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Clinical Article

Multimodal Therapy for Patients with Acute Ischemic Stroke : Outcomes and Related Prognostic Factors

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Objective : The objectives of this study were to analyze the recanalization rates and outcomes of multimodal therapy that consisted of sequential intravenous (IV)/intra-arterial (IA) thrombolysis, mechanical thrombolysis including mechanical clot disruption using microcatheters and microwires, balloon angioplasty, and stenting for acute ischemic stroke, and to evaluate the prognostic factors related to the outcome.
Methods : Fifty patients who were admitted to the hospital within 8 hours from ischemic symptom onset were retrospectively analyzed. Initial IV thrombolysis and subsequent cerebral angiography were performed in all patients. If successful recanalization was not achieved by IV thrombolysis, additional IA thrombolysis with mechanical thrombolysis, including balloon angioplasty and stenting, were performed. The outcomes were assessed by the National Institute of Health Stroke Scale (NIHSS) change and modified Rankin scale (mRS) and prognostic factors were analyzed.
Results : Successful recanalization was achieved in 42 (84%) of 50 patients, which consisted of 8 patients after IV thrombolysis, 19 patients after IA thrombolysis with mechanical clot disruption, and 15 patients after balloon angioplasty or stenting. Symptomatic hemorrhage occurred in 4 (8%) patients. Good outcomes were achieved in 76% and 70% of patients upon discharge, and 93% and 84% of patients after 3 months according to the NIHSS change and mRS. The initial clinical status, recanalization achievement, and presence of symptomatic hemorrhage were statistically related to the outcomes.
Conclusion : Multimodal therapy may be an effective and safe treatment modality for acute ischemic stroke. Balloon angioplasty and stenting is effective for acute thrombolysis, and produce higher recanalization rates with better outcomes.

KEY WORDS : Acute ischemic stroke · Mechanical thrombolysis · Balloon angioplasty · Stenting · Prognostic factors.

INTRODUCTION

Stroke is one of the leading causes of death among Koreans[9]. Various thrombolytic therapies to recanalize the occluded artery, such as intravenous (IV) recombinant tissue plasminogen activator (rt-PA), intraarterial (IA) thrombolysis, combined IV/IA thrombolysis, and mechanical thrombolysis have been reported up to recently[3,4,7,8,10,12,15,20,22-26]. Single-modality approaches are often inadequate, though, as a result of heterogeneous nature of ischemic stroke[1,5]. We treated 50 patients with a multimodal approach combining sequential IV and IA thrombolysis with mechanical thrombolysis, including angioplasty and stenting, after acute ischemic stroke. We also analyzed the relationship between prognostic factors and outcomes.

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MATERIALS AND METHODS

Patients

We analyzed 50 consecutive acute ischemic stroke patients who underwent multimodal therapy between April, 2006, and June, 2008. All patients were admitted to the hospital within 8 hours from ischemic symptom onset. They all suffered from sudden-onset measurable neurological deficits, such as mental change, significant hemiparesis, hemisensory disturbance, dysarthria or aphasia, and hemianopsia.

All patients underwent brain computed tomography (CT). The exclusion criteria on initial CT were a hyperdense lesion consistent with hemorrhage, a significant mass effect, marked hypodense lesions, and any other intracranial lesion. All patients without exclusion criteria underwent computed tomography angiography (CTA) and three-dimensional

CTA (3D-CTA) reconstruction was obtained. The study covered only 50 patients who revealed complete or near-complete occlusion of their proximal intracranial artery, such as middle cerebral artery (MCA : M1 and M2), posterior cerebral artery (PCA : P1), basilar artery (BA), vertebral artery (VA), or internal carotid artery (ICA : proximal or distal) on 3D-CTA. The patients who showed occlusion of a distal intracranial artery (distal to M2 and P1), or anterior cerebral artery were excluded from the study due to endovascular inaccessibility.

CTA demonstrated complete or near-complete occlusion of M1 in 25 patients, M2 in 10, P1 in 2, BA in 2, VA in 1, proximal ICA in 5, and distal ICA in 5. We made an effort to detect true occlusions and to eliminate radiological artifacts by carefully examining the 3D-CTA and 1-mm-sliced CTA source images.

Table 1. General characteristics of patients (n=50)

Characteristic	Results
Age, mean (range), years	64 (38-84)
Sex, men : women	34:16
Time from symptom to hospital arrival, mean (range), minutes	123 (20-430)
Time from symptom to IV thrombolysis, mean (range), minutes	146 (42-454)
rt-PA	92 (42-165)
UK	255 (190-454)
Time from symptom to IA thrombolysis, mean (range), minutes	233 (87-528)
Pre-thrombolytic NIHSS, mean (range)	13.8 (6-28)
Initial occlusion site on CTA	
M1	25
M2	10
P1	2
BA	2
VA	1
Proxiaml ICA	5
Distal ICA	5
Initial IV thrombolytic agent	
rt-PA	32
UK	18

IV : intravenous, IA : intraarterial, NIHSS : National Institute Health Stroke Scale, CTA : computed tomography angiongraphy, rt-PA : recombinant tissue plasminogen activator, UK : urokinase

The general characteristics of patients were shown in Table 1.

Initial IV thrombolysis

Patients who arrived at the hospital within 3 hours from ischemic symptom onset were treated using IV rt-PA (Actilyse, Boehringer Ingelheim, Germany), and those who arrived between 3 and 8 hours were treated using IV urokinase (UK : Urokinase, Yuhan Pharmaceutical Co, Korea). The mean time from ischemic symptom onset to IV rt-PA was 92 minutes (range : 42-165 minutes) and to IV UK was 255 minutes (range : 190-454 minutes). The total IV rt-PA dose was 0.9 mg/kg (10% of which was delivered via a bolus IV injection and 90%, via continuous IV injection for an hour). The total IV UK dose was 300,000 units, which was delivered via continuous IV injection for 24 h. IV rt-PA was used in 32 patients, and IV UK was used in 18 patients. During IV thrombolysis therapy, cerebral angiography was prepared as soon as possible. If cerebral angiography was ready, CT was then performed to detect any hemorrhage, and patient was immediately transferred to the angiographic room regardless of the status of the IV thrombolytic agent injection, with remaining agent continuously injected during IA thrombolysis. We shortened the time from admission to angiography for effective IA thrombolysis. Symptomatic hemorrhage was defined as a homogenous hemorrhagic area on CT, and concomitant neurological deterioration with increase in the NIHSS of ≥3 points[8,15]. If any hemorrhage was detected on CT before cerebral angiography, additional interventions were not performed and conservative therapy or decompressive craniectomy was considered.

Angiography and IA thrombolysis with mechanical thrombolysis

All patients underwent cerebral digital subtraction angiography (DSA). The angiographic recanalization was assessed according to the thrombolysis in myocardial infarction (TIMI) grades, as complete occlusion (grade 0), contrast penetration with minimal perfusion (grade I), recanalization of some, but not all of the occluded arteries (grade II), and complete recanalization with normal opacification of all occluded arteries (grade III). We defined successful recanalization as grade II or III; partial recanalization, as grade I; and no recanalization, as grade 0, for reference of previous literature[9,14].

If patients showed successful recanalization (grade II or III) in the initial DSA, no other interventions were performed. Patients with absent or partial recanalization (grade 0 or I) in the initial DSA received additional IA thrombolysis using UK and concomitant mechanical clot disruption using a microwire and a microcatheter. This procedure was performed with simple to-and-fro passages through the clot with microwire and microcatheter, followed by disruptions with a pigtail-shaped wire tip with alternating small-dose injections of UK distal, within, and proximal to the clot. The median total IA UK dose was 257,000 units (range : 100,000-400,000). When dense contrast extravasation occurred, procedures were halted and the patient was immediately referred for CT.

If recanalization still did not occur (grade 0), no other interventions were performed, and conservative therapy or decompressive craniectomy was considered. Partial recanalization (grade I) from incomplete thrombolysis with remnant thrombus, or from complete thrombolysis but with recurrent stenosis or thrombus formation from a preexisting atherosclerotic stenosis of the occluded artery prompted a balloon angioplasty. When balloon angioplasty failed to achieve successful recanalization, additional stenting was considered. However, although preexisting atherosclerotic stenosis was detected, if successful recanalization was achieved, balloon angioplasty or stenting was not immediately performed even though preexisting atherosclerotic stenosis was detected but was considered later.

All procedures were performed under local anesthesia.

Post-thrombolytic care and outcome evaluation

A final DSA was performed, and immediately followed by CT to detect any hemorrhage. During the first 3 days after thrombolytic therapy, all patients underwent close neurological observation in the Neurological Intensive Care Unit. Conventional brain magnetic resonance imaging (MRI) with diffusion-weighted images, apparent diffusion coefficient map, and fluid-attenuated inversion of the recovery images were obtained on hospital day 2, to determine the baseline extent of the infarcted area and associated perilesional edema, and to detect any delayed hemorrhage. Also, CT was evaluated routinely on hospital day 7, but when neurological deterioration was detected, emergent CT was performed to detect any hemorrhage or progression of the infarcted area, which could result in serious intracranial hypertension.

The appropriate anti-platelet agent (aspirin with clopidogrel or cilostazol) was administered 24 hours after termination of thrombolytic therapy in all patients. Decompressive craniectomy was performed on patients who showed severe intracranial hypertension or a mass effect on CT, regardless of recanalization. This operation was determined by considering the general conditions appropriate for anesthesia, and was performed after permission was obtained from the patient's family.

The mean follow-up period was 16 months (range : 4-28). The brain magnetic resonance angiography (MRA) or CTA was evaluated upon discharge and after 3 months to determine the arterial patency of the previously occluded artery. The NIHSS (National Institute of Health Stroke Scale) was obtained at pre-thrombolytic, post-thrombolytic, upon discharge, and after 3 months. The mRS (modified Rankin scale) was obtained upon discharge and after 3 months. The NIHSS at pre-thrombolytic was compared with the NIHSS upon discharge and after 3 months. The mRS upon discharge and after 3 months was analyzed. A good outcome was defined as a 4-point decrement in NIHSS, and as a mRS score of 2 or less[6,25].

Prognostic factors related to the outcomes

The prognostic factors included were age; the length of time from ischemic symptom onset to patient's arrival at hospital, to IV thrombolysis, and to IA thrombolysis; the initial IV thrombolytic agent; the initial clinical status assessed by pre-thrombolytic NIHSS; the site of arterial occlusion; the recanalization achievement assessed by post-thrombolytic TIMI grade; and the presence of symptomatic hemorrhage. Each of these factors was analyzed with related outcomes according to the NIHSS change and mRS upon discharge. The factors were not analyzed after 3 months, however, because patients showed poor outcomes such as death and loss of follow-up. A χ^2 test was performed using the SPSS (Statistical Package for Social Science) to analyze the differences in outcomes. A p value less than 0.05 was considered statistically significant.

RESULTS

Angiography and IA thrombolysis with mechanical thrombolysis (Table 2, Fig. 1)

Among 32 patients treated with IV rt-PA, successful recanalization was achieved in 8 (25%) patients at initial DSA without additional interventions. There were M1 occlusions in 3 (12%) of 25 patients; P1 in 2 (100%) of 2 patients; and M2 in 3 (30%) of 10 patients. Recanalization was unsuccessful in all patients who had BA, VA, and proximal and distal ICA occlusions by IV rt-PA. On the other hand, among 18 patients treated by IV UK, successful recanalization was not achieved in all patients. Any hemorrhage did not occur after IV rt-PA, or IV UK. As a result, 8 (16%) of 50 patients achieved successful recanalization by IV thrombolysis, and the other 42 patients did not. Also, IV rt-PA alone was effective and safe for some patients, but relatively low successful recanalization rates (25%) were obtained.

Among the remaining 42 patients with unsuccessful recanalization despite IV thrombolysis, additional IA thrombolysis using UK and concomitant mechanical clot disruption were performed. Successful recanalization was achieved in 19 (45%) patients; partial recanalization with remnant or recurrent stenosis, in 21 (50%) patients; and no recanalization, in 2 (5%) patients. The 2 patients who showed no recanalization showed distal ICA and BA occlusions, and decompressive craniectomy was considered. As a result, successful recanalization was achieved in only 27 (54%) of 50 patients by IV/IA thrombolysis with mechanical clot disruption, so additional interventions were required.

Balloon angioplasty was performed in 21 patients who showed partial recanalization after IV/IA thrombolysis with mechanical clot disruption. Eighteen patients showed incomplete thrombolysis with remnant thrombus, and 3 patients showed complete thrombolysis but with recurrent stenosis or thrombus formation from preexisting atherosclerotic stenosis. Successful recanalization was achieved in 10 (48%) of these 21 patients (Fig. 2). Also, the 10 (55%) of 18 patients with remnant thrombus achieved successful recanalization, but the 3 patients with recurrent stenosis or thrombus formation from preexisting atherosclerotic stenosis did not. Balloon angioplasty was effective for thrombolysis of remnant thrombus, but relatively ineffective for pre existing atherosclerotic stenosis.

Stenting was then considered for the 11 patients who showed unsuccessful recanalization after balloon angioplasty. However, stenting was contraindicated in 3 patients with M2, distal ICA, and BA stenosis, and in 2 patients with M1 stenosis because of inappropriate arterial diameter, severe arterial tortuosity, and other technical problems. Stenting was performed in the remaining 3 patients with proximal ICA stenosis using an extracranial stent, 1 patient with extracranial VA origin stenosis using a balloon expandable stent, and 2 patients with M1 stenosis using an intra-cranial stent. Four patients showed incomplete thrombolysis with remnant thrombus, and 2 patients showed complete thrombolysis but with recurrent stenosis or thrombus

Table 2. Recanalization and hemorrhage rates

Parameter	Recanalization (n=50)			Hemorrhage (n=50)	
	Successful	Unsuccessful		Symptomatic	Asymptomatic
	(TIMI GII, III)	TIMI GI	TIMI G0		
IV thrombolysis (n=50)	8 (16%)	42 (84%)			
rt-PA (n=32)	8	24		0	0
UK (n=18)	0	18			
IA UK with mechanical clot disruption (n=42)	19 (45%)	21 (50%)	2 (5%)		
Balloon angioplasty (n=21)	10 (48%)	11 (52%)		4	13
Contraindicated stenting		5			
Indicated stenting		6			
Stenting (n=6)	5 (83%)	1 (17%)			
Total	42 (84%)	8 (16%)		4 (8%)	13 (26%)

TIMI : Thrombolysis in myocardial infarction

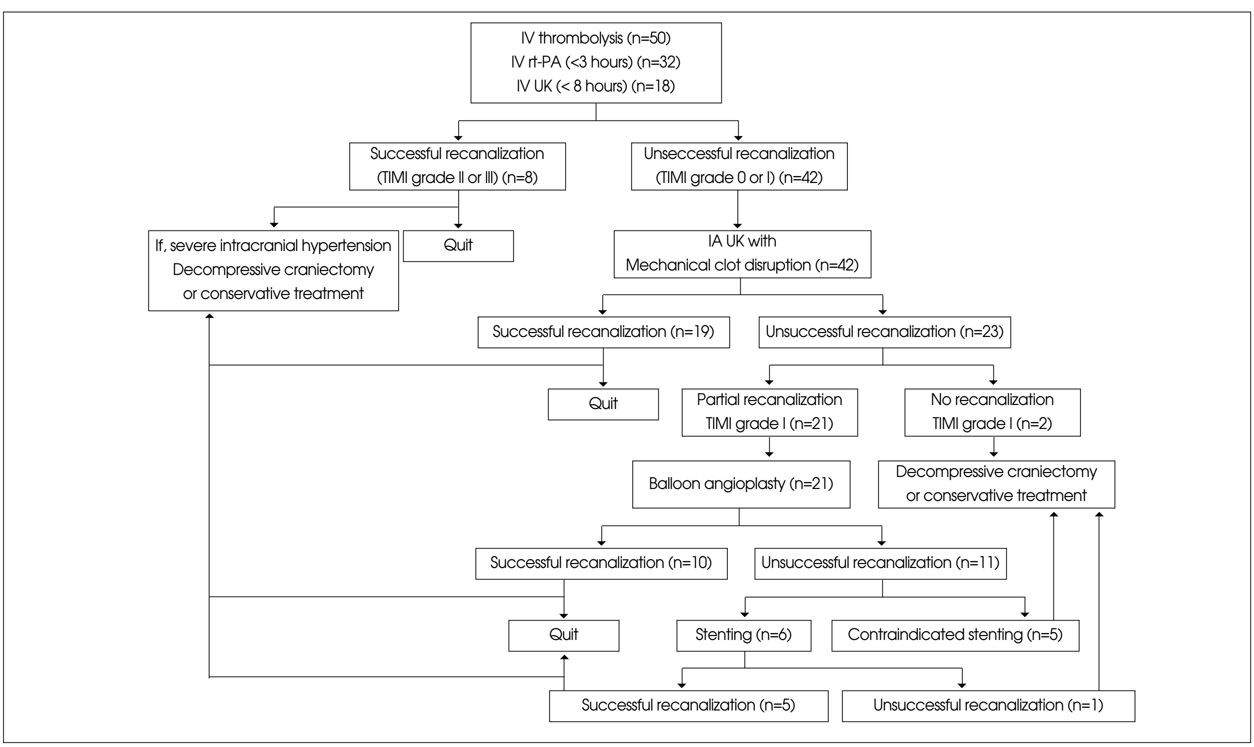

Fig. 1. Flowchart showing multimodal therapy. TIMI : thrombolysis in myocardial infarction

formation from preexisting atherosclerotic stenosis after balloon angioplasty. Successful recanalization was achieved in 5 (83%) of 6 patients except VA stenosis after stenting (Fig. 3). Also, the all patients with remnant thrombous achieved successful recanalization, but the 1 (50%) of 2 patients with recurrent stenosis or thrombus formation from preexisting atherosclerotic stenosis achieved successful recanalization. Stenting was effective for thrombolysis of remnant thrombous like as balloon angioplasty, and may be effective for preexisting atherosclerotic stenosis.

As a result, we achieved high successful recanalization in 15 (71%) of 21 patients by performing additional balloon angioplasty or stenting. Also, balloon angioplasty and stenting was more effective for thrombolysis of remnant thrombous than preexisting atherosclerotic stenosis in acute ischemic stroke.

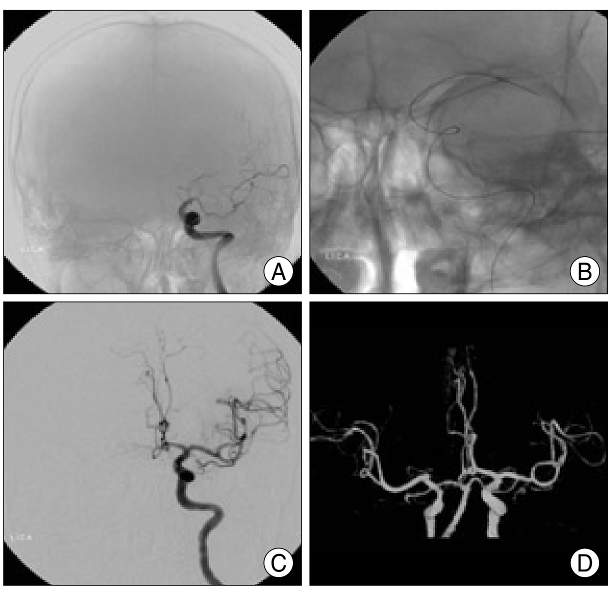

Fig. 2. Case of 63-year-old man with acute onset of right hemiparesis. A : After intravenous recombinant tissue plasminogen activator, angiography shows a near-complete occlusion of left distal internal carotid artery (ICA). B : A intra-arterial urokinase with mechanical clot disruption, and followed balloon angioplasty was performed. C : A final angiography shows a successful recanalization of the left distal ICA. D : Computed tomography angiography after 3 months shows a good arterial patency.

In final DSA, 42 (84%) of 50 patients achieved successful recanalization. Among them, 23 (92%) of 25 patients showed M1 occlusions; 9 (90%) of 10 patients, M2 occlusion; 2 (100%) of 2 patients, P1 occlusion; 5 (100%) of 5 patients, proximal ICA occlusion; 3 (60%) of 5 patients, distal ICA occlusion; and none (0%) of 3 patients, VA and BA occlusion. The occlusions of the anterior cerebral circulation and ICA were more responsive to multimodal therapy and had higher successful recanalization rates than posterior cerebral circulation. In the remaining 6 patients without successful recanalization, a conservative treatment or decompressive craniectomy was considered.

In this study, unsatisfactory rates (54%) of successful recanalization were achieved by IV/IA thrombolysis with mechanical clot disruption, but balloon angioplasty and stenting increased recanalization rates to 84%. Balloon angioplasty and stenting may help treat acute ischemic stroke patients.

Post-thrombolytic care and outcome evaluation

Hemorrhage was detected in 17 (34%) of 50 patients, with symptomatic hemorrhage in only 4 (8%) patients, and asymptomatic hemorrhage in 13 (26%) patients. Hemorrhage occurred in no patients after IV thrombolysis, and in 17 patients after IA thrombolysis and mechanical clot disruption, balloon angioplasty, or stenting (Table 2). Also, CT at hospital day 7 showed no delayed hemorrhage. Multimodal therapy with balloon angioplasty and stenting may be a safe treatment modality for acute ischemic stroke.

Three-month follow-up was obtained in 45 of 50 patients, because 2 (4%) patients died and 3 (6%) patients were lost during follow-up. One patient died due to severe intracranial hypertension resulting from failed recanalization and massive hemorrhage, and the other patient died due to sudden cardiac arrest from severe pulmonary thromboembolism despite partial recanalization with mild neurological improvement. The 3 patients lost during follow-up

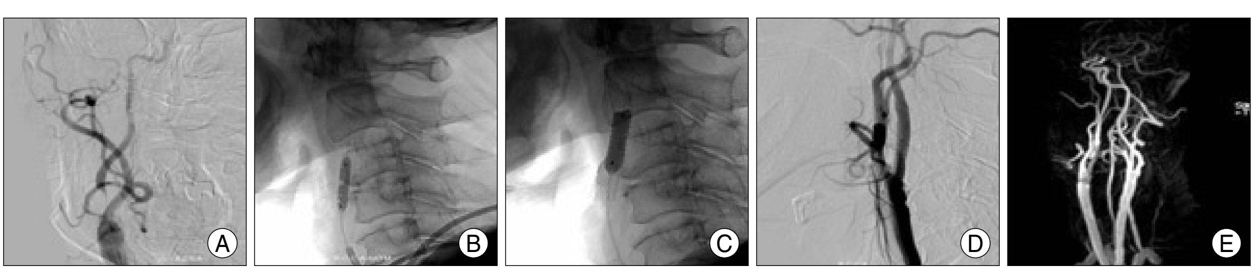

Fig. 3. Case of 74-year-old man with acute onset of left hemiparesis. A : After intravenous recombinant tissue plasminogen activator, intra-arterial urokinase with mechanical clot disruption and balloon angioplasty, angiography shows a partial recanalization with severe recurrent stenosis of the right proximal internal carotid artery (ICA) origin. B : A pre-dilatation balloon angioplasty was performed. C : Stenting and post-dilatation balloon angioplasty was performed. D : A final angiography shows a successful recanalization of the right proximal ICA origin. E : Magnetic resonance angiography after 3 months shows a good arterial patency.

showed progression of the infracted area on CT, but their families rejected decompressive craniectomy.

The median NIHSS was 13.8 at pre-thrombolytic, 10.2 at post-thrombolytic, 7.3 upon discharge and 3.5 after 3 months. The median mRS was 2.12 upon discharge and 2.09 after 3 months. Good outcomes were achieved in 38 (76%) patients upon discharge, and in 42 (93%) patients after 3 months for NIHSS change, and in 35 (70%) patients upon discharge, and in 38 (84%) patients after 3 months for mRS (Table 3, Fig. 4). Patients with good outcomes at discharge showed no progressive neurological deterioration after 3 months. Furthermore, recurrent stenosis or occlusion of successful recanalized artery were not detected on MRA or CTA upon discharge and after 3 months. We therefore achieved overall good outcomes with low hemorrhagic risk for more than 3 months.

Table 3. Overall outcomes

Outcome	Upon discharge (n=50)		After 3 months (n=45)	
	NIHSS (%)	mRS (%)	NIHSS (%)	mRS (%)
Good	38 (76)	35 (70)	42 (93)	38 (84)
Poor	12 (24)	15 (30)	3 (7)	7 (16)

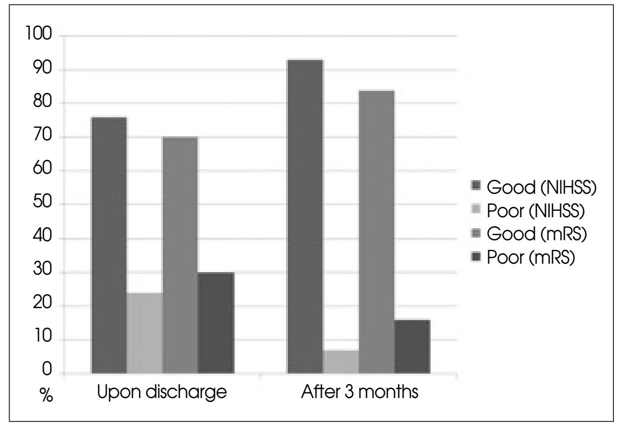

Fig. 4. Bar graph showing overall outcomes upon discharge and after 3 months.

Prognostic factors related to the outcomes (Fig. 5)

The outcomes were analyzed according to age; the length of time from ischemic symptom onset to patient's arrival at hospital, to IV thrombolysis, and to IA thrombolysis; the initial IV thrombolytic agent; and the site of arterial occlusion. However, there was no statistically significant relationship between the outcomes and these factors (p>0.05).

Next, the outcomes were analyzed according to the initial clinical status assessed by pre-thrombolytic NIHSS. Among the 16 patients whose NIHSS was below 10, good outcomes were achieved in 11 (69%) and 13 (81%) patients by NIHSS change and mRS, respectively. Among the 30 patients whose NIHSS was 11-20, good outcomes were achieved in 26 (86%) and 22 (73%) patients, in NIHSS change and mRS, respectively. For the 4 patients whose NIHSS was above 21, good outcomes were achieved in 1 (25%) and 0 (0%) patient by NIHSS change and mRS, respectively. The patients with relatively low pre-thrombolytic NIHSS and good initial clinical status showed better outcomes than those with high scores (p<.05).

The outcomes were then analyzed according to recanalization assessed by post-thrombolytic TIMI grade. Among the 42 patients who showed successful recanalization with higher TIMI grade (II or III), good outcomes were achieved in 36 (86%) and 34 (81%) patients by NIHSS change and mRS. Among the 8 patients with unsuccessful recanalization with lower TIMI grade (0 or I), good outcomes were achieved in 2 (25%) and 1 (12%) patient, respectively. The patients with higher TIMI grade and successful recanalization showed better outcomes than those with lower TIMI grades (p<.05).

The outcomes were then analyzed according to the presence of symptomatic hemorrhage. Among the 33 patients without any hemorrhage, good outcomes were achieved in 27 (82%) and 26 (79%) patients by NIHSS change and mRS, respectively. Among the 13 patients with asymptomatic hemorrhage, good outcomes were achieved in 11 (84%) and 9 (69%) patients, respectively. On the other hand, among the 4 patients with symptomatic hemorrhage, good outcomes were achieved in no patients. The patients with symptomatic hemorrhage showed poorer outcomes than those with asymptomatic or no hemorrhage (p<.05).

Good initial clinical status, successful recanalization, and the absence of symptomatic hemorrhage produced better outcomes.

DISCUSSION

The flowchart of our multimodal therapy is shown in Fig. 1.

In the rt-PA Stroke Trial of the National Institute of Neurological Disorders and Strokes (NINDS), IV rt-PA improved clinical outcomes after 3 months, despite an increased incidence of symptomatic hemorrhage[1]. In this study, IV rt-PA-induced successful recanalization in 25% of patients, and no patients showed symptomatic hemorrhage. IV rt-PA alone was safe and effective for some patients.

No large clinical trial has shown that IV UK is effective, but it is relatively safe[16,21]. In Korea, continuous IV UK infusion has been applied empirically in many hospitals[2].

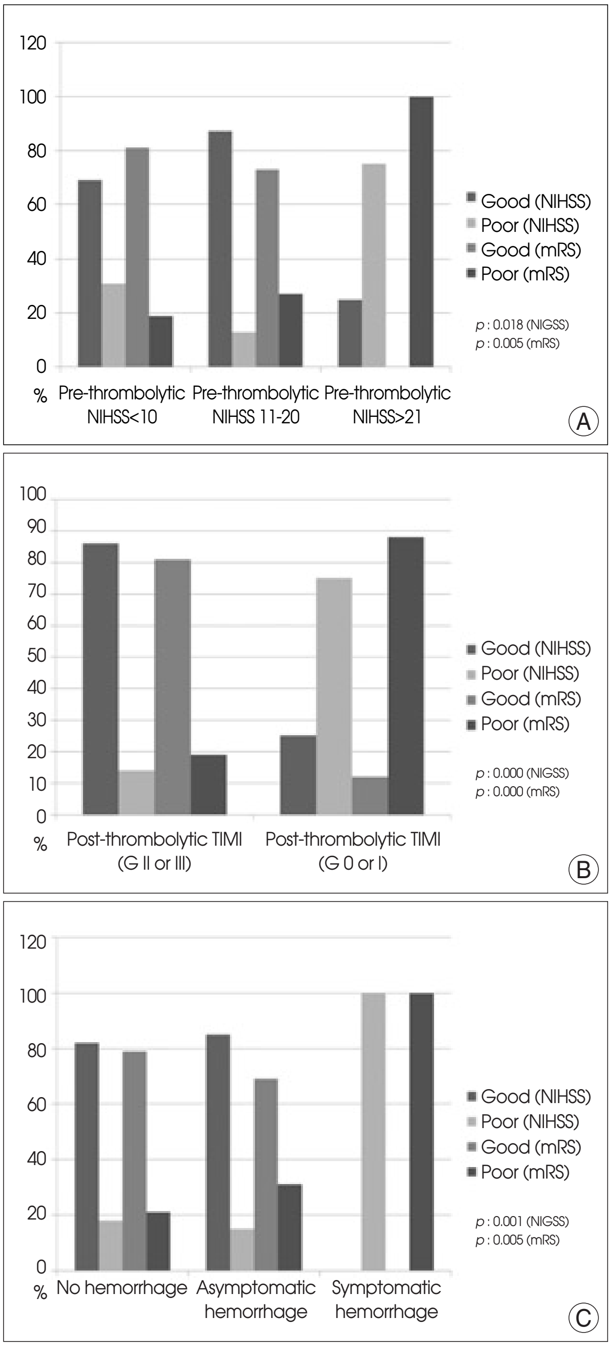

Fig. 5. Bar graph showing the relationship between prognosis and pre-thrombolytic National Institute of Health Stroke Scale (A), post-thrombolytic thrombolysis in myocardial infarction grade (B), and hemorrhage(C).

Although we did not achieve successful recanalization with IV UK alone, it is thus thought that appropriate initial IV thrombolysis with rt-PA or UK is the basis of successful recanalization and good outcomes, if combined with other therapy.

The use of IV rt-PA is limited by low recanalization rates and short treatment time window, within 3 hours as in this study[3,4,23]. Many previous studies reported the effectiveness of combined IV/IA thrombolysis and mechanical thrombolysis[10,12,15,20,22-26]. We used a full dose (0.9 mg/kg) of IV rt-PA and sequential combined IA UK, instead of combined IV/IA rt-PA[10]. We also performed concomitant mechanical clot disruption[22]. Shaltoni et al.[20] reported that IA UK after full-dose IV rt-PA was safe and effective compared with IV rt-PA alone or low-dose IV rt-PA followed by IA rt-PA, and they achieved high rates of recanalization (72%), favorable outcomes (55%), and low hemorrhagic risk (5.8%). Noser et al.[15] reported that aggressive mechanical clot disruption with IA thrombolysis was performed safely with comparable hemorrhage and mortality rates, and led to immediate recanalization in one-third of their subject patients. In this study, full-dose IV rt-PA and subsequent IA UK with mechanical clot disruption is feasible, safe, and effective. However, successful recanalization was obtained in only 45% of patients, so additional treatment modalities were considered to achieve higher rates.

As in previous studies, the therapeutic time window of combined IV and IA therapy for occlusion of anterior cerebral circulation was defined as within 6 hours after ischemic symptom attack[10,12,15,20]. In this study, however, we treated 2 patients with M1 occlusion who arrived at the hospital between 6 and 8 hours after ischemic symptoms attack. One patient showed successful recanalization and good outcomes, but the other patient did not. Our multimodal therapy may be beneficial for some patients with occlusion of anterior cerebral occlusion who arrived at hospital within 8 hours after ischemic symptom attack, but further evidence is needed.

Angioplasty and stenting may be adjuvant treatment modalities to thrombolytic therapy because as many as 40% of patients are resistant to local thrombolytic infusion[6,13,14,17]. Ringer et al.[17] reported that balloon angioplasty is a safe, effective adjuvant therapy in patients who are resistant to IA thrombolysis, and the use of balloon angioplasty may prevent reocclusion in a stenotic artery and permit distal infusion of thrombolytic agents. Jovin et al.[6] purposed that angioplasty and stenting of acute ICA occlusion appears to have a high recanalization rate (92%) and be relatively safe in the patients with acute ICA occlusion. We achieved high successful recanalization rates (71%) and low symptomatic hemorrhagic risk (8%) with additional balloon angioplasty and stenting, with no recurrent stenosis or occlusion on subsequent MRA or CTA upon discharge and after 3 months. Also, we could achieve better outcomes by increasing successful recanalization rates. Balloon angioplasty and stenting was more effective for thrombolysis of remnant thrombus than recurrent stenosis or thrombus formation from preexisting atherosclerotic stenosis. As a result, balloon angioplasty and stenting are safe and effective treatment modalities for patients who are resistant to combined IV/IA thrombolysis with mechanical clot disruption.

Prognostic factors for outcomes include the site of arterial occlusion and time to thrombolysis[3,11,26]. We were not able to identify these factors as influencing outcomes, but good initial clinical status, successful recanalization, and the absence of symptomatic hemorrhage did influence outcomes.

We obtained the overall high successful recanalization rates (84%) and good outcomes (76% upon discharge and 93% after 3 months) with acceptable mortality (4%) and symptomatic hemorrhagic risk (8%) using multimodal therapy for patients with acute ischemic stroke. The key of this satisfactory results has been thought that strict choice of the indicated patients according to the time from ischemic symptom onset, general medical status, and initial radiologic findings; shortening of the time to initiation of IV thrombolysis, cerebral angiography, and IA thrombolysis; careful selection of therapy for each patients; appropriate supportive care, such as strict blood pressure, glucose, and lipid control with increased intracranial pressure management. Moreover, we performed additional balloon angioplasty and stenting for acute arterial occlusion to achieve higher recanalization rates with better outcomes than previous studies.

Study limitations

Perfusion-diffusion mismatch studies could not be performed before thrombolytic therapy because of time and equipment limitations at our hospital. Many previous studies demonstrated that thrombolytic therapy based on perfusion-diffusion mismatch studies is safe and effective[18,19]. Although MRI-based thrombolysis seems to be superior to CT and CTA-based thrombolysis, stroke MRI at present is fully available only in major stroke centers. In particular, most patients with acute ischemic stroke are treated in general hospitals that do not have this access to MRI, and CT is more cost-effective than stroke MRI and often located in the emergency departments of even smaller community hospitals. Furthermore, CT and CTA can be performed rapidly with fewer movement artifacts, especially in severely ill patients.

In this study, sudden-onset measurable neurological deficit indicating compromised blood flow in a large part of the territory of affected vessel, and absence of any hemorrhage, marked hypodense lesion or mass effect on CT with complete or near-complete occlusion of proximal intracranial artery or ICA on 3D-CTA lead to determination of thrombolytic therapy. As a result, we achieved high recanalization rates and overall good outcomes without significant symptomatic hemorrhagic risk. We designed most appropriate treatment protocol for patients with acute ischemic stroke, when diffusion-perfusion mismatch studies were not available in general hospital.

Due to the differences in baseline characteristics, the lack of control group, the presence of heterogeneous arterial lesions, and the small number of cases, however, our results may not be justified to draw a definitive conclusion. Future large-scale prospective randomized studies are required to confirm the results of this study.

CONCLUSION

Multimodal therapy consisting of IV/IA thrombolysis, mechanical thrombolysis including mechanical clot disruption using microcatherters and microwires, balloon angioplasty, and stenting may be a safe and effective treatment modality for acute ischemic stroke. Balloon angioplasty and stenting are effective, when combined IV/IA thrombolysis with mechanical clot disruption is unsuccessful. Also, the good initial clinical status, the achievement of successful recanalization and the absence of symptomatic hemorrhage is related to the better outcome with statistically significance.

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