Stenting as a Rescue Treatment After Failure of Mechanical Thrombectomy for Anterior Circulation Large Artery Occlusion

Jang-Hyun Baek, MD; Byung Moon Kim, MD; Dong Joon Kim, MD; Ji Hoe Heo, MD; Hyo Suk Nam, MD; Joonsang Yoo, MD

Background and Purpose—We hypothesized that permanent stenting may be a rescue treatment for stentriever-failed anterior circulation large artery occlusion. We compared the outcomes among patients with permanent stenting and those without stenting after stentriever failure.

Methods—We retrospectively evaluated 208 patients who underwent stentriever thrombectomy for anterior circulation large artery occlusion between September 2010 and September 2015. Modified thrombolysis in cerebral ischemia 2b-3 recanalization was achieved with stentriever alone or in combination with Penumbra device in 155 patients (74.5%). An additional 8 patients (3.8%) obtained modified thrombolysis in cerebral ischemia 2b-3 with urokinase or glycoprotein IIb/IIIa inhibitor infusion. Of the remaining 45 patients (21.6%), 17 underwent stenting (stenting group; mean age, 68 years), whereas 28 did not undergo stenting (nonstenting group; mean age, 72 years). The rate of modified thrombolysis in cerebral ischemia 2b-3 in stenting group was assessed, and clinical outcomes were compared between groups.

Results—There were no differences in clinical and laboratory findings, initial National Institute of Health Stroke Scale score, location of anterior circulation large artery occlusion, and onset-to-puncture time between groups. Modified thrombolysis in cerebral ischemia 2b-3 was achieved in 14 members (83.3%) of the stenting group. Stenting group had more favorable outcomes (modified Rankin Scale score 0–2, 35.3%) and less cerebral herniation (11.8%) than nonstenting group (modified Rankin Scale score 0–2, 7.1%; cerebral herniation, 42.9%; P<0.05 for both). Symptomatic intracranial hemorrhage and mortality rates did not differ between stenting group (symptomatic intracranial hemorrhage, 11.8%; mortality, 23.5%) and nonstenting group (symptomatic intracranial hemorrhage, 14.3%; mortality, 39.3%).

Conclusions—Permanent stenting may be a rescue modality for stentriever-failed anterior circulation large artery occlusion. A large prospective study is necessary for confirmation because of the small sample size of this study. (Stroke. 2016;47:2360-2363. DOI: 10.1161/STROKEAHA.116.014073.)

Key Words: stents ■ stroke ■ thrombectomy

Because recent randomized, controlled trials proved the efficacy and safety of intra-arterial recanalization therapy (IART) via mechanical thrombectomy predominantly using stentriever, stentriever thrombectomy has been recommended as the first-line method in IART for acute anterior circulation large artery occlusion (AC-LAO).1–4 Nevertheless, stentriever thrombectomy fails to achieve successful recanalization (modified thrombolysis in cerebral ischemia [mTICI], 2b-3) in ≈30% of cases.5 Permanent self-expanding stent placement has been suggested as an another primary approach or as a rescue tool for recanalization of acute intracranial LAO.6–8 We hypothesized that permanent self-expanding stent placement may be a rescue treatment for AC-LAO refractory to stentriever thrombectomy. This study aimed to test the hypothesis that stenting might further recanalize stentriever-failed AC-LAO, resulting in a significantly more favorable outcome in the stenting group (SG) than in the nonstenting group (NSG), without an increase in symptomatic intracranial hemorrhage (sICH) and mortality rates.

Methods
We retrospectively evaluated the data for 208 consecutive patients with acute stroke attributable to AC-LAO who underwent stentriever thrombectomy in a comprehensive stroke center between September 2010 and September 2015. All patients who underwent IART for acute stroke were registered in the prospectively maintained stroke registry and neurointerventional database at the hospital. The indication for IART was an initial National Institute of Health Stroke Scale (NIHSS) score of ≥4 within 6 hours of symptom onset. If indicated, tissue-type plasminogen activator was administered intravenously, and IART was subsequently performed in the nonresponders to tissue-type plasminogen activator. AC-LAO
was defined as occlusion of the intracranial internal carotid artery (ICA) and middle cerebral artery M1 or M2 proximal portion before second bifurcation. Cases of AC-LAO because of intracranial arterial dissection were excluded.

Our institutional review board approved this study and waived patient-informed consent for study inclusion based on the retrospective design.

IART for AC-LAO
IART was performed under local anesthesia. IART was initiated after completion of 4-vessel angiography for evaluation of collaterals in all cases before June 2013; however, for all cases thereafter, the occluded target vessel on computed tomography (CT) angiography was first approached to reduce the time from puncture to recanalization. A balloon guiding catheter (8F or 9F Cello; Covidien/ev3, Irvine, CA) was used in all cases after its introduction early in 2012. The 2 neurointerventionalists who had treated all AC-LAO cases also performed IART according to identical endovascular protocol. Briefly, an 8F or 9F balloon guiding catheter was placed in the relevant cervical ICA. In patients who had a large number of clots in the extracranial ICA, suction thrombectomy using the balloon guiding catheter was first attempted, and then, stentriever (Solitaire AB/FR; Covidien/ev3) thrombectomy was performed for the remnant occlusion. In patients who had no clots in the extracranial ICA, stentriever thrombectomy was first attempted. After waiting for 3 to 5 minutes after stentriever deployment, the balloon guiding catheter was inflated, and the stentriever was then retrieved. During the retrieval of the stentriever, the balloon guiding catheter was manually suctioned by an assistant. If the occlusion remained on the control angiogram immediately after the retrieval of the stentriever, the procedure was repeated. For patients who had refractory occlusion after 3 to 7 stentriever thrombectomy attempts, a Penumbra device (Penumbra, Alameda, CA), urokinase, or glycoprotein IIb/IIIa inhibitor was used at the operator’s discretion. Finally, permanent stenting was conducted. The decision to perform permanent stenting and the type of stent used depended on the operator’s preference. Specifically, 1 of the 2 neurointerventionalists who performed the IART procedures favored permanent stenting for stentriever-failed cases, whereas the other did not. In the SG, glycoprotein IIb/IIIa inhibitor (Reopro, 5–10 mg) was bolus injected intra-arterially and maintained for at least 24 hours to prevent acute in-stent thrombosis, with the exception of one patient who had suspected biliary sepsis because of bile duct cancer. Successful recanalization was defined when mTICI 2b-3 recanalization was persistent on an angiogram taken after at least 10 minutes.

Clinical and Imaging Follow-Up
All patients who underwent IART were examined via magnetic resonance imaging, including T2*, Flair, and diffusion-weighted imaging and 3-dimensional time-of-flight and contrast-enhanced magnetic resonance angiography within 24 hours. When the patient’s neurological status abruptly deteriorated, a CT scan was immediately obtained. In the SG, stent patency was evaluated via magnetic resonance angiography or CT angiography obtained within 24 hours and then followed up with catheter angiography or CT angiography at 3 to 12 months post stenting. ICH was evaluated on CT or T2* magnetic resonance images. ICH was regarded as symptomatic (sICH) if the patient’s NIHSS score increased to ≥4 and no different causes for the increased NIHSS score were evident. Clinical outcomes were evaluated via NIHSS score daily during the first week and at discharge and via modified Rankin scale score at discharge and 3 months. The SG and NSG were compared with respect to the rates of sICH and cerebral herniation requiring decompression craniectomy or causing death, as well as modified Rankin scale score and mortality at 3 months.

Results
mTICI 2b-3 recanalization was achieved in 155 patients (74.5%) after stentriever thrombectomy alone or in combination with a Penumbra device. Additionally, 8 patients achieved recanalization with intra-arterial infusion of thrombolytic (urokinase, 50 000–200 000 IU) or glycoprotein IIb/IIIa inhibitor (Reopro, 5.0–10.0 mg). Finally, 45 patients remained non-recanalized after stentriever thrombectomy alone (n=24) or stentriever thrombectomy plus Penumbra (n=21). Of these 45 patients, 17 were treated with permanent stenting, whereas 28 patients were left nonrecanalized without stenting (Figure 1). The Solitaire-AB/FR stentriever was permanently detached in 10 patients (Figure 2), whereas a Wingspan stent was alternatively used in 7 patients. Pre- or poststenting balloon angioplasty was performed in 7 cases (41.2%).

There were no differences in clinical and laboratory findings, initial NIHSS score, location of AC-LAO, and onset-to-puncture time between the SG and the NSG (Table). mTICI 2b-3 recanalization was obtained in 14 patients (83.3%) of the SG. Follow-up vascular imaging was obtained in all patients at least once via magnetic resonance angiography, CT angiography, or digital subtraction angiography 1 day to 12 months after stenting. All stented arteries were patent with the exception of 1 patient who did not receive intravenous glycoprotein IIb/IIIa inhibitor maintenance because of biliary sepsis. The rate of favorable outcome (modified Rankin scale score, 0–2) was significantly higher in the SG (35.5%) than in the NSG (7.1%), and cerebral herniation was significantly lower (SG: 11.8%; NSG: 42.9%). There was no difference in sICH between the SG (n=2, 11.8%) and the NSG (n=4, 14.3%). Fifteen patients (33.3%) died at 3 months. There was no difference in the mortality rate between the SG (n=4, 23.5%) and the NSG (n=11, 39.3%; Table).

Discussion
The results of this study showed that, in patients with acute AC-LAO that was refractory to stentriever thrombectomy, permanent stenting achieved mTICI 2b-3 recanalization in 83.3% of cases, and the stent group had a significantly higher favorable outcome rate than the nonstent group without an increase in sICH or mortality. This suggests that permanent stenting may be a rescue treatment modality for stentriever-failed AC-LAO. The efficacy and safety of permanent stenting for recanalization of acute stroke were evaluated in several
In the era of stentriever thrombectomy, however, the efficacy of permanent stenting for stentriever-failed AC-LAO has remained unclear. To our knowledge, this is the first report comparing an SG with an NSG in patients with stentriever-failed AC-LAO, although the study performed was retrospective in nature.

In ≈30% of AC-LAO cases, stentriever thrombectomy failed to achieve mTICI 2b-3 recanalization. In 25.5% of the AC-LAO cases in this study, the use of stentriever thrombectomy alone or in combination with a Penumbra device failed to achieve mTICI 2b-3 recanalization. Irrespective of the cause of the refractoriness of AC-LAO, a rescue modality is needed for such refractory cases. One modality that we used was intra-arterial infusion of thrombolytic or glycoprotein IIb/IIIa inhibitor, which achieved further mTICI 2b-3 recanalization in 3.8% of cases. The final rescue modality that we considered was permanent stenting. In the literature, the mTICI 2 to 3 recanalization rate of permanent stenting ranged from 75% to 100%, and the favorable outcome rate ranged from 25% to 50%, with a sICH rate of 0 to 16.0% and a mortality rate of 10.5%–38.9%. These outcomes were not superior to those of stentriever thrombectomy. In addition, permanent stenting has the drawback that it requires antplatelet medication during or immediately after the treatment in an acute stroke setting. Therefore, stentriever thrombectomy is currently the first-choice method for IART. However, in the setting of stentriever failure, permanent stenting might be reappraised as a rescue option. One major concern of permanent stenting is that antplatelet medication might increase the rate of sICH. In this study, all patients except one received glycoprotein IIb/IIIa inhibitor during the procedure for resolution or prevention of acute in-stent thrombosis, and dual antplatelet medication was subsequently maintained for at least 3 months. The rate of sICH of the SG (11.8%) was within the range of previous studies and lower than that of the NSG (14.3%) in this study, although this difference was not significant. Furthermore, the rate of cerebral herniation caused by malignant edema or sICH was significantly lower in the SG (11.8%) than in the previous studies.

### Table. Comparison of Clinical and Laboratory Findings and Outcomes Between Stenting and Nonstenting Groups

<table>
<thead>
<tr>
<th>Factors</th>
<th>Stenting Group (n=17)</th>
<th>Nonstenting Group (n=28)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>68.5±11.2</td>
<td>72.8±11.1</td>
<td>0.214</td>
</tr>
<tr>
<td>Male sex</td>
<td>8 (47.1%)</td>
<td>14 (50.0%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>14 (82.9%)</td>
<td>25 (89.3%)</td>
<td>0.658</td>
</tr>
<tr>
<td>DM</td>
<td>8 (47.1%)</td>
<td>15 (53.6%)</td>
<td>0.763</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>2 (11.8%)</td>
<td>5 (17.9%)</td>
<td>0.693</td>
</tr>
<tr>
<td>Smoking</td>
<td>6 (35.3%)</td>
<td>11 (39.3%)</td>
<td>1.0</td>
</tr>
<tr>
<td>CAOD</td>
<td>7 (41.2%)</td>
<td>5 (17.9%)</td>
<td>0.163</td>
</tr>
<tr>
<td>PAOD</td>
<td>2 (11.8%)</td>
<td>2 (7.1%)</td>
<td>0.626</td>
</tr>
<tr>
<td>Location</td>
<td>7 (41.2%)</td>
<td>13 (46.4%)</td>
<td>0.767</td>
</tr>
<tr>
<td>i-NIHSS, median (range)</td>
<td>19 (7–22)</td>
<td>16 (6–28)</td>
<td>0.888</td>
</tr>
<tr>
<td>IV-tPA</td>
<td>5 (29.4%)</td>
<td>9 (32.1%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Onset-to-puncture time, min</td>
<td>230.1±90.4</td>
<td>208.1±68.2</td>
<td>0.359</td>
</tr>
<tr>
<td>Number of stentriever passes, mean±SD</td>
<td>4.4±2.1</td>
<td>5.1±2.5</td>
<td>0.345</td>
</tr>
<tr>
<td>Penumbra use</td>
<td>8 (47.1%)</td>
<td>13 (46.4%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Urokinase use</td>
<td>4 (23.5%)</td>
<td>7 (25.0%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Glycoprotein IIb/IIIa inhibitor use</td>
<td>6 (35.3%)</td>
<td>3 (10.7%)</td>
<td>0.063</td>
</tr>
<tr>
<td>Procedure time, min</td>
<td>155.3±64.0</td>
<td>152.8±51.9</td>
<td>0.886</td>
</tr>
<tr>
<td>mTICI 2b-3</td>
<td>14 (83.3%)</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>sICH</td>
<td>2 (11.8%)</td>
<td>4 (14.3%)</td>
<td>1.0</td>
</tr>
<tr>
<td>CH</td>
<td>2 (11.8%)</td>
<td>12 (42.9%)</td>
<td>0.046</td>
</tr>
<tr>
<td>mRS, 0–2</td>
<td>6 (35.3%)</td>
<td>2 (7.1%)</td>
<td>0.039</td>
</tr>
<tr>
<td>Mortality</td>
<td>4 (23.5%)</td>
<td>11 (39.3%)</td>
<td>0.341</td>
</tr>
</tbody>
</table>

CAOD indicates coronary artery occlusive disease; CH, cerebral herniation; CI, confidence interval; DM, diabetes mellitus; ICA, internal carotid artery; i-NIHSS, initial National Institute of Health Stroke Scale; IV-tPA, intravenous tissue-type plasminogen activator; MCA, middle cerebral artery; mTICI, modified thrombolysis in cerebral ischemia; PAOD, peripheral artery occlusive disease; and sICH, symptomatic intracranial hemorrhage.
NSG (42.9%), leading to lower mortality in the SG (23.5%) than in the NSG (39.3%). These results could be derived from the high mTICI 2b-3 recanalization rate (83.3%) of the SG, whereas the recanalization rate of the NSG was 0%. In other words, the benefit of recanalization success by permanent stenting might overcome its drawbacks in patients with stentriever-failed AC-LAO that was otherwise left nonrecanalized. These results seem to reemphasize that recanalization success is one of the most important factors for improving functional outcome and reducing mortality.1,8,15

This study had several limitations inherent to its retrospective nature. Patient selection for permanent stenting depended on the operators’ preference. Specifically, between the 2 operators, one favored permanent stenting for stentriever-failed AC-LAO, whereas the other did not. There were, however, no differences in clinical and laboratory findings, presenting stroke severity (initial NIHSS score), location of AC-LAO (ICA or middle cerebral artery), and onset-to-puncture time between the 2 groups; therefore, it seems unlikely that patient selection bias affected the results. Another limitation was the relatively small sample size from a single center. Our findings warrant a prospective randomized multicenter study with a large sample size to determine the value of permanent stenting for stentriever-failed AC-LAO.

Conclusions
Among patients with stentriever-failed AC-LAO, the SG had a significantly more favorable outcome and less cerebral herniation than the NSG, without an increase in sICH and mortality rates. Permanent stenting may be a feasible rescue modality for stentriever-failed AC-LAO. A large prospective study is necessary for confirmation because of the small sample size of this study.

Disclosures
Dr D.J. Kim received a speaker honorarium from Medtronic. The other authors report no conflicts.

References
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