Occlusion Status on Magnetic Resonance Angiography Is Associated with Risk of Delayed Ischemic Events in Cerebral Aneurysms Treated with Stent-Assisted Coiling

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■ OBJECTIVE: **Management after stent-assisted coiling (SAC) for unruptured intracranial aneurysm is sometimes difficult because close monitoring for ischemic events for a long period of time after the procedure is necessary. The purpose of this study was to clarify the usefulness of magnetic resonance angiography (MRA) at follow-up after SAC.**

■ METHODS: **Sixty-six consecutive cases of SAC for unruptured intracranial aneurysm in our institute and affiliated hospitals were retrospectively reviewed for a delayed ischemic event. Occlusion status of the aneurysm and stent apposition on time-of-flight (TOF)-MRA, patient demographics, and characteristics of the aneurysms were analyzed for a possible relationship to delayed ischemic events.**

■ RESULTS: **Over a median follow-up of 755 days, 14 patients had delayed ischemic events after a median follow-up of 230.5 days. All of the ischemic events were transient or asymptomatic. Univariate analysis revealed that the history of hypertension ($P = 0.042$) and the occlusion status of the aneurysm ($P = 0.006$) were significantly associated with delayed ischemic events. Multivariate analysis indicated that dome filling had a hazard ratio of 4.96 (95% confidence interval [CI], 1.30–23.60) and 3.74 (95% CI, 1.10–13.34), compared with neck remnant and complete obliteration, respectively. Six of 7 patients who had persistent dome filling during follow-up developed a delayed ischemic event.**

■ CONCLUSIONS: **In this preliminary study, dome filling on follow-up TOF-MRA is a possible risk factor for delayed ischemic events. TOF-MRA could be a modality for tailored management after SAC.**

INTRODUCTION

Stent-assisted coiling (SAC) has become an important treatment modality for unruptured large or wide-necked intracranial aneurysms.[1-3] One of the major concerns in managing patients after SAC is the maintenance of antiplatelet agents. There is still no consensus on optimal postoperative antiplatelet management while preoperative multiple antiplatelet therapy (APT) has been reported as mandatory to prevent periprocedural thromboembolic complications.[4,5] Previous reports concerning SAC using the Enterprise VRD (Codman Neurovascular, Raynham, Massachusetts, USA) have suggested that insufficient stent apposition is a risk factor associated with delayed ischemic events.[6,7] Furthermore, angiographic results of the treated aneurysm are a possible risk factor for delayed ischemic events.[8] However, digital subtraction angiography (DSA) cannot be repeatedly performed because of its invasiveness, although spatial resolution remains superior to the other modalities.

Time-of-flight magnetic resonance angiography (TOF-MRA) is a noninvasive method for diagnosing intracranial arterial diseases. Because of its noninvasiveness, TOF-MRA has been increasingly used and has replaced DSA, especially in the situation of follow-up

Key words
- Intracranial aneurysm
- Ischemic stroke
- Magnetic resonance angiography
- Stent-assisted coil embolization

Abbreviations and Acronyms
APT: Antiplatelet therapy
ASA: Acetylsalicylic acid
DAPT: Dual antiplatelet therapy
DF: Dome filling
DSA: Digital subtraction angiography
SAC: Stent-assisted coiling
TOF-MRA: Time-of-flight magnetic resonance angiography

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examinations. This method has also been reported to be useful in evaluating intra-aneurysmal flow after coil embolization. The susceptibility artifacts of coils do not interfere with evaluation of the occlusion status.[9-12] In addition, a recent study revealed TOF-MRA was also useful in evaluating stent apposition in the parent artery.[6] However, it remains unknown whether the occlusion status of aneurysms on TOF-MRA is associated with delayed ischemic events. In this study, findings of TOF-MRA after SAC, as well as patient demographics and the characteristics of the treated aneurysm, were investigated to clarify the usefulness of TOF-MRA on postoperative management of SAC, paying particular attention to the risk of delayed ischemic events.

MATERIALS AND METHODS

From July 2010 to November 2014, 86 SAC procedures for unruptured intracranial aneurysm were performed in our institute and our affiliated hospitals. Stent usage was indicated for wide-necked (≥4 mm in maximum neck width or dome-to-neck ratio ≤2) aneurysms with a large dome size (≥7 mm in maximum diameter). Among these procedures, a total of 66 patients were followed for more than 3 months. Three patients were unable to obtain postoperative magnetic resonance imaging (MRI) because of a ferromagnetic clip previously applied to another intracranial aneurysm. Sixty-three patients were included in the final analysis. All ischemic events were extracted during the follow-up. A delayed ischemic event was defined as an episode of transient neurologic symptoms, which could be explained by ischemia of the treated vessels, without MRI findings; cerebral infarction demonstrated both on neurologic examination and on MRI; asymptomatic infarction newly found on follow-up MRI; or in-stent thrombosis or parent artery occlusion revealed by DSA. Events that occurred within 2 days after the endovascular procedure were regarded as periprocedural events and were excluded from this study.[13] This study was approved by the Institutional Review Board Committee at Kyoto University Graduate School of Medicine (IRB No. R0058).

Antiplatelet Management

Dual antiplatelet therapy (DAPT) consisting of acetylsalicylic acid (ASA) 81 mg and clopidogrel sulfate 75 mg daily was initiated 5–7 days before the procedure. No platelet aggregation test or other platelet aggregation assay was performed in this study. During follow-up, if MRI after 6 months revealed no signs of in-stent stenosis or new ischemic lesions, clopidogrel administration was terminated and single APT with ASA 81 mg daily was continued. If 1-year follow-up DSA and MRI revealed good patency of the stent and no signs of ischemic lesions, APT was discontinued. In patients with an aneurysmal location at or distal to M1 or P1, ASA was continued for 1 additional year.

Endovascular Procedures

Our standard endovascular procedure consisted of local anesthesia, a transfemoral approach with a 7-French guiding catheter using a coaxial system, and systemic heparinization to maintain the activated clotting time over 250 seconds. A single stent was deployed after microcatheter introduction into the aneurysm. If packing of an aneurysm was considered insufficient, additional coils were inserted through the microcatheter, which was reintroduced through the stent strut. When recanalization was confirmed during follow-up, retreatment was considered. Patients who were not suitable for retreatment due to technical difficulties or systemic problems (e.g., chronic renal failure) were kept for observation.

Magnetic Resonance Imaging Analysis

MRI was performed with a whole-body 3-T scanner (Siemens, Erlangen, Germany) within 2 days, 6 months, and 12 months after the procedure. TOF-MRA images were scanned as axial sections using a 32-channel head coil with the following parameters: repetition time, 20 ms; echo time, 3.7 ms; 18-degree flip angle; 0.7-mm slice thickness; 220 × 186 mm field of view with a 384 × 326 matrix; pixel size, 0.57 × 0.57 mm. We also performed DSA at 12 months after the procedure, but the results were blinded and were not used in this study. TOF-MRA was evaluated for the postoperative condition of the aneurysm and stent apposition. Multiplanar axial, coronal, and sagittal reconstruction images were created using AquariusNET (TeraRecon Inc., Foster City, California, USA); implemented in the picture-archiving and communication system of our institute; and reviewed by 2 neurointerventionalists who were not involved in the patients' treatment and were blinded for the ischemic events. If these 3-direction images were inappropriate for evaluation, arbitrary planar images were also created and reviewed. The occlusion status of the aneurysm was classified into 1 of 3 groups based on conventional DSA assessment after coil embolization: complete obliteration (no flow signal within the treated aneurysm), neck remnant (intra-aneurysmal flow signal confined to the neck), and dome filling (intra-aneurysmal flow signal in both the dome and the neck, DF). Stent apposition was evaluated as incomplete if the flow signal was identified in the "extra-stent lumen" in the parent artery, not related to the aneurysmal neck. The extrastent lumen was defined as the lumen located outside of the signal artifact made by the stent.[6] If 2 reviewers' judgment differed, the third reviewer, blinded for the judgment, was employed. The judgment on which 2 reviewers agreed was adopted as final judgment.

Statistical Analysis

Patient demographics, aneurysm locations, dome sizes and neck widths of aneurysms, and results of postoperative MRIs were evaluated to clarify the factors associated with delayed ischemic events. Statistical analysis was performed using JMP version 11 software (SAS Institute Inc., Cary, North Carolina, USA). The Fisher exact test and Mann-Whitney U test were used for the appropriate situation. The cumulative event-free rate was plotted using the Kaplan-Meier method, and intergroup differences were tested with the log-rank test. Cox proportional hazards model was used for multivariate analysis. The 95% confidence interval (95% CI) was calculated to analyze the hazard ratio for delayed ischemic events. $P < 0.05$ was considered significant.

RESULTS

Overall patient demographics are shown in **Table 1**. Median follow-up duration was 755 days (177–1531 days). We used the Enterprise VRD in 49 patients and Neuroform EZ (Stryker, Kalamazoo, Michigan, USA) in 14 patients. Half of the patients