Asymptomatic Ischemic Risks in Microsurgical Clipping for Unruptured Intracranial Aneurysms in Anterior Circulation

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■ BACKGROUND: **The ischemic risk in prophylactic treatments of unruptured intracranial aneurysms (UIAs) is a serious health concern.**

■ OBJECTIVE: **The aim of this study was to elucidate the incidence and characteristics of ischemic events in microsurgical clipping of anterior circulation UIAs.**

■ METHODS: **Ischemic events were prospectively evaluated before and after surgery between April 2011 and March 2017. The location, volume, minimum value of apparent diffusion coefficient in high-intensity spots (HIS) on 3-T magnetic resonance diffusion-weighted imaging (DWI), and radiographic outcomes were analyzed. The relationships between DWI positivity and patient demographics, surgical procedures, and intraoperative vessel features were assessed.**

■ RESULTS: **Overall, 78 consecutive patients including 29 men and 49 women (median age, 62 years; range, 24–77 years) with 99 UIAs were analyzed. A total of 10 in 78 craniotomies (13%) detected HIS on DWI, which were all asymptomatic. Seventeen HIS were shown, 5 of which were located in the basal ganglia, 6 in the white matter, and 6 in the cortex. The volume and minimum value of apparent diffusion coefficient were 180.4 ± 31.2 mm^3 and 0.56 ± 0.03 × 10^{-3} mm^2/second, respectively. Radiographic outcomes at follow-up showed that 71% of HIS on DWI led to irreversible brain ischemia. The maximum diameter of aneurysms, atherosclerotic features of the aneurysm wall, and procedure-related factors were associated with DWI positivity.**

■ CONCLUSIONS: **The asymptomatic ischemic risk associated with microsurgical clipping was not low and most lesions were irreversible. Although the mechanism could be various, the use of clips for atherosclerosis of the aneurysm and/or parental vessels requires much attention.**

INTRODUCTION

In the prophylactic treatment of unruptured intracranial aneurysms (UIAs), procedure-related risks such as hemorrhagic and ischemic events are noteworthy to ensure the patients' benefit. According to ISUIA (International Study of Unruptured Intracranial Aneurysms), overall incidence of complications and death were 12% and 1.5% in microsurgical clipping versus 7.3% and 1.8% in endovascular coiling, respectively.[1] In previous studies, the rate of aneurysmal rupture during the procedure was similar (around 1%) in both treatments. On the contrary, the specific ischemic event associated with treatments seems to reflect each characteristic of treatments. The prospective ISUIA study showed cerebral infarction in 11% of microsurgical clipping and 5% of endovascular coiling.[1] A recent

Key words
- Atherosclerosis
- Clipping
- Diffusion-weighted imaging
- Intracranial aneurysm
- Ischemic events

Abbreviations and Acronyms
ADC: Apparent diffusion coefficient
ADC_{MIN}: Minimum value of apparent diffusion coefficient
CT: Computed tomography
DWI: Diffusion-weighted imaging
FLAIR: Fluid-attenuated inversion recovery
HIS: High-intensity spots
MRI: Magnetic resonance imaging
UIAs: Unruptured intracranial aneurysms

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endovascular meta-analysis[2] showed that thromboembolic events detected on diffusion-weighted imaging (DWI) in endovascular coiling accounted for 49% of patients, most of which were considered silent. Regarding microsurgical clipping a few studies have shown periprocedural ischemic events as well; however, little is known about the characteristics of the events evaluated using magnetic resonance imaging (MRI).[3-11] The aim of this study was to elucidate the incidence and characteristics of ischemic events in microsurgical clipping of UIAs.

METHODS

Patients

This study was approved by the local university institutional review board. Considering patients' preference in primary and interdisciplinary consensus with an interventional neuroradiologist (S.S.) on aneurysmal morphologic assessments, the treatment of choice was performed. Patients with UIAs who were treated by microsurgical clipping were prospectively scanned between April 2011 and March 2017. Exclusion criteria were 1) cardiac pacemaker or any other electronic implants or other MRI exclusion criterion, 2) pregnancy or breastfeeding, or 3) claustrophobia.

Data Collection of Patients and Aneurysms

Patient demographics, comorbidities, and aneurysmal geometric data were reviewed in the patients' medical records. According to comorbidities, hypertension was defined as systolic blood pressure at rest of >140 mm Hg or medicated. The diagnostic criteria for dyslipidemia were defined according to the Japanese atherosclerosis guidelines: fasting plasma lipid levels suggesting low-density lipoprotein cholesterol >140mg/dL or high-density lipoprotein cholesterol <40 mg/dL or triglycerides >150 mg/dL.[12] Patients with a history of dyslipidemia who took any type of statin were also diagnosed as having dyslipidemia. Current as well as past smokers were defined as having a smoking history. Aneurysmal geometry was assessed using three-dimensional rotation digital subtraction angiography and the maximum diameter of the aneurysm sac was also measured.

Surgical Procedure

All aneurysm operations were performed under somatosensory evoked potential and motor evoked potential monitoring. Except for aneurysms arising from the anterior communicating artery, the operation was performed via a pterional approach. An interhemispheric approach was routinely performed for anterior communicating artery aneurysms. The microscopic operative field was recorded, and the presence of atherosclerosis (yellowish) of the aneurysm wall and relevant vessels to the treated aneurysm were objectively evaluated by an experienced neurosurgeon (T.O.). Regardless of aneurysmal diameter, temporary clips were used for aneurysms adhesive to branching arteries or surrounding brain tissue to mobilize and achieve the repair. Each occlusion time was recorded. The closure of the aneurysm neck and the patency of the relevant vessels were confirmed using intraoperative indocyanine green videoangiography.

MRI

MRI was performed using a 3.0-T scanner (Signa Excite HD 3.0 T [GE Healthcare, Milwaukee, Wisconsin, USA]) or (Titan 3.0T [Toshiba, Tokyo, Japan]). Diffusion-weighted MRI were obtained 1 day before surgery and within 5 days after surgery. Conventional MRI such as T1-weighted, T2-weighted, and/or fluid-attenuated inversion recovery (FLAIR) images were obtained at the outpatient follow-up. All images were acquired in the axial anterior clinoid–posterior clinoid plane to ensure identical section positioning through sequential MRI sessions. Diffusion-weighted images were acquired with spin echo planar imaging sequences oriented in the axial plane, with coverage of the whole brain with a slice thickness of 6 mm.

MRI Analysis

Radiographic outcomes were evaluated using computed tomography (CT) or conventional MRI including T1-weighted, T2-weighted, or FLAIR imaging at the outpatient clinic follow-up within 12 months after the surgery. Image evaluation was performed, using a freeware program (AZE Virtualplace Fujin [AZE Ltd., Tokyo, Japan]), by 2 experienced neurosurgeons (T.M. and D.I.), reported as a consensus reading. Ischemic lesions were identified as focal high-intensity spots (HIS) on DWI. The appearance of HIS on DWI was evaluated by comparing postoperative DWI with preoperative DWI. The 2 neurosurgeons also analyzed the characteristics of HIS on DWI. Regions of interest corresponding to the location of the new HIS were placed on apparent diffusion coefficient (ADC) maps, and the location, volume, and absolute minimum value of ADC (ADC_{MIN}) were recorded. The ADC was obtained from DWI with the power of standard (b = 1000 seconds/mm^2). The volume was calculated by multiplying the selected area by the section thickness. Each DWI HIS was analyzed on a dual-screen monitor to ascertain whether or not it corresponded to permanent signs of brain damage on CT or T1-weighted, T2-weighted, or FLAIR images obtained at the follow-up.

Statistical Analysis

Statistical analyses were performed using the JMP statistical package (JMP version 13 [SAS Institute Inc., Cary, North Carolina, USA]). To compare differences between the 2 groups, we used the χ^2 test for categorical factors and the Mann-Whitney U test for quantitative variables. Statistical significance was assigned for $P < 0.05$. Multiple logistic regression analysis was in addition performed when a variable suggested a relationship with $P < 0.1$. Statistical significance was assigned for $P < 0.05$.

RESULTS

Patient Cohort

Overall, 90 patients were treated surgically, including 78 clipping and 12 trap and bypass surgery, whereas 131 patients underwent endovascular coiling. In a total of 78 patients, 99 UIAs were eligible for analysis, including 29 men and 49 women, with a median age of 62 years (range, 24–77 years). Fifteen patients harbored multiple UIAs (2 or 3), which could be treated simultaneously during 1 craniotomy. Patient demographics and comorbidities are summarized in Table 1. Hypertension, diabetes, and