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Stent-Assisted Recanalization for Acute Ischemic Stroke

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ABSTRACT

Objective : Acute ischemic stroke attributable to major cerebral arteries occlusion is frequently associated with severe disability or death. Pharmacological or mechanical thrombolysis may achieve better results if the treatment can be performed within 3 hours of stroke onset. If failed thrombolysis, stent-assisted recanalization may improve recanalization rates. **Methods** : We reviewed retrospectively 9 patients with acute ischemic stroke resistant to standard thromolytic therapy, who received stent-assisted recanalization from January 2002 to December 2005. Dermographics, clinical, and radiographic presentation and outcomes were studied. **Results** : Five men and four women with a median baseline National Institutes of Health Stroke Scale (NIHSS) score of 15 (range, 12-20) were included. Five lesions were located in the extracranial internal carotid artery, two in the middle cerebral artery, one in the common carotid artery, and one in the mid-basilar artery. Mean time to treatment was 9.8±14.6 hours from symptom onset. All occlusions were successfully recanalized with thrombolysis and stent placement, and the stenotic ratio was reduced from 91% (pre-stenting) to 5% (post-stenting) on average. Procedure-related complications occurred in two patients (22%): distal embolism in one and subacute thrombotic occlusion in the other. NIHSS score at discharge showed significant improvement ($P < 0.05$, Wilcoxon rank sum test). **Conclusion** : Emergency stent angioplasty for acute ischemic stroke with failed thrombolysis appears to have a high recanalization rate and to improve outcome in our retrospective study. This study reveals that emergency stent angioplasty could be considered as an optimal treatment for recalcitrant arterial occlusions. **(Kor J Cerebrovascular Surgery 8:254-9, 2006)**

KEY WORDS : Acute stroke · Ischemic · Thrombolysis · Stent

Introduction

The delayed, ineffective management of acute ischemic stroke result in high rates of morbidity and mortality. For patients with acute ischemic stroke who present with serious neurologic symptoms on admission or continue to deteriorate neurologically due to total occlusion despite maximal medical treatment, an effective intervention to improve their neurologic symptoms and clinical outcome has not yet been established. Intravenous tissue plasminogen activator (t-PA) has been approved for the treatment of acute ischemic stroke within 3 hours after symptoms onset by the United States Food and Drug Administration (FDA).[20] Drawbacks associated with intravenous t-PA thrombolysis include the fact that most patients are not seen within 3 hours, patients with baseline National Institutes of Health Stroke Scale (NIHSS) scores of 10 or greater do not fare as well as those with baseline scores of less than 10.[1] Additionally, only 8% of patients with internal carotid artery (ICA) occlusion receiving intravenous t-PA treatment have shown early recanalization.[4][22] Recently, intra-arterial thrombolysis has been demonstrated to extend the time window for the treatment of acute ischemic stroke to 6 hours but has not been approved by the FDA.[7] During the first hours and days after a stroke, the risk of reocclusion or recurrent arterio-arterial embolism remains. Alternative

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treatment for acute ischemic stroke patients includes endovascular mechanical revascularization.[8] In acute atherothrombotic occlusions with underlying stenosis, mechanical thrombolysis had a low recanalization rate and reocclusion at initial recanlization site. For patients with acute ischemic stroke who fail intra-arterial thrombolysis and mechanical clot disruption, there are few options. In the case of atherothrombotic occlusion, mechanical thrombolysis with stent angioplasty may be necessary to decrease underlying chronic vessel stenosis. We report a retrospective study to investigate feasibility and outcome of endovascular stent angioplasty after failed intra-arterial pharmacological and mechanical thrombolysis for acute ischemic stroke at our institution.

Patients and Methods

1. Patients

From January 2002 to July 2005 at one cerebrovascular center, we identified 9 patients who underwent stent angioplasty immediately after failed pharmacologic and/or mechanical thrombolysis in the setting of an acute ischemic stroke as defined by clinical, radiological findings at presentation. Clinical and radiographic data included the following: demographic information, National Institutes of Health Stroke Scale (NIHSS) score before endovascular procedures, time to treatment, location of occlusion, treatment before stenting including pharmacological and mechanical thrombolysis, and degree of stenosis after thrombolysis. Poststenting angiographic results were by degree of stenosis after stenting. Complications felt to be a result of the procedure were recorded. NIHSS score at the time of discharge was also recorded.

2. Techniques of Stent Placement Procedure

A transfemoral approach was used to performed diagnostic cerebral angiography with a standard 5-French (Fr) catheter. Digital subtraction angiography of the ipsilateral and contralateral common carotid arteries and of the vertebral artery was performed to demonstrate the occlusion site and to assess potential collateral routes. After complete occlusion was demonstrated, the diagnostic catheter was exchanged for a 6-Fr guide catheter that was placed over a 0.038-inch diameter exchange length wire. Microcatheters and microwires of different dimensions were navigated through the guide catheter to access the site of occlusion. Before crossing the occlusion, the patients were given intravenous heparin for systemic anticoagulant at a dose of 60 units per kg body weight or 30 units per kg body weight if intravenous thrombolytic agents had been administered. A loading dose (0.4 ug/kg/min) and maintenance dose (0.1 ug/kg/min) of tirofiban was administered intravenously to three patients at the discretion of the physician performing the procedure. Through the microcatheter, intra-arterial thrombolytic therapy was performed with urokinase (500,000 units), t-PA (up to 20 mg) or abciximab (up to 4 units). Mechanical thrombolysis was attempted with balloon angioplasty and the microcatheter wire. After failure of pharmacological and/or mechanical thrombolysis, angioplasty with stent placement was considered especially in case with the underlying severe vessel stenosis and atherothrombotic occlusion.

For the performance of stent angioplasty, a 0.014-inch exchange length microwire was maintained distal to the vessel occlusion, and stent sized to the target vessel diameter were navigated to the occlusion site. Two different balloon expandable stents of various lengths and diameters were used for the basilar artery (BA) and MCA: 1) Driver (Medtronic, Santa Rosa, CA) and 2) Flexmaster (JoMed International, Helsinborg, Sweden). Deployment of a self-expandable Precise nitinol stent (JoMed) in 5 patients or Zilver (Cook) in 1 patient was performed for ICA occlusion. Immediately after stent placement, all of the patients were given an oral dose of clopidogrel (300 mg) and aspirin (325 mg) and were maintained on clopidogrel (75 mg/day) and aspirin (325 mg/day). Clopidogrel therapy was discontinued after 1 month, and patients were maintained on aspirin indefinitely.

Results

The clinical summary was listed in Table 1. The cause of lesion in all patients was atherothrombotic occlusion with underlying high-grade vascular stenosis. The mean age of our study of five men and four women was 58 ± 12 years (range 34 to 71 years). The median baseline NIHSS score was 15 (range 12 to 20) and mean time to treatment was 9.8 $\pm$ 14.6 hours from symptom onset. Five lesions were located

Table 1. Clinical summary of nine patients underwent stent−assisted recanalization for acute ischemic stroke

Patient No.	Age(yr) /Sex	Location of occlusion	NIHSS before procedure	Time to treatment (hrs)	Treatment before stenting	Degree of stenosis after thrombolysis (%)	Stent devices (mm)	Procedure−related complications	Degree of stenosis after stenting (%)	NIHSS at discharge
1	58/M	Rt. MCA	12	48	Urokinase, Tirofiban Balloon angiopplasty	95	Driver 2.5×12	None	0	7
2	47/F	Lt. ICA	15	10	Urokinase, Balloon angioplasty	80	Precise 4 × 60	None	5	10
3	65/M	Lt. ICA	15	5	Urokinase, Tirofiban Balloon angioplasty	95	Precise 8 × 30	None	0	6
4	34/F	Rt. CCA	20	6	Urokinase, Tirofiban Balloon angioplasty	95	Precise 6 × 40	Distal embolism	20	18
5	65/M	Lt. ICA	12	2	t−PA Balloon angioplasty	95	Precise 8 × 30	None	0	10
6	66/F	Lt. ICA	15	3	t−PA	95	Precise 7 × 30	None	10	7
7	56/F	Lt. ICA	14	4	Urokinase Balloon angioplasty	95	Zilver 8 × 30	None	5	5
8	71/M	Mid BA	17	2	t−PA, Reopro	80	Driver 3.5 × 15	Thrombotic occlusion	5	15
9	64/M	Lt. MCA	15	8	Urokinse Balloon angioplasty	90	Flexmaster 2.5 × 12	None	0	7

MCA: middle cerebral artery, ICA: internal carotid artery, CCA: common carotid artery, BA: basilar artery, t−PA: tissue plasminogen activator

in the ICA, two were in the MCA, one was in the common carotid artery, and one was in the mid-BA. Intravenous tirofiban was administered in three of nine (33%) patients. Intra-arterial thrombolysis was performed with urokinase in six patients, and t-PA in three patients, and abciximab in one patient. Balloon angioplasty was performed in seven patients. All patients underwent successful crossing of the occlusion site and subsequent stent angioplasty. The stenotic ratio was reduced from 91% (pre-stenting) to 5% (post-stenting) on average. Procedure-related complications occurred in two patients (22%): distal embolism in one and subacute thrombotic occlusion in the other. Seven of nine patients (78%) exhibited a dramatic clinical improvement in their NIHSS score at discharge. However, the complicated two patients showed severe disabilities and their NIHSS scores at discharge were similar to one on admission. At discharge, median NIHSS score was 9 (range 5 to 18). These results showed statistically significant clinical improvement ($P < 0.05$, Wilcoxon rank sum test).

Discussion

This report with the preliminary results demonstrates that stent angioplasty can be utilized as an option for patients with lesions recalcitrant to pharmacological and mechanical thrombolysis in acute athrothrombotic stroke. In addition, this intervention may also improve survival and reduce morbidity by restoration of blood flow to penumbral areas and decreasing stroke volume. The lack of a control or alternative treatment group does not allow us to assess whether this approach is clinically beneficial but does provide pilot data for subsequent study.

Intra-arterial thrombolysis provides an alternative to intravenous thrombolysis in selected patients with acute ischemic stroke. Rapid, local delivery of fibrinolytic agents or immediate access of thrombolytic devices is now feasible with recent advances in the field of neurointervention. Intra-arterial thrombolysis has been used most successfully in patients with acute MCA occlusion. There is evidence that the treatment window for intra-arterial thrombolysis can be extended to at least 6 hours from stroke onset in patients with MCA occlusion. Other potential candidates for intra-arterial candidates for intra-arterial thrombolysis include patients with extracranial ICA occlusion, intracranial ICA

"T" occlusion, or basilar artery occlusion. Two randomized, multicenter, controlled trials of intra-arterial thrombolysis in acute MCA stroke have been reported so far, the Prolyse in Acute Cerebral Thromboembolism Trial (PROACT-I) and PROACT-II.[4)7)] PROACT-II study revealed that recanalization rates of 66% in the treatment group versus 18% in the control group (P<0.001).[7)] Conversely, symptomatic hemorrhage occurred in 10% of the prourokinase group versus 2% in the control group. In PROACT-II, despite the higher early symptomatic intracranial hemorrhage rate, patients overall benefited from therapy, and there was no excess mortality (prourokinase group 24%, control group 27%) in the "intention-to-treat" analysis. The major issues with intra-arterial thrombolysis has been the rate of hemorrhage, inability to effectively dissolve platelet-rich clots, and lengthy times to recanalization.[3)7)] Mechanical device trials were initiated in the hopes of addressing these concerns. Mechanical thrombolysis have included clot maceration with the microcatheter or microwire, thrombus or embolus removal, intra-arterial ultrasound, and balloon angioplasty.[2)8)14)15)17)] In the Mechanical Embolus Removal in Cerebral Ischemia (MERCI) phase I trial, successful recanalization was demonstrated in cerebral vessels in 18 (64%) patients with or without intra-arterial t-PA therapy.[8)] Sorimachi et al. reported the recanalization rate was 46% using the Merci clot

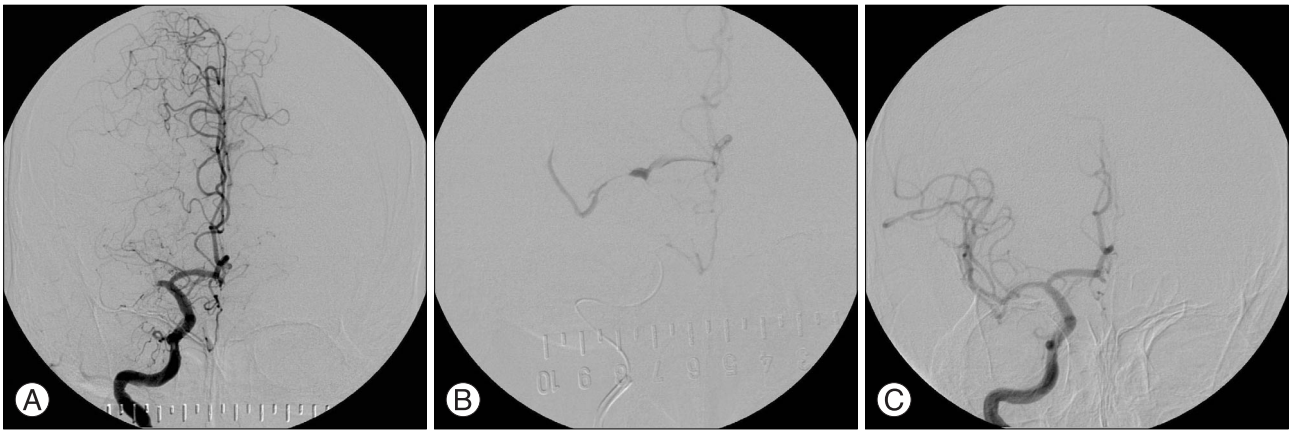

Fig. 1. Patient 1 presented with left hemiparesis 48 hours from stroke attack. A : Angiogram revealed complete occlusion of the right middle cerebral artery. B : Severe stenosis appeared on angiogram obtained immediately after pharmacological and balloon angioplasty. Blood flow was very weak through the stenosis. C : After satisfactory and uneventful stent deployment, angiogram showed a normal caliber of the right middle cerebral artery.

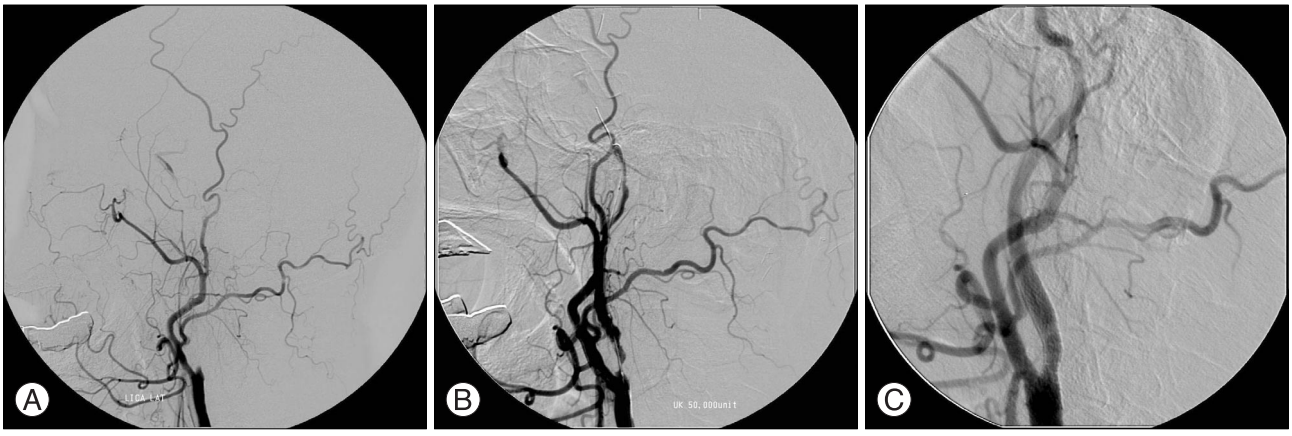

Fig. 2. Patient 3 presented with right hemiparesis and mental change 5 hours from stroke attack. A : A diagnostic angiogram confirmed the presence of a left carotid occlusion at the bifurcation. B : The occlusion was crossed with a 0.014-inch microwire and microcatheter injection confirmed severe stenosis at the occlusion site. C : Poststenting and angioplasty revealed a normal caliber left carotid and patent intracranial circulation.

retriever.[17] Mechanical thrombolysis may reduce the need for incremental doses of thrombolytics, thus minimizing the hemorrhage risk. To date, there is insufficient evidence to suggest a dose threshold at which hemorrhagic transformation occurs.

In most instances of acute vascular occlusions, the cause is embolic in the absence of an underlying vascular stenosis. However, plaque rupture in an underlying stenosis lead to acute vascular occlusions. In our series with an underlying vascular stenosis and acute thrombotic occlusion, angioplasty was found to have temporary recanalizing effect and thrombosis and reocclusion recurred during the angioplasty. An occlusive lesion consisting of thrombus superimposed on atherosclerotic plaque is more vulnerable to reocclusion.[16] Dissolution of the thrombus leads to exposure of the thrombogenic plaque surface, thereby providing a template for the reformation of thrombus. Theoretically, stenting minimizes the risk of acute closure by compression of the intimal flap, or trapping plaque material between the stent and the vessel wall. Therefore, it is considered stenting is better tool for vascular recanalization than mechanical angioplasty. In the setting of acute myocardial infarction, stenting began to replace angioplasty as the primary means of revascularization for acute coronary syndrome.[10][18][21] In one multicenter, randomized trial comparing stenting with angioplasty for acute myocardial infarction, implantation of a stent has clinical benefits beyond those of angioplasty alone.[9] There have been several reports about stent-assisted recanalization for acute stroke.[6][11-13][19] These reports concluded that stent-assisted recanalization for acute stroke resulting from atherothrombotic occlusion is associated with a high recanalization rate and low intracranial hemorrhage rate. These preliminary results suggest that stenting may be an alternative option for recalcitrant cerebral artery occlusions. However, they have limitations largely derived from its retrospective nature. Future prospective studies are necessary to determine which patients are most likely to benefit from this form of therapy.

Problems about stenting are vessel rupture, dissection, reperfusion hemorrhage, distal embolism, or subacute occlusion. We experienced two complicated cases; distal embolism and subacute occlusion. These risks can be minimized by limiting the time from onset to revascularization to limit reperfusion injury, by using experienced operators to reduce the risk of vessel dissection, by maintaining thrombolytic or antithrombotic therapy for several days to prevent subacute occlusion, and by using devices to prevent distal embolization. In addition, there is the longer-term risk of stent restenosis, although this is less concerning given that patients are being treated for a disease with a high probability of severe disability and mortality.

Conclusions

Our preliminary results suggest that stent-assisted

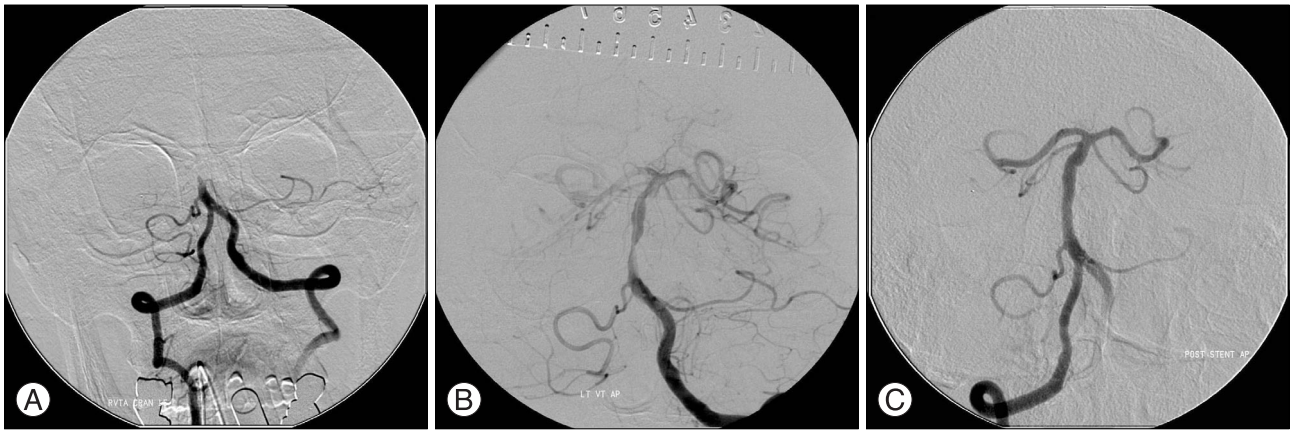

Fig. 3. Patient 8 presented with mental change 2 hours from stroke attack. The patient had known medical history of basilar artery stenosis. A : A diagnostic angiogram confirmed the complete occlusion of mid basilar artery. B : After pharmacological thrombolysis, moderate to severe stenosis was identified on mid-basilar portion. C : Poststenting and angioplasty showed a complete recanalization of the stenotic basilar artery.

recanalization for acute atherothrombotic stroke with an underlying vessel stenosis were fairly good from the viewpoints of clinical and angiographic follow-up results. This procedure can be considered an alternative to pharmacological and mechanical thrombolysis in selected patients.

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