INTRODUCTION

The stroke remains 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. The primary aim of acute ischemic stroke therapy is to re-establish blood flow to critically ischemic but salvageable brain tissue within the ischemic penumbra. Timely treatment and intervention can minimize the long-term disability by salvaging the at-risk penumbra and, consequently, reducing the associated morbidity and mortality.

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. Despite treatment with intravenous rt-PA, 58% of the patients still ended up with death or disability as a consequence of the stroke. 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. However, a large proportion of patients are admitted or notified after the 3 hours time window.

Endovascular therapy has several theoretic advantages over intravenous rt-PA, it includes site specificity, longer treatment windows, and higher recanalization rates. 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 be achieved.
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 to 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 examine 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 computed 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, Alameda, 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

| 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.
Among the procedures for stroke, mechanical thrombolysis techniques have been applied by using a number of apparatus, but it is considered most important 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 occlusion site, move to the distal portion and melt down.

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### DISCUSSION

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### 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) | 15.2/24.5     | 12.95/15.76       |
| (at discharge)           |               |                   |
| 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.

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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