Current Status of Recanalization Therapy in Acute Ischemic Stroke with Symptomatic Intracranial Arterial Occlusion in Korea

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Background: Recent methodological advances in recanalization therapy may alter recanalization strategies and clinical outcomes in patients with symptomatic occlusion of intracranial cerebral arteries. However, few studies have analyzed these changes at a national level, with none conducted in Korea. Methods: On the basis of a prospective multicenter stroke registry database in Korea, 642 consecutive patients hospitalized within 12 hours of the onset with symptomatic occlusion of intracranial major cerebral arteries between March 2010 and November 2011 were identified. Recanalization therapy was used in 48% (n = 307) of patients; intravenous thrombolysis only (IVT) in 46%, intra-arterial thrombolysis only (IAT) in 16%, and combined thrombolysis (CMT) in 38%. Of the 166 patients treated by IAT or CMT, the Penumbra system or the Solitaire was used in 58% of patients. Results: Early neurologic improvement (ENI), 3-month modified Rankin scale (mRS) score of 2 or less, and symptomatic hemorrhagic transformation (SHT) were observed in 43%, 39%, and 9% of the patients in the IVT group; 52%, 27%, and 12% of the patients in the IAT group; and 54%, 39%, and 12% of the patients in the CMT group, respectively. Compared with no treatment, adjusted odd ratios (95% confidence intervals) of recanalization therapy were 1.59 (1.04-2.42) for ENI,

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1.37 (.81-2.30) for 3-month mRS score of 2 or less, and 2.58 (1.12-5.91) for SHT. *Conclusions:* The variety and active use of endovascular approaches were quite noticeable. As a whole, recanalization therapy tended to contribute to favorable outcomes despite a significant increase of symptomatic hemorrhage. **Key Words:** Recanalization therapy—endovascular treatment—thrombolysis—acute ischemic stroke—intracranial arterial occlusion—Korea—outcome—registry. © 2014 by National Stroke Association

Introduction

Intracranial large vessel occlusion accounts for up to 40% of ischemic stroke and is known as an independent predictor of poor outcome.^{1,2} The recent advances in endovascular devices have made them a major emerging target for stroke intervention.^{3,4}

The unsatisfactory efficacy of intravenous tissue plasminogen activator (IV t-PA) can be partly attributed to low reperfusion rates.⁵⁻⁷ New mechanical thrombectomy devices have been developed to achieve higher recanalization and lower hemorrhagic transformation rates.^{3,4,8,9} The success of these devices is change the practice; in the United States, the use of endovascular devices increased 6-fold between 2004 and 2009.¹⁰ However, this technical success has not been proven to improve a clinical outcome through adequately powered randomized clinical trials.¹¹

Few studies described how acute intracranial large vessel occlusion was treated and what the treatment outcome was in a nationally representative population.^{5,12,13} Furthermore, these few studies had a limitation that they did not compare various recanalization strategies with respect to clinical outcomes.

Aims

The aims of the present study were to describe—among ischemic stroke patients who presented within 12 hours of the onset, when diagnosed with symptomatic intracranial occlusion of major cerebral arteries and were hospitalized to nationally representative regional stroke centers in South Korea—the following: (1) which of the patients were treated with recanalization therapy; (2) what strategies were applied to them; and (3) what were the treatment outcomes.

Methods

Study Subjects

A consecutive series of patients who were hospitalized because of acute ischemic stroke between March 1, 2010 and November 31, 2011 were identified from a prospective, multicenter, nationwide web-based acute stroke registry database in Korea.^{14,15} Ten university hospitals or regional centers participated in this study. They are

scattered throughout a major part of South Korea; 5 metropolitan areas: Seoul (the largest one), Pusan (the second largest one), Daegu, Kwangju, and Daejeon and the largest provincial area, Gyeonggi; more than 60% of the Korean population resides in these areas (Supplementary Figure 1).

Among these patients, those who met the following criteria were included in this study: (1) the time interval from their first symptom onset to arrival at 12 hours or earlier, (2) a clinical diagnosis of acute ischemic stroke confirmed by relevant lesions on brain images; and (3) intracranial major cerebral artery occlusion on initial angiographic evaluation including magnetic resonance angiography, computed tomography angiography, or digital subtraction angiography. Intracranial major cerebral arteries were defined as the distal portion of the internal carotid artery (d-ICA), anterior cerebral artery, middle cerebral artery (MCA), posterior cerebral artery (PCA), or basilar artery (BA). Patients who did not undergo angiographic evaluation or who had occlusion of proximal ICA or proximal vertebral artery were excluded. Patients who received recanalization therapy were divided into 2 groups: an intravenous thrombolysis only (IVT) group and an endovascular treatment (EVT) group. EVT included intra-arterial use of chemical thrombolytic agents, clot maceration by multiple passages of a microcatheter/microwire through the clot,¹⁶ use of mechanical thrombectomy devices, and stent placement. The EVT group was further divided into an intra-arterial thrombolysis only (IAT) group and a combined thrombolysis (CMT) group.

In all participating centers, approval was obtained from the institutional review boards for collection of anonymized clinical data without patients' consent into the stroke registry database to improve the quality of stroke care. We got further approval for collection of additional data and the use of the registry database for this study.

Data Collection

Patients' clinical and laboratory information and 3month functional outcome were obtained directly from the registry database or by reviewing medical records. Digital subtraction angiography images of patients who underwent EVT were collected from each center, and

CURRENT STATUS OF RECANALIZATION THERAPY

successful recanalization, defined as achieving thrombolysis in cerebral infarction IIa, IIb, or III flow¹⁷ in all treatable vessels, was determined by independent assessment of 2 stroke neurologists (M.U.J, J-H.H) who were blinded to clinical outcomes. The discrepancies in thrombolysis in cerebral infarction scoring were resolved by consensus (kappa value = .83).

Early neurologic improvement (ENI) was defined as a discharge National Institutes of Health stroke scale (NIHSS) score of 0 or 1 or an improvement of 8 or more in the NIHSS score from the baseline to the discharge.¹⁸ Favorable functional outcome was defined as a 3-month modified Rankin scale (mRS) score of 2 or less. Safety

outcome was symptomatic intracranial hemorrhage (SHT) defined as any hemorrhage plus a neurologic deterioration of 4 points or more in the NIHSS score from the baseline or from the lowest NIHSS value after the baseline, or leading to death.¹⁹

Statistical Analysis

Comparisons of baseline characteristics and clinical outcomes were made between patients who had recanalization therapy and those who did not, between the IVT and EVT groups, between the IAT and CMT groups, and according to major endovascular devices in the EVT

No recanalization therapy $(n = 335)$		Recanalization therapy $(n = 307)$	P value*	
Age (y)				
Mean \pm SD	68.3 ± 13.9	68.8 ± 11.7	.67	
Age < 80	260 (77.6%)	249 (81.1%)	.27	
$Age \ge 80$	75 (22.4%)	58 (18.9%)		
Sex (male)	178 (53.1%)	189 (61.6%)	.03	
Onset to arrival [†]				
Mean \pm SD	5.26 ± 3.32	2.40 ± 2.47	<.001	
\leq 3 h	103 (30.7%)	228 (74.3%)	<.001	
>3 and ≤ 4.5 h	53 (15.8%)	34 (11.1%)		
>4.5 and ≤ 6 h	43 (12.8%)	13 (4.2%)		
>6 h	136 (40.6%)	32 (10.4%)		
Initial NIHSS				
Median (IQR)	9 (3, 15)	15 (9, 19)	<.001	
0-3	99 (29.6%)	14 (4.6%)	<.001	
4-9	78 (23.3%)	68 (22.1%)		
10-25	154 (46.0%)	213 (69.4%)		
26-44	4 (1.2%)	12 (3.9%)		
Occluded artery				
d-ICA	42 (42.9%)	56 (57.1%)	.045	
ACA	20 (60.6%)	13 (39.4%)	.320	
MCA	213 (51.0%)	205 (49.0%)	.396	
PCA	64 (70.3%)	27 (29.7%)	<.01	
BA	34 (47.9%)	37 (52.1%)	.443	
Prestroke mRS	· · ·		.01	
0	262 (78.2%)	264 (86.0%)		
≥1	73 (21.8)	43 (14.0%)		
Risk factors				
HTN	198 (59.1%)	208 (67.8%)	.01	
DM	65 (19.4%)	77 (25.1%)	.08	
HL	51 (15.2%)	56 (18.2%)	.30	
Smoking	106 (31.6%)	87 (28.3%)	.36	
A-fib	128 (38.2%)	176 (57.3%)	<.001	

Abbreviations: ACA, anterior cerebral artery; A-fib, atrial fibrillation; BA, basilar artery; d-ICA, distal portion of the internal carotid artery; DM, diabetes mellitus; HL, hyperlipidemia; HTN, hypertension; IQR, interquartile range; MCA, middle cerebral artery; mRS, modified Rankin scale; NIHHS, National Institutes of Health Stroke Scale; PCA, posterior cerebral artery; SD, standard deviation.

Values are number of patients (%) if not indicated.

*P values are calculated by the Student t test, Pearson chi-square test, and Mann–Whitney U test, whichever appropriate.

[†]Time interval from last normal time to arrival at hospitals.

‡Values are the number of the occluded vessels, which can be overlapped in patients who have multiple occlusions. *P* values were calculated by comparison of proportion of treatment between patients with and without each occlusion.

group. In comparisons by endovascular devices, the final device used was chosen as representative and the analyses were limited to the cases in which the final device could be determined clearly. Three-month mRS score, ENI, and SHT were used as outcome variables. Recanalization rate was adopted as an outcome variable to analyze those who underwent EVT. Patients whose 3-month mRS scores were unavailable (n = 64) were excluded from the analysis when 3-month mRS score was an outcome variable.

Multivariable logistic regression models were developed for estimating the adjusted odds ratios (ORs) of recanalization therapy compared with that of no therapy, the OR of EVT compared with that of IVT, and the OR of CMT compared with that of IAT for the previously mentioned outcome variables. Variables for adjustment in each model were selected on the basis of (1) $P \le .20$ in comparisons according to methods of recanalization therapy or (2) clinical relevance of their associations with stroke outcomes. In the models in which SHT was an outcome variable, we confined the number of variables for adjustment to no greater than 4. All analyses were performed using IBM SPSS 19.0.1 (IBM Corporation, Armonk, NY). A 2-tailed P < .05 was considered a minimum level of statistical significance.

Results

General Characteristics

During the study period, among 6070 patients who presented with acute ischemic stroke, 642 patients met the eligibility criteria (Supplementary Figure 2). The occluded vessels were MCA in 65% of patients, d-ICA in 15%, PCA in 14%, BA in 11%, and anterior cerebral artery in 5%. Overall, intravenous tissue plasminogen activator (IV t-PA) was used in 257 patients (40.0%); .9 mg/kg in 54% and .6 mg/kg in 46% (Supplementary Table 1). The 77% of the patients in the IVT group used .9 mg/kg and the 73% in the CMT group used .6 mg/kg.

Recanalization Therapy versus no Recanalization Therapy

Compared with patients without recanalization therapy, those with recanalization therapy were mostly male, arrived at hospitals earlier, and had higher initial NIHSS scores (Table 1). Seventy-four percent of patients who had recanalization therapy arrived within 3 hours of the onset, whereas 41% of those who did not have recanalization therapy arrived after 6 hours. Recanalization therapy was preferred in d-ICA occlusion, and no therapy was preferred in PCA occlusion. ENI and SHT

	Number of patients	Adjusted odds ratio	95% CI	P valu
ENI*				
No recanalization therapy	105/335 (31.3%)	1		
Recanalization therapy	150/307 (48.9%)	1.59*	1.04-2.42	.03
IVT	61/141 (43.3%)	1		
EVT	89/166 (53.6%)	1.17*	.71-1.93	.54
IAT	26/50 (52.0%)	1		
CMT	63/116 (54.3%)	1.04*	.43-2.52	.93
3-month mRS ≤ 2				
No recanalization therapy	131/293 (44.7%)	1		
Recanalization therapy	106/285 (37.2%)	1.37*	.81-2.30	.24
IVT	50/127 (39.4%)	1		
EVT	56/158 (35.4%)	1.54*	.85-2.77	.15
IAT	13/48 (27.1%)	1		
CMT	43/110 (39.1%)	1.35*	.48-3.78	.57
SHT†				
No recanalization therapy	11/335 (3.3%)	1		
Recanalization therapy	32/307 (10.4%)	2.58†	1.12-5.91	.03
IVT	12/141 (8.5%)	1		
EVT	20/166 (12.0%)	1.16†	.52-2.60	.71
IAT	6/50 (12.0%)			
CMT	14/116 (12.1%)	1.20†	.35-4.20	.77

 Table 2. Clinical outcomes according to methods of recanalization therapy

Abbreviations: A-fib, atrial fibrillation; CI, confidence interval; CMT, combined thrombolysis; DM, diabetes mellitus; ENI, early neurologic improvement; EVT, endovascular therapy; IAT, intra-arterial thrombolysis only; IVT, intravenous thrombolysis only; mRS, modified Rankin scale; NIHHS, National Institutes of Health Stroke Scale; SHT, symptomatic hemorrhagic transformation.

Values are number of patients (%) if not indicated.

*Adjusted for sex, onset to arrival, initial NIHSS, prestroke mRS, A-fib, and DM.

†Adjusted for onset to arrival, initial NIHSS, A-fib, and DM.

developed more frequently in patients treated with recanalization therapy (*P* values <.001), and the proportion of 3-month mRS score of 2 or less was slightly higher in untreated patients (P = .16) (Table 2). Multivariable analyses demonstrated that recanalization therapy increased the odds of ENI and SHT significantly, but not the odds of 3-month mRS score of 2 or less.

IVT versus EVT

Of the 307 patients who underwent recanalization therapy, 46% were treated with IVT and 54% with EVT. Compared with the IVT group, the EVT group was more likely to be less than 80-years old, arrive late at hospitals, and had higher initial NIHSS scores (Table 3). EVT was preferred in BA occlusion, and IVT was preferred in PCA occlusion. ENI tended to develop more frequently in the EVT group than in the IVT group (P = .07); however, the proportion who had SHT and 3-month mRS score of 2 or less was not different between the 2 groups (Table 2). Multivariable analyses revealed no significant association between EVT and the clinical outcomes.

IAT versus CMT

Of the 166 patients in the EVT group, 30% received IAT and 70% received CMT. The CMT group was more likely to arrive at hospitals earlier and had higher initial NIHSS scores than the IAT group (Table 4). CMT was preferred in d-ICA and MCA occlusions. The ENI and SHT rates and the proportion of mRS score of 2 or less were not significantly different between the 2 groups (Table 2). The recanalization rate was not different too (P = .38).

Methods of EVT and Comparisons According to Endovascular Devices

Chemical thrombolytics were used in 74% of the patients in the EVT group, and urokinase was the most commonly used thrombolytic agent (91%) (Supplementary Table 1). Endovascular devices were applied in 95% of the patients in the EVT group and the microcatheter/microwire was used most frequently. The new generation thrombectomy devices, such as the Penumbra system and the Solitaire, were used in 58% of the patients in the EVT group. Comparisons

Table 3. Comparisons of baseline characteristics between IVT and EVT groups			
	IVT $(n = 141)$	EVT $(n = 166)$	P value*
Age (y)			
Mean \pm SD	70.0 ± 12.4	67.8 ± 11.1	.41
Age < 80	106 (75.2%)	143 (86.1%)	.01
$Age \ge 80$	35 (24.8%)	23 (13.9%)	
Sex (male)	93 (66.0%)	96 (57.8%)	.15
Onset to arrival			
Mean \pm SD	2.00 ± 1.72	2.74 ± 2.93	.01
≤3 h	111 (78.7%)	117 (70.5%)	.01
>3 and \leq 4.5 h	15 (10.6%)	19 (11.4%)	
>4.5 and ≤ 6 h	10 (7.1%)	3 (1.8%)	
>6 h	5 (3.5%)	27 (16.3%)	
Initial NIHSS			
Median (IQR)	12 (7, 17.5)	16.5 (11, 20)	<.001
0-3	7 (5.0%)	7 (4.2%)	<.001
4-9	47 (33.3%)	21 (12.7%)	
10-25	83 (58.9%)	130 (78.3%)	
26-44	4 (2.8%)	8 (4.8%)	
Occluded artery		· · · ·	
d-ICA	22 (39.3%)	34 (60.7%)	.27
ACA	9 (69.2%)	4 (30.8%)	.09
MCA	96 (46.8%)	109 (53.2%)	.65
PCA	20 (74.1%)	7 (25.9%)	<.01
BA	10 (27.0%)	27 (73.0%)	.01
Door-to-needle time (min)	22.5 ± 200.5	$39.7 \pm 166.125 (n = 115)^{\dagger}$.32
Door-to-puncture time (min)		147.5 ± 178.4	
1			

Abbreviations: ACA, anterior cerebral artery; BA, basilar artery; CMT, combined thrombolysis; d-ICA, distal portion of the internal carotid artery; EVT, endovascular therapy; IQR, interquartile range; IVT, intravenous thrombolysis only; MCA, middle cerebral artery; NIHHS, National Institutes of Health Stroke Scale; PCA, posterior cerebral artery; SD, standard deviation.

Values are number of patients (%) if not indicated.

*P values are calculated by the Student t test, Pearson chi-square test, and Mann–Whitney U test, whichever appropriate.

†Values were obtained from patients receiving IVT in the CMT group.

	IAT $(n = 50)$	CMT $(n = 116)$	P value*
Age (y)			
Mean \pm SD	69.3 ± 10.8	67.2 ± 1.0	.53
<80	42 (84.0%)	101 (87.1%)	.60
≥ 80	8 (16.0%)	15 (12.9%)	
Male sex	24 (48.0)	72 (62.1)	.09
Onset to arrival			
Mean \pm SD	4.96 ± 3.53	1.79 ± 2.93	<.01
<3 h	9 (18.0%)	98 (84.5%)	<.001
>3 and \leq 4.5 h	9 (18.0%)	10 (8.6%)	
>4.5 and ≤ 6 h	0 (.0%)	3 (2.6%)	
>6 h	22 (44.0%)	5 (4.3%)	
Initial NIHSS			
Median (IQR)	16 (10-21)	17 (12-20)	.895
0-3	4 (8.0%)	3 (2.6%)	<.001
4-9	7 (14.0%)	14 (12.1%)	
10-25	36 (72.0%)	94 (81.0%)	
26-44	3 (6.0%)	5 (4.3%)	
Occluded artery			
d-ICA	15 (44.1%)	19 (55.9%)	.046
ACA	1 (25.0%)	3 (75.0%)	.82
MCA	26 (23.9%)	83 (76.1%)	.02
PCA	2 (28.6%)	5 (71.4%)	.93
BA	12 (44.4%)	15 (55.6%)	.08
Door-to-puncture time (min)	149.2 ± 194.2	146.7 ± 172.0	.94
Recanalization rate	38 (76.0%)	95 (81.9%)	.38

Table 4. Comparisons of baseline characteristics between IAT and CMT groups

Abbreviations: ACA, anterior cerebral artery; BA, basilar artery; CMT, combined thrombolysis; d-ICA, distal portion of the internal carotid artery; IAT, intra-arterial thrombolysis only; MCA, middle cerebral artery; NIHHS, National Institutes of Health Stroke Scale; PCA, posterior cerebral artery; SD, standard deviation.

Values are number of patients (%) if not indicated.

*P values are calculated by the Student t test, Pearson chi-square test, whichever appropriate.

of baseline characteristics and clinical outcomes according to the EVT devices are presented in Supplementary Table 1. Recanalization rates ranged from 80%-86% and were comparable among the EVT devices. The proportions of 3month mRS score of 2 or less and the ENI and SHT rates were not different among the 3 groups.

Discussion

The proportion of patients treated with recanalization therapy within the first 3 hours was 74%. This proportion decreased to 25% beyond this time window (79 of 311 patients: IVT in 30, IAT in 31, and CMT in 18 patients; Tables 1, 3, and 4), but was still high. In a recent Japanese study, less than 10% of patients were treated with recanalization therapy, mostly by IAT.¹²

The proportion of EVT to recanalization therapy in this study was 56%, which is higher than 34% in the Japanese study³ and 8% in a Swiss study.²⁰ The differences may be explained partly by the more aggressive application of EVT beyond the 3-hour window (62%) compared with within the 3-hour window (51%) in this study (Table 3).

More than 10% of patients with the NIHSS score less than 4 and almost half of those with NIHSS score of 4 or more but less than 10 received recanalization therapy. These findings represent that physicians in real practice do not always withhold recanalization therapy in mild stroke patients. The present guidelines recommend avoiding recanalization therapy in patients who have minor and isolated symptoms.²¹

Recanalization therapy increased the odds of ENI and SHT significantly. The increase of ENI by recanalization therapy was reported in the Safe Implementation of Treatment in Stroke–International Stroke Thrombolysis Register¹⁸ and the National Institute of Neurological Disorders and Stroke (NINDS) trial,¹ although these 2 studies enrolled subjects without any knowledge of vascular status. No difference between the IVT and EVT groups is compatible with the failures seen in recent EVT trials.²²⁻²⁴

Comparison of the IAT and CMT groups also showed no improvement in clinical outcomes by precedent IVT. However, the imbalance of baseline characteristics and possibilities of residual and unmeasured confounders prevent generalization of these results.

	Microcatheter ($n = 54$)	Penumbra ($n = 25$)	Solitaire ($n = 78$)	P value [†]
Onset to arrival, mean \pm SD	3.17 ± 3.27	3.51 ± 3.26	2.26 ± 2.47	.09
Initial NIHSS, median (IQR)	15 (18-20)	14 (7-18)	16 (10-20)	.01
Occluded artery				
d-ICA	10 (31.2%)	5 (15.6%)	17 (53.1%)	.90
ACA	2 (50.0%)	0	2 (50.0%)	.62
MCA	35 (35.0%)	15 (15.0%)	50 (50.0%)	.91
PCA	2 (28.6%)	1 (14.3%)	4 (57.1%)	.92
BA	10 (37.0%)	6 (22.2%)	11 (40.7%)	.50
Outcomes				
Recanalization rate (TICI \ge 2A)	43 (79.6%)	21 (84.0%)	67 (85.9%)	.63
ENI	34 (63.0%)	13 (52.0%)	39 (50.0%)	.32
3-month mRS ≤ 2 §	16 (29.6%)	9 (37.5%)	27 (37.5%)	.62
SHT	7 (13.0%)	2 (8.0%)	11 (14.1%)	.73

Table 5. Comparisons according to EVT devices*

Abbreviations: ACA, anterior cerebral artery; BA, basilar artery; d-ICA, distal portion of the internal carotid artery; ENI, early neurologic improvement; EVT, endovascular therapy; MCA, middle cerebral artery; NIHHS, National Institutes of Health Stroke Scale; PCA, posterior cerebral artery; SD, standard deviation; SHT, symptomatic hemorrhagic transformation; TICI, thrombolysis in cerebral infarction.

Values are the number of patients (%) if not indicated.

*Analysis was made on the basis of the final device used in the cases in which multiple devices were used, and 9 patients in whom the Wingspan stent was the final device were excluded from the analysis.

†P values are calculated by a 1-way analysis of variance, Kruskal–Wallis test, and Pearson chi-square test, whichever appropriate.

‡Values are the number of the occluded vessels, which can be overlapped in patients who have multiple occlusions.

 β Patients whose 3-month mRS scores were unavailable (n = 7) were excluded from the analysis.

With respect to the methods of mechanical EVT, the traditional microcatheter/microwire method¹⁶ was still used most commonly; however, a large proportion used new generation devices. The recanalization rates of those new generation devices were quite high, although the proportions of 3-month mRS score of 2 or less and the ENI and SHT rates were not different among these 3 commonly used EVT methods (Table 5).

Among the EVT group, the proportion of those treated by CMT was more than 2 times of those treated by IAT (Table 4). The recanalization rates of the CMT and IAT groups (82% and 76%, respectively) were higher than that of the prourokinase trial $(66\%)^{25}$ and slightly lower than those observed in recent new generation device trials (83% and 86%).^{3,4} The negligible difference in recanalization rates between the CMT and IAT groups may explain the difference in the clinical outcomes (Table 2).

Significant increase of SHT and nonsignificant improvement of the 3-month functional outcome despite increase in the odds of ENI can be interpreted as that the recanalization strategies for symptomatic intracranial occlusion in this study do not improve the clinical outcome overall. However, high recanalization rates in the EVT group especially with new generation devices and combined methods and without increase of SHT suggest that the recent technical advances can bring about improvement of clinical outcomes in this population.²⁶

This study has limitations. First, it was a retrospective observational study, although a prospectively collected database was used. Second, the hospitals participating in this study were mostly classified as comprehensive stroke centers, which may raise concerns about the representativeness of this study at a national level. Third, because catheter-guided angiography was performed only in the EVT group, we could not directly compare the IVT group with the EVT group with respect to the recanalization rate. Fourth, it should be noted that 3month clinical outcomes were unavailable in 10% of patients.

In conclusion, this study demonstrated the current situation of recanalization strategies for acute symptomatic occlusion of intracranial cerebral arteries in Korea. The variety and active use of endovascular approaches were quite noticeable. Exploration of newer endovascular strategies in the clinical trial setting is warranted.

Supplementary Data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2013.12. 027.

References

- Brown DL, Johnston KC, Wagner DP, et al. Predicting major neurological improvement with intravenous recombinant tissue plasminogen activator treatment of stroke. Stroke 2004;35:147-150.
- Smith WS, Tsao JW, Billings ME, et al. Prognostic significance of angiographically confirmed large vessel intracranial occlusion in patients presenting with acute brain ischemia. Neurocrit Care 2006;4:14-17.

- **3.** Saver JL, Jahan R, Levy EI, et al. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallelgroup, non-inferiority trial. Lancet 2012;380:1241-1249.
- Nogueira RG, Lutsep HL, Gupta R, et al. Trevo versus Merci retrievers for thrombectomy revascularisation of large vessel occlusions in acute ischaemic stroke (TREVO 2): a randomised trial. Lancet 2012;380:1231-1240.
- Mazighi M, Serfaty JM, Labreuche J, et al. Comparison of intravenous alteplase with a combined intravenousendovascular approach in patients with stroke and confirmed arterial occlusion (RECANALISE study): a prospective cohort study. Lancet Neurol 2009;8:802-809.
- 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. Bhatia R, Hill MD, Shobha N, et al. Low rates of acute recanalization with intravenous recombinant tissue plasminogen activator in ischemic stroke: real-world experience and a call for action. Stroke 2010;41:2254-2258.
- 8. Smith WS, Sung G, Saver J, et al. Mechanical thrombectomy for acute ischemic stroke: final results of the Multi MERCI trial. Stroke 2008;39:1205-1212.
- 9. Grunwald IQ, Wakhloo AK, Walter S, et al. Endovascular stroke treatment today. AJNR Am J Neuroradiol 2011; 32:238-243.
- **10.** Hassan AE, Chaudhry SA, Grigoryan M, et al. National trends in utilization and outcomes of endovascular treatment of acute ischemic stroke patients in the mechanical thrombectomy era. Stroke 2012;43:3012-3017.
- 11. Hennerici MG, Kern R, Szabo K. Non-pharmacological strategies for the treatment of acute ischaemic stroke. Lancet Neurol 2013;12:572-584.
- 12. Yoshimura S, Egashira Y, Sakai N, et al. Recovery by Endovascular Salvage for Cerebral Ultra-acute Embolism-Japan retrospective survey group. Retrospective nationwide survey of acute stroke due to large vessel occlusion in Japan: a review of 1,963 patients and the impact of endovascular treatment. Cerebrovasc Dis 2011;32:219-226.
- 13. Chao AC, Hsu HY, Chung CP, et al. Outcomes of thrombolytic therapy for acute ischemic stroke in Chinese patients: the Taiwan Thrombolytic Therapy for Acute Ischemic Stroke (TTT-AIS) Study. Stroke 2010;41:885-890.
- Kim BJ, Han MK, Park TH, et al. Current status of acute stroke management in Korea: a report on a multicenter,

comprehensive acute stroke registry. Int J Stroke 2013. Nov 21 [Epub ahead of print.].

- 15. Hong K-S, Bang OY, Kang D-W, et al. Stroke statistics in Korea: part I. Epidemiology and risk factors: a report from the Korean Stroke Society and Clinical Research Center for stroke. J Stroke 2013;15:2-20.
- **16.** Noser EA, Shaltoni HM, Hall CE, et al. Aggressive mechanical clot disruption: a safe adjunct to thrombolytic therapy in acute stroke? Stroke 2005;36:292-296.
- 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.
- **18.** Kharitonova T, Mikulik R, Roine RO, et al. Association of early national institutes of health stroke scale improvement with vessel recanalization and functional outcome after intravenous thrombolysis in ischemic stroke. Stroke 2011;42:1638-1643.
- 19. Larrue V, von Kummer RR, Muller A, et al. Risk factors for severe hemorrhagic transformation in ischemic stroke patients treated with recombinant tissue plasminogen activator: a secondary analysis of the European-Australasian Acute Stroke Study (ECASS II). Stroke 2001;32:438-441.
- Michel P, Odier C, Rutgers M, et al. The Acute STroke Registry and Analysis of Lausanne (ASTRAL): design and baseline analysis of an ischemic stroke registry including acute multimodal imaging. Stroke 2010;41:2491-2498.
- Jauch EC, Saver JL, Adams HP Jr, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2013;44:870-947.
- 22. Kidwell CS, Jahan R, Gornbein J, et al. A trial of imaging selection and endovascular treatment for ischemic stroke. N Engl J Med 2013;368:914-923.
- Ciccone A, Valvassori L, Nichelatti M, et al. Endovascular treatment for acute ischemic stroke. N Engl J Med 2013; 368:904-913.
- Broderick JP, Palesch YY, Demchuk AM, et al. Endovascular therapy after intravenous t-PA versus t-PA alone for stroke. N Engl J Med 2013;368:893-903.
- 25. Furlan A, Higashida R, Wechsler L, et al. Intra-arterial prourokinase for acute ischemic stroke. The PROACT II study: a randomized controlled trial. Prolyse in acute cerebral thromboembolism. JAMA 1999;282:2003-2011.
- 26. Rha JH, Saver JL. The impact of recanalization on ischemic stroke outcome: a meta-analysis. Stroke 2007;38:967-973.