Endovascular Therapy of Cerebral Arterial Occlusions: Intracranial Atherosclerosis versus Embolism

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Background: Treatment strategy for acute arterial occlusions due to intracranial atherosclerotic disease (IAD) may differ from those due to embolism (embolic). The aims were to differentiate and classify angiographically defined occlusion due to IAD versus embolism and identify baseline clinical factors associated with IAD-related occlusion. *Methods:* Acute ischemic stroke patients with large cerebral artery occlusions on computed tomography angiography who underwent transfemoral cerebral angiography for endovascular treatment were included. Patients were categorized as the embolic (no evidence of focal stenosis after recanalization) or IAD group (significant fixed focal stenosis in the occlusion site, evidenced in the final angiography or during the endovascular treatment procedure) based on transfemoral cerebral angiography findings. *Results:* In total, 158 patients were included. The IAD group patients (n = 24) were younger ($P = .005$), more often male ($P < .001$) and smokers ($P < .001$), and had a higher total cholesterol level ($P = .001$) than patients in the embolic group (n = 134). The posterior circulation was more frequently involved in the IAD group ($P = .001$). Independent predictors of IAD on multivariable analysis were male sex (odds ratio, 6.42 [95% confidence interval, 1.25-32.97], $P = .026$), posterior circulation involvement (3.57 [1.09-11.75], $P = .036$), and high total cholesterol levels (1.02 [1.01-1.03], $P = .008$). *Conclusions:* Male sex, hypercholesterolemia, and posterior circulation involvement are associated with higher likelihood of underlying IAD as the etiology for the intracranial arterial occlusion. In patients with these characteristics, underlying IAD may have to be considered and the endovascular treatment strategy may have to be modified. **Key Words:** Intracranial atherosclerosis—intracranial embolism—cerebrovascular disorders—thrombectomy—thrombolytic therapy—acute ischemic stroke.

Although intravenous tissue plasminogen activator (IV rt-PA) is a standard therapy for acute ischemic stroke,[1-3] it has limited efficacy in recanalizing large-artery occlusions.[4,5] Endovascular treatment improves the rate of recanalization compared with IV rt-PA.[6] Although previous phase 3 clinical trials on endovascular treatment in which conventional treatment methods were mostly used have failed to show successful outcomes,[7-9] recent

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clinical trials using newer devices such as stent retrievers have shown successful outcomes.[10-12]

In the Western society, large-artery occlusions are generally because of embolism from proximal sources. This is not the case in Asian patients in whom intracranial atherosclerotic disease (IAD) is common.[13] Residual vascular stenosis associated with IAD is often encountered during endovascular revascularization treatment for large-artery occlusions. This may have important implications for endovascular treatment because emerging approaches using thrombectomy via a stent retriever may be less successful if significant IAD is associated with the occlusion. Reocclusion tendency of IAD is also a problem, which needs additional rescue treatments.[14] However, the frequency of IAD and clinical factors predicting IAD have not been identified.

The aim of the present study was to categorize intracranial occlusion into either embolic or IAD-related occlusions based on postreperfusion cerebral angiography findings and to identify factors associated with IAD-related occlusion.

Methods

Patient Enrollment

Among consecutive patients with ischemic stroke admitted to Ajou University Hospital, Suwon, Korea between January 2010 and March 2014, we included patients (1) with acute ischemic stroke due to large cerebral artery occlusion on computed tomography (CT) angiography, (2) who underwent transfemoral cerebral angiography for endovascular reperfusion therapy, and (3) whose onset-to-puncture time was within 8 hours. This time limitation was based on the phase 2 clinical trials with stent retriever (SWIFT and TREVO 2 studies).[15,16] Patients were excluded if (1) the cause of stroke was dissection, Moyamoya disease, or vasculitis; (2) the ipsilesional extracranial internal carotid artery was chronically occluded; or (3) the arterial lesion status could not be reliably assessed because of either persistent occlusion or incomplete recanalization.

Operational Definition of IAD and Embolic Etiologies for Occlusion

The authors discussed operational definition regarding angiographic classification comparing IAD and embolism. IAD was defined as significant fixed focal stenosis in the occlusion site, evidenced in the final angiography or during endovascular treatment (Fig 1 and Table 1). Significant stenosis was defined as (1) a degree of fixed stenosis >70%, or (2) a degree of fixed stenosis >50 in addition to either flow and perfusion impairment on angiography or an evident reocclusion tendency even after sufficient treatment with stent retrievers.[14,17] When angioplasty or stent insertion was used for intracranial stenosis and it was fully recanalized, the case was classified as an IAD. Arterial stenoses due to vessel wall injury or iatrogenic dissection were not classified as an IAD and excluded from the study population. Embolism was defined when there was no evidence of focal stenosis after thrombolysis or thrombectomy. When full recanalization of the occlusion site was evident in short-term repeat CT angiography, it was also classified as embolism.[14] For defining embolic occlusions, minimal stenosis with sufficient blood flow and without reocclusion tendency was allowed. Two experienced neurologists (K.S.L. and H.I.S.) reviewed the angiographic data blinded to the patients' clinical information. Final determination was based on consensus among them and the other interventional neurologist (J.S.L.).

Protocols

For acute ischemic stroke treatment, a bridging endovascular treatment protocol based on noncontrast CT and CT angiography has been used. CT scans (including noncontrast and postcontrast axial parenchymal images) and CT angiography scans (SOMATOM Sensation 16, Siemens, Erlangen, Germany) were obtained for each patient on admission to the emergency department. The CT angiography source images were postprocessed to create coronal, sagittal, and axial multiplanar reformats in maximum intensity projection images and volume-rendered 3-dimensional images. Patients who met the criteria for IV rt-PA within 3-4.5 hours of onset were treated with .9 mg/kg IV rt-PA. If an intracranial large artery corresponding to the stroke signs was observed to be occluded on CT angiography, the patients were brought to the angiography room for endovascular treatment. Patients in whom intracranial large-artery occlusion was identified despite IV rt-PA treatment and those who were ineligible to receive IV rt-PA or who were late for the IV rt-PA time window were considered candidates for endovascular treatment. The time window for endovascular treatment was less than 6 hours of onset-to-puncture time. If the time window was expected to be 6-8 hours, the decision to perform endovascular treatment was based on diffusion-weighted image–perfusion-weighted image mismatch. If the onset was unclear (for example, wake-up stroke), the decision was based on diffusion-weighted image–fluid-attenuated inversion recovery mismatch.

The methods of endovascular treatment were determined at the treating physicians' discretion. For mechanical thrombectomy, the clot aspiration method with the Penumbra system (Penumbra, Alameda, CA) was used in the early study period, whereas the embolus retrieval method with the Solitaire stent system (Covidien, Irvine, CA) was mostly used after 2011. Endovascular treatment was not considered when there were signs of large ischemic damage such as frank hypodense lesions on noncontrast CT.

Informed consent was obtained from all patients or their relatives before they received IV rt-PA or intra-arterial