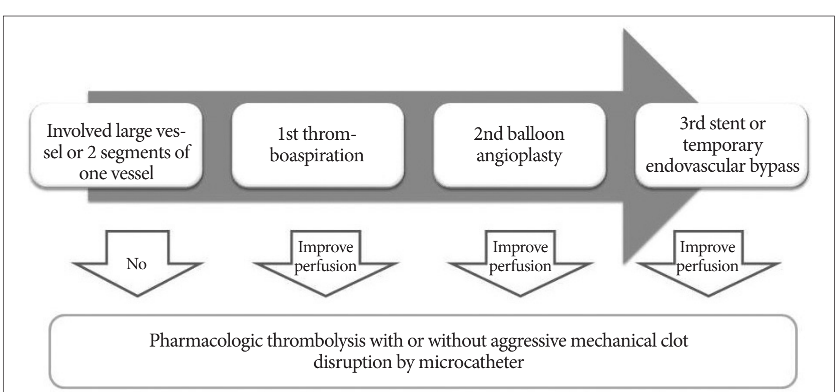

Fig. 1. Treatment sequence of mechanical thrombolysis.

was an improvement in TICI grade, the microcatheter was used to dissolve the clot, with the thrombolytic agent being administered. In case of reperfusion failure, balloon angioplasty was selected. However, this procedure was not used in the regions of perforating vessels. When reperfusion was not achieved even by balloon angioplasty, we attempted reperfusion by using a stent and sometimes adopted a temporary endovascular bypass technique (Fig. 1).

RESULTS

Thirty-six patients out of 935 patients with acute ischemic stroke were treated with intra-arterial thrombolysis (Table 1). Fifteen patients underwent aggressive mechanical clot disruption as the first treatment and the other 21 received thrombus aspiration. All the patients had hyper-acute ischemic stroke caused by intracranial vessel occlusion and their mean age was

Table 1. Summary of the patients

Case	Sex/Age	Initial mental status	NIHSS*	Occluded vessel	DTN (hour)	DTP (hour)	DTR (hour)	Tx. modality	mRS
1	F/73	Semicoma	23, D	VA	1.5	4.2	5.3	AMCD	6
2	F/69	Drowsy	15, D	T-seg.	2.06	5	No	AMCD	6
3	F/88	Semicoma	25, D	BA	No	4.5	5.6	AMCD	6
4	M/86	Drowsy	8, 2	VA	1.25	2.9	5	AMCD	2
5	M/67	Drowsy	15, D	VA	No	4.3	6.3	AMCD	6
6	M/51	Drowsy	11, D	M1, Rt.	No	2.56	No	AMCD	6
7	M/65	Stupor	31, 15	BA	No	2	5.5	AMCD	2
8	M/42	Drowsy	8, 0	M2	No	3	4.5	AMCD	0
9	M/78	Drowsy	15, 15	T-seg.	0.88	3.71	No	AMCD	3
10	M/87	Drowsy	12, 15	M2	No	2.38	No	AMCD	3
11	F/82	Stupor	18, 38	T-seg.	0.75	3.6	6.6	AMCD	5
12	M/72	Drowsy	11, 15	M2	No	1.95	No	AMCD	3
13	F/70	Drowsy	9, D	T-seg.	1.4	4	No	AMCD	6
14	F/66	Drowsy	17, 9	M1	No	2.63	4	AMCD	3
15	F/73	Drowsy	10, 3	M1	1.18	2.1	No	AMCD	2
16	F/86	Drowsy	11, 16	M1	0.88	3.61	5.16	Thromboaspiration	2
17	F/82	Drowsy	12, 21	T-seg.	1	3	No	Thromboaspiration	4
18	F/81	Stupor	23, D	T-seg.	1.56	4	No	Thromboaspiration	6
19	F/69	Drowsy	5, 0	M2	No	4	5.5	Thromboaspiration	0
20	M/61	Drowsy	15, 22	M2	No	3	6	Thromboaspiration	5
21	M/58	Drowsy	9, 0	BA	No	4.03	6.75	Thromboaspiration	0
22	M/51	Drowsy	4, 1	M2	No	2.5	5.2	Thromboaspiration	1
23	M/40	Stupor	23, D	VA	0.9	3.4	5.13	Thromboaspiration	6
24	M/66	Drowsy	20, 30	VA	0.86	3	5	Thromboaspiration	5
25	F/87	Stupor	20, 20	M2	0.96	2.83	5	Thromboaspiration	4
26	M/73	Drowsy	5, 1	M1	No	2.4	5.21	Thromboaspiration	1
27	M/72	Semicoma	26, 16	BA	No	4.4	7.6	Thromboaspiration	3
28	M/42	Stupor	23, 1	VA	No	4.5	10.5	Thromboaspiration	1
29	M/72	Drowsy	3, 1	M2	No	3	5	Thromboaspiration	1
30	F/37	Drowsy	16, 1	T-seg.	0.71	2.25	4.03	Thromboaspiration	1
31	M/71	Drowsy	13, D	T-seg.	0.68	4.26	No	Thromboaspiration	6
32	M/72	Drowsy	8, 3	M1	0.98	4.13	6.36	Thromboaspiration	1
33	M/48	Drowsy	10, D	M1	0.83	4	4.91	Thromboaspiration	6
34	M/70	Drowsy	11, 38	M1	1.56	4.98	No	Thromboaspiration	5
35	M/62	Drowsy	8, 1	M2	1.5	3.35	4.08	Thromboaspiration	1
36	M/58	Drowsy	7, 1	M1	No	3.53	5.27	Thromboaspiration	1

*Initial number is NIHSS at admission and second number is NIHSS at discharge. AMCD : aggressive mechanical clot disruption, BA : basilar artery, CAS : carotid angioplasty, D : death, DTN : door to needle, the time from admission to I.V. tissue plasminogen activator (t-PA), DTP : door to puncture, the time from admission to femoral puncture, DTR : door to recanalization, the time from admission to recanalization that occluded vessel is opened. F : female, ICA : internal cerebral artery, NIHSS : National Institutes of Health Stroke Scale, M : male, M1 : middle cerebral artery segment 1, M2 : middle cerebral artery segment 2, M3 : middle cerebral artery segment 3, mRS : modified Rankin score, O : do as the protocol that I mentioned, T-seg. : ICA bifurcation, Tx : treatment, VA : vertebral artery, X : do not as the protocol that I mentioned

67.42. The male-to-female ratio of the patients was 22 : 14. The mean NIHSS at admission was 13.89 and 26 patients showed occlusion in the anterior circulation of the brain and 10 patients showed occlusion in the posterior circulation. Out of the 36 patients, intravenous rt-PA was injected in 19 patients with mean arrival to injection time of 1.13 hours. The mean arrival to femoral artery puncture was 3.41 hours, and after puncture was performed, mean 2.18 hours was required for circulation.

The mRS at three months after discharge was closely related to NIHSS, especially to NIHSS at 24-hours after procedure (p=0.000) and was improved with the use of rt-PA (p=0.028). The patients with spouse definitely had greater chance of receiving rt-PA because of the presence of their caretaker (p=0.022).

In relation to the time taken until the recirculation after femoral artery puncture, the time taken was shorter in case that rt-PA was used. It should be noted that, more remarkable difference was found in the case that thrombus aspiration was performed as the first thrombolysis procedure (Table 2). When thrombus aspiration was used as the first treatment, the recanalization rate was 80.85%, higher than in the group who thromboaspiration was not used, and the possibility of cerebral hemorrhage and complications by reperfusion after the operation was 0.09%. Also, mortality was lower in patient who received thromboaspiration, 19.04% compared to AMCD, 40%.

Thromboaspiration group of the mean NIHSS at discharge and mRS (15.76, 2.85, respectively) were lower than AMCD group (24.5, 3.93, respectively). But, the difference between the thromboaspiration group and the AMCD group is not statistically significant.

DISCUSSION

Among the procedures for stroke, mechanical thrombolysis techniques have been applied by using a number of apparatuses, but it is considered most import to adopt an optimum treatment for the patient. Before the reperfusion catheter of the Penumbra system was introduced, there were some problems in using thrombus aspiration, which include the difficulty of reaching occlusion site and bending or closing of the catheter due to weak resistance to negative pressure. However, those problems have been solved by the reperfusion catheter. The brand-new catheter can reach the distal occlusion site easily and withstand a strong negative pressure, and thus thrombus aspiration can be performed more effectively.

The different sized reperfusion catheters were available, which are 0.026 inch, 0.032 inch and 0.041 inch. We selected the shortest one in diameter. The reason was that most of the patients had developed arteriosclerosis, so we thought that it would be difficult for a large-diameter catheter to reach up to desired portion whereas a small-diameter catheter is more flexible and can pass weak portion of the blood clot better. We also thought that the smaller-diameter catheter would be able to easily break blood clot once reperfusion is done and that the blood clot would move to the distal portion and melt down.

After performing angiography, we located a reperfusion catheter in the proximal portion of the occlusion site, got a microwire pass through the occlusion site, and then, located a reperfusion catheter up to the distal portion. At this time, we assumed that the microwire would pass through the softest portion of blood clot, and we also thought that the existence of the soft portion means that the clot itself is not hard. After that, through guiding catheter and reperfusion catheter, we injected a contrast medium and carried out double angiogram. The contrast medium, which came from the reperfusion catheter located in the distal portion, flow backwards to the proximal portion, through which we could see the range of the blood clot that caused occlusion (Fig. 2). The reperfusion catheter provides effect of macerating blood clot while passing through the occlusion site with the contrast medium when double angiogram was given. Through this we can predict the composition of blood clot. That is, we can presume that occlusion was caused by hard clot if cut-off in distal thrombus was found on the double angiogram, and presence of soft blood clot was presumed if the occlusion site was filled with the contrast medium even a little. In order to shorten the time for operation, we located the reperfusion catheter in the distal portion of blood clot, connected a 20 cc syringe, and gave a negative pressure (Fig. 3). After that, we took out the catheter to the proximal portion of the blood clot. When the catheter passed through the blood clot, blood regurgitated into the syringe fast. Then, we removed the catheter and conducted angiography.

Table 2. Comparison between mechanical clot disruption and thromboaspiration as first line treatment

	AMCD	Thromboaspiration
Mean age	71.26	64.67
Sex (M/F)	8/7	14/7
Mean NIHSS (at admission/at discharge)	15.2/24.5	12.95/15.76
Lesion site (A/P)	10/5	16/5
rt-PA or no use	7/8	12/9
Recanalization rate	53%	80.85%
Hemorrhagic formation	26%	0.09%
PTR (hours)	With rt-PA : 2.07	With rt-PA : 1.64
	Without rt-PA : 2.0	Without rt-PA : 2.85
Mortality	40%	19.04%
mRS	3.93	2.85

A : anterior circulation, AMCD : Aggressive Mechanical Clot Disruption, F : Female, M : Male, mRS : modified Rankin Score, NIHSS : National Institutes of Health Stroke Scale, P : posterior circulation, PTR : puncture to recanalization, the time between femoral puncture time and recanalization time, rt-PA : recombinant tissue plasminogen activator

Thrombus aspiration reduces the quantity of blood clot, prevents blood clot from migrating while the procedure is performed, and also reduces the time taken for using a suction device in penumbra system. We also thought that aspiration could be done without blocking blood flow in the proximal portion during aspiration.

In recanalization was not established even after above procedures, interventionists had to make difficult choice about next procedure. There is a guideline that balloon dilatation cannot be used for segments that make branching vessels because if balloon dilatation is performed in the portion that has many perforating vessels, blood clot can cause occlusion in branches. Therefore, we selected balloon dilatation for the segment that has no branches, and we selected a stent or temporary endovascular bypass for the portion which has a lot of perforating vessels. Selecting this sequential procedure method will help both interventionist and patient not to waste time and for better patient's prognosis, respectively. However, for occlusion of the internal carotid artery (ICA) bifurcation, other method may be necessary because we experienced that in this case, thrombus aspiration allowed the circulation successful recanalization, but after balloon dilatation, blood clot moved and caused anterior cerebral artery occlusion. Thus, we think that the quantity of blood clot in ICA bifurcation is greater than that in other cerebral arteries and also has the hardest composition. Therefore, for the patients with occlusion of the ICA bifurcation, blood flow occlusion in the proximal portion may be necessary when thrombus aspiration or other procedures is performed.

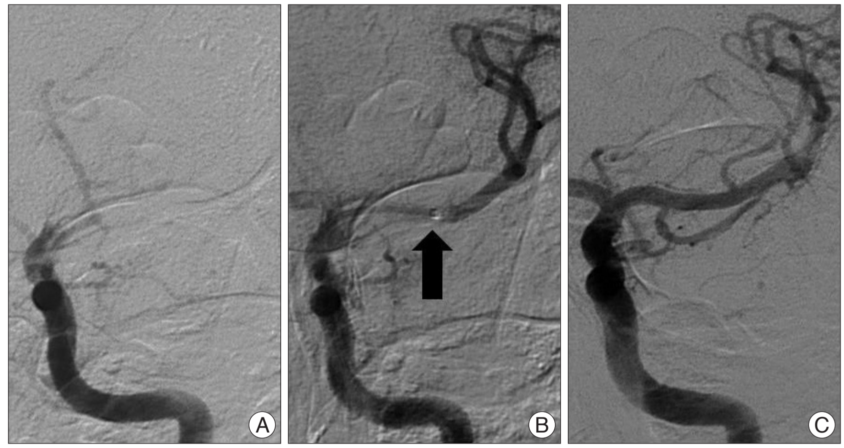

Fig. 2. The angiogram of the Mechanical thrombolysis. A : This angiogram shows the T-segment occlusion of left carotid artery. B : The angiogram was performed through the guiding catheter and the reperfusion catheter. The black arrow indicates the back flow to the distal thrombus. C : After thromboaspiration and balloon angioplasty, the occlusion of the T-segment was recanalized in the status of TICI grade 3.

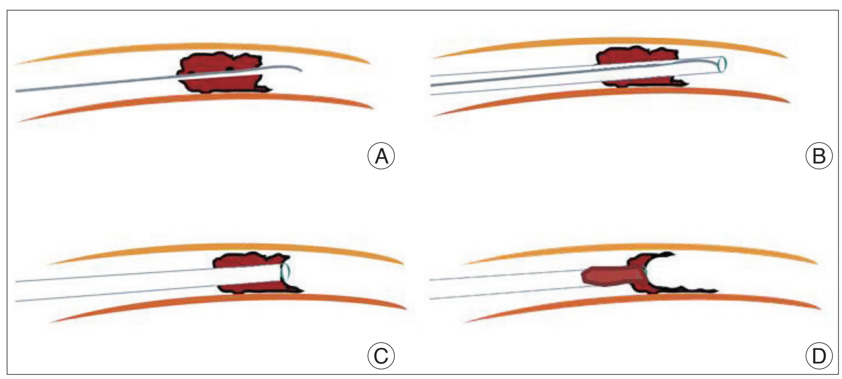

Fig. 3. The process of the thromboaspiration. A : The microwire passing through the occlusion site. B : The reperfusion catheter passing through the occlusion site along the microwire. C : The reperfusion catheter located in the distal portion of the occlusion site. D : The thrombus aspirated by the negative pressure.

We believe that when a patient arrives quickly at the hospital and rt-PA is applied, recanalization can be established through intra-arterial thrombolysis faster. After recanalization, the patient's NIHSS was improved in an average of six hours, so it is thought that patients' prognosis will be mostly determined within six hours.

CONCLUSION

We have assessed intra-arterial thrombolysis treatment in hyperacute stroke patients for the past three years since the opening of our hospital's stroke center. The initial treatment of choice couldn't be determined because of the limited statistical data we have gathered. But revascularization rate is higher and complication rate is lower on the thromboaspiration treatment group than the AMCD group. Follow up study with sufficient data is required to get more statistical significance and to support our conclusion.

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