Clinical and Radiological Outcomes After Treatment of Unruptured Paraophthalmic Internal Carotid Artery Aneurysms: a Comparative and Pooled Analysis of Single-Center Experiences

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■ OBJECTIVE: **Unruptured paraophthalmic aneurysms present unique challenges, and the ideal management remains unknown.**

■ METHODS: **We performed a pooled analysis of single-center experiences to compare the risks and effectiveness involving patients with unruptured paraophthalmic aneurysms treated with clipping, coiling alone, stent-assisted coiling, and flow-diversion. The MEDLINE database was searched and thirty-three series (including our institutional experience) were included.**

■ RESULTS: **Clipping caused more intracranial hemorrhage (ICH) and neurologic complications (NCs) than coiling alone (ICH: odds ratio [OR] = 3.058, $P = 0.013$; NC: OR = 5.809, $P < 0.001$), stent-assisted coiling (ICH: P = 0.018; NC: OR = 7.367, $P < 0.001$), and flow-diversion (ICH: $P = 0.006$; NC: OR = 16.954, $P < 0.001$). Clipping also caused more unfavorable visual outcomes than both coiling alone (OR = 3.037, $P = 0.001$) and stent-assisted coiling (OR = 6.055, $P = 0.005$). Clipping resulted in a lower reoperation rate than coiling alone in large/giant aneurysm group, which approached statistical significance (OR = 0.133, $P = 0.057$). Clipping, stent-assisted coiling, and flow-diversion all showed higher occlusion rates compared with coiling alone (OR [clipping vs. coiling alone] = 2.852, $P \leq 0.001$; OR [coiling alone vs. stent-assisted coiling] = 0.302, $P = 0.003$; OR [coiling alone vs. flow-diversion] = 0.400, $P = 0.013$). Flow-diversion showed comparative complication rate, clinical outcomes, and angiographic result compared with stent-assisted coiling. No significant differences were found among all 4 treatment modalities on mortality and poor outcome.**

■ CONCLUSIONS: **Endovascular therapies have benefits over surgical clipping in terms of fewer intracranial hemorrhage complications, fewer NCs, and lower unfavorable visual outcome rate. Flow diversion showed comparative safety and effectiveness to stent-assisted coiling, and they both achieved better radiologic results than coiling alone. Further validation by randomized cohort studies is still needed to provide robust evidence.**

INTRODUCTION

Unruptured intracranial aneurysms (UIAs) have been diagnosed with greater frequency in the most recent decade. As a result of the continuing evolution of endovascular therapy, treatment strategies for UIAs have substantially changed and more aneurysms are now referred for endovascular coiling. However, the management of unruptured paraophthalmic aneurysms remains controversial. From the perspective of microsurgical clipping, several characteristics of paraophthalmic aneurysms, including their proximal location, close relationships with the cavernous sinus, and the covering of

Key words
- Clip
- Coil
- Flow diversion
- Outcomes
- Paraophthalmic aneurysm
- Stent-assisted coil
- Unruptured intracranial aneurysm

Abbreviations and Acronyms
GOS: Glasgow Outcome Scale
ICH: Intracranial hemorrhage
mRS: modified Rankin Scale
NC: Neurologic complications
UIAs: Unruptured intracranial aneurysms

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Citation: World Neurosurg. (2015) 84, 6:1726-1738.
http://dx.doi.org/10.1016/j.wneu.2015.07.036

*Journal homepage: **www.WORLDNEUROSURGERY.org***

*Available online: **www.sciencedirect.com***

the aneurysm base by the optic nerve, can all add technical challenges to the treatment and make clipping rather risky (7, 24, 39). In contrast, paraophthalmic aneurysm embolization may also lead to hazardous results, such as retinal artery occlusion and delayed optic ischemia (38, 43). Moreover, visual function outcome and completeness of occlusion are major concerns of endovascular therapy. The advent of stent-assisted coiling and flow diversion offered new strategies for the treatment of aneurysms, especially for those large and complex aneurysms or aneurysms with wide necks (5); however, the safety issues and efficiency of these technologies remain a major concern.

Therefore in this study we retrospectively analyzed our single-center experience of 13 cases with paraophthalmic UIAs over a 4-year period, and a pooled analysis of the literature was performed to compare the benefits and risks among neurosurgical clipping, coiling alone, stent-assisted coiling, and flow diversion in treating patients with unruptured paraophthalmic aneurysms.

MATERIALS AND METHODS

Current Series

Between January 2009 and October 2013, a total of 13 patients were diagnosed with unruptured paraophthalmic intracranial aneurysms and treated in our institution. All patients underwent digital subtraction angiography before treatment, and formal neuro-ophthalmologic examinations before and after surgery were performed if possible. At the time of the initial angiogram, paraophthalmic aneurysms were distinguished from other aneurysms by the principal neurosurgeon. The indication for treatment was based mainly on "Guidelines for the Management of Unruptured Intracranial Aneurysms" (23), our own clinical experience, and the patient's decision. Additionally, patients with the following situations were referred for treatment in our institution: 1) UIAs were accompanied with subarachnoid hemorrhage caused by other ruptured aneurysms; 2) patients had a family history of aneurysmal subarachnoid hemorrhage; and 3) patients who insisted on receiving treatment, whether or not meeting the treatment indications, after a careful and thorough explanation. The decision of the treatment (clip or coil) was made in individual cases by an interdisciplinary approach with effective collaborations between experienced microneurosurgeons and endovascular neurosurgeons on a cerebrovascular team. Endovascular coil embolization was performed without stent deployment when the aneurysm neck was favorable; however, if the aneurysm dome-to-neck ratio was <2, greater difficulty and a higher risk for conventional coil embolization were likely and a stent would be placed across the aneurysm neck. Finally, all 13 patients were treated via endovascular therapy, in whom 8 received stent-assisted coiling while the remaining 5 were treated with coiling alone.

The hospital records, operative reports, and radiologic reports of the 13 patients were reviewed, and complications were identified. Finally, clinical outcomes, including visual outcomes, were evaluated at the time of discharge from the hospital and at the latest follow-up evaluation.

Systematic Literature Search

Using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines, 2 reviewers (Y. Z. and J. P.) performed an independent and systematic MEDLINE search of the published studies written in English through June 2015. The following key words were used in relevant combinations: "intracranial aneurysm(s)," "unruptured," "C6," "C5," "ophthalmic segment," "carotid-ophthalmic," "carotid artery ophthalmic," "ophthalmic artery," "superior hypophyseal," "paraclinoid," "paraophthalmic," "carotid cave," "transitional," "surgery," "neurosurgery," "clipping," "endovascular," "coiling," "flow-diversion," "flow-diverting," "pipeline embolization," and "embolization."

All studies reporting patients with unruptured paraophthalmic aneurysms treated with endovascular coiling (coiling alone, stent-assisted coiling, or flow diversion) or surgical clipping were selected, and all reference sections of eligible studies and pertinent reviews were hand-reviewed for potential studies. To be considered, studies had to be published in English and report >5 cases, with clinical outcomes and treatment modalities for each case described (clipping, coiling alone, stent-assisted coiling, or flow diversion). Paraophthalmic aneurysms were defined as aneurysms arising from the roof of the cavernous sinus to the origin of the posterior communicating artery; thus intracavernous aneurysms were excluded from this study. Specifically, studies including both ruptured and unruptured aneurysms and studies including aneurysm locations differing from the paraophthalmic were only considered eligible when these unruptured aneurysms could clearly be separated from the entire cohort. For each study, we extracted the following information: mortality; clinical outcomes; visual outcomes; angiographic occlusion rates at follow-up; reoperations caused by failure of the initial treatment, aneurysm recurrence, or coil compaction; and complications, including intracranial hemorrhage, ischemic events, and neurologic complications (NCs). Mortality was defined as all-cause postprocedural mortality. Clinical outcomes were specified by modified Rankin Scale (mRS) (4) and Glasgow Outcome Scale (GOS) score (19) when possible. When the author described a deficit without specifying the outcome, an mRS or GOS score from the description was assigned. A "poor" outcome was defined as a GOS score of 1–3 or an mRS of 3–6. Postoperative intracranial hemorrhage, ischemic events, and NCs were independently determined. In assessing visual outcomes, "unfavorable" was defined as worsening of visual symptoms on admission on either visual acuity or visual fields or the occurrence of new postprocedural visual deficits. Specifically, data concerning postoperative visual fields/acuity defects/deteriorations were also combined with the data for NCs. Data on aneurysm occlusion included the number of patients treated with coiling alone, stent-assisted coiling, flow diversion, and patients treated with clipping with postprocedural imaging. The results were categorized as total/near-total (95%–100%) or partial ($<95\%$) occlusion.

Statistical Analysis

Statistical data analyses were conducted using SPSS (version 18 database; SPSS Institute, Inc., Chicago, Illinois, USA). From each study, we assessed the cumulative incidence (event rate) and 95% CI for each outcome. Event rates were pooled across studies. The unpaired t-test was used for parametric statistics. Categorical variables were analyzed in contingency tables using the Pearson