

# The Impact of the Endovascular Treatment of Cerebral Aneurysms on Headaches

Mitra Assadi, MD, FAAN,\* Mandy Binning, MD, † Kenneth Liebman, MD, FACS, †  
and Erol Veznedaroglu, MD, FACS, FAHA †

**Objective:** The co-occurrence of headaches and cerebral aneurysms is common in clinical practice, although a clear causal relationship has not been ascertained. We aimed to investigate the impact of endovascular obliteration of aneurysms on headaches using a cross-sectional, prospective, open-label protocol. We also sought to characterize the preexisting headaches in patients harboring cerebral aneurysms using the International Classification of Headache Disorders criteria.

**Methods:** A total of 33 patients were recruited into the study and underwent endovascular treatment for obliteration of their aneurysms. A standardized survey was administered before and 3 to 6 months after the procedure, documenting the HIT-6 scores as well as the headache frequency.

**Results:** The study cohort included 25 women and 8 men. In 61% of cases, the aneurysms were located in the posterior circulation. We achieved grade 0 or 1 obliteration of aneurysms in 100% of cases and there were no complications. The mean for HIT-6 scores were 52.3 at baseline and 49.6 postprocedure (student *t* test,  $P < 0.047$ ). The headache frequency measured as total headache days per month did not demonstrate statistical significance. Our data indicated that more than half of our cohort had preexisting headaches which fulfilled the criteria for a primary headache disorder. These individuals showed a more robust response to the intervention compared with the remainder of the group, although the *P*-value per se was not considered statistically significant due to the small sample size.

**Conclusions:** Endovascular treatment of the aneurysms mitigates the headache-related disability.

**Key Words:** cerebral aneurysms, headache, endovascular coiling of aneurysms

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Cerebral aneurysms represent a frequently encountered condition within the general population. It is estimated that approximately 15 million Americans harbor intracranial aneurysms.<sup>1</sup> It is therefore not surprising that the diagnosis of headache, being a common condition, may overlap with cerebral aneurysms. The lifetime prevalence of tension type headache (TTH) is estimated to be about 80%,<sup>2–4</sup> and 12% of the population suffers from migraine.<sup>5,6</sup> By far, headache is the most common complaint which leads to a diagnosis of aneurysms as reported by Deruty et al<sup>7</sup> and many other authors. Brain imaging studies are often used for the evaluation of patients with headaches. The number of unruptured

aneurysms recognized in the general population is increasing due to the enhanced sophistication and accessibility of non-invasive imaging methods. As such, the co-occurrence of headaches and aneurysms may be entirely incidental; a clear causal relation between the 2 conditions has never been established. For large aneurysms, measuring >1 cm in diameter, a hypothetical causal effect on headaches has been assumed, although the definition of “large aneurysm” in headache research remains elusive. The risk of aneurysmal rupture is directly related to its size. The annual risk of hemorrhage in aneurysms measuring >1 cm is 0.5% to 1%. Giant aneurysms, measuring >2 cm in diameter, have an annual rupture risk of 6%.<sup>8</sup>

This study aimed to investigate the following hypothesis: there exists a causal relation between the presence of unruptured aneurysms and headaches, which may be mitigated by endovascular interventions leading to obliteration of the aneurysm. We also aimed to investigate the headache characteristics and classifications in our cohort using the International Classification of Headache Disorders, second edition (ICHD-II) criteria and correlate the treatment response following the endovascular intervention in the context of the primary headache disorders.

## METHODS

This is a cross-sectional, prospective, open-label study to examine the impact of the endovascular treatment of cerebral aneurysms on headaches. All patients diagnosed with cerebral aneurysms were evaluated by the staff neurosurgeons and underwent conventional angiogram at baseline to determine the exact size, location, and shape of the aneurysm/s. The treatment decision for endovascular intervention versus open craniotomy was made based on the location and size of the aneurysm according to the current neurosurgical literature and guidelines.<sup>7,8</sup> All of the patients who qualified for the endovascular intervention were invited to participate in the study. The background information recorded on each patient included age, sex, comorbidities, concomitant medicines, and smoking status.

A validated survey was administered before the endovascular procedure and during the 3 to 6 months follow-up visit. The questionnaire inquired about the presence of all headache-related characteristics as well as nonpain features including nausea, vomiting, light/sound sensitivity, aura and autonomic features as specified by the ICHD-II. We inquired about previous history of headaches as well as the age of onset of headaches. The survey also included HIT-6, a standardized questionnaire which is used to estimate the impact of headache on daily function. The scale consists of 6 questions that cover various areas reflected in health-related quality of life, including pain, social functioning, role functioning, vitality, cognitive functioning, and psychological distress. The response to each of the 6 questions include the following options: “never,” “rarely,”

From the \*Capital Neurological Institute, Pennington, NJ; and †Department of Neurosurgery, School of Medicine, Drexel University, Philadelphia, PA.

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Reprints: Mitra Assadi, MD, FAAN, Capital Neurological Institute, 2 Capital Way, Pennington, NJ 08534. E-mail: massadi@capitalhealth.org.

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“sometimes,” “very often,” or “always,” for which 6, 8, 10, 11, or 13 points are assigned, respectively. These points are summed up to produce a total score ranging from 36 to 78 and higher scores indicate higher headache-related disability. The survey also documents headache frequency measured as headache days per month.

### INCLUSION CRITERIA

- (1) Patients with nonruptured cerebral aneurysms that necessitated treatment, regardless of presenting complaint which may or may not have included headaches.
- (2) The aneurysm's size, shape, and location were considered amenable to endovascular procedures.
- (3) Patient given informed consent for endovascular procedure and the study.

### EXCLUSION CRITERIA

- (1) Inability to obtain informed consent.
- (2) Contraindication to anticoagulation.
- (3) Cancer or other terminal illness likely to cause death within 2 years or less.
- (4) Patients presenting with subarachnoid bleeding.
- (5) Aneurysm is not considered amenable to coiling due to its size, shape or location.
- (6) Subjects with concurrent intracranial pathology such as brain tumor, vascular malformations or hemorrhage.
- (7) Significant atherosclerotic disease of the parent arteries necessary to traverse to coil the target aneurysm.

The selected patients underwent endovascular treatments using to the appropriate methods according to neurosurgical guidelines.<sup>7,8</sup> The following standardized grading system<sup>9</sup> was used to report the degree of aneurysmal obliteration achieved by the procedure:

- grade 0: complete and total aneurysm occlusion;
- grade 1:  $\geq 90\%$  volumetric aneurysm occlusion;
- grade 2: 70% to 89% volumetric aneurysm occlusion;
- grade 3: 50% to 69% volumetric aneurysm occlusion;
- grade 4: 25% to 49% volumetric aneurysm occlusion;
- grade 5:  $<25\%$  volumetric aneurysm occlusion.

We extracted the survey results at baseline and 3 to 6 months posttreatment in a database in Excel format. The pre-existing headaches were categorized to migraine, trigeminal autonomic cephalalgia or TTH according to the ICHD-II criteria. For each subject, the HIT-6 score at baseline and 3 to 6 months postprocedure was calculated and entered into the database. Similarly, headache frequencies at baseline and 3 to 6 months follow-up was entered into the Excel sheet.

None of the patients in the study cohort were receiving any preventative treatments for headaches before the study. This protocol did not aim to initiate any medical treatment for headaches and therefore no preventive medications were offered during the study period. Several of the patients opted to seek a neurological consultation for headache management during the 3 to 6 months follow-up visit.

Descriptive statistics were prepared using Excel, and inferential statistics related to means and frequency tables were computed using Stata version 10.0, College Station, TX. Differences within the frequency tables were evaluated via  $\chi^2$  analysis or *t* tests.

### RESULTS

A total of 60 patients with unruptured aneurysms were evaluated in our institution between spring of 2012 through 2015. A total of 15 patients did not require any interventions

due to small aneurysm size, and 12 patients underwent open craniotomy procedures. A total of 33 cases met the inclusion criteria and were recruited into the study.

The study cohort included 25 women (75%) and 8 men (25%). Smokers comprised 70% of the cases. Half of the cohort had a diagnosis of hypertension. A total of 16 patients (48%) had been referred for imaging due to headaches, 24% for follow-up on previous aneurysms, 18% for transient ischemic attack symptoms and the remainder for minor head trauma. A total of 10 cases (30.3%) had large aneurysms which measured 10 mm or larger. In 61% of cases the aneurysms were located in the posterior circulation and in 39% in the anterior circulation. In 28% of cases more than 1 aneurysm was detected by the imaging studies. In all of these cases, the second aneurysms were small measuring 2 to 4 mm in diameter and did not necessitate any procedures.

Table 1 summarizes the procedures used in the study cohort. The procedures yielded 100% occlusion of the aneurysm (grade 0) in 50% of cases and  $>90\%$  (grade 1) in the other half.

Figure 1 depicts several samples of our cohort at baseline and following the obliteration of the aneurysm.

The mean for the HIT-6 scores were 52.39 at baseline and 49.60 during the follow-up. A student *t* test showed statistical significance with a *P*-value of 0.047. The HIT-6 scores in the 10 cases with large aneurysm before and after the procedure were 51.3 versus 47.1. Statistical significance was not achieved due to the small sample size.

The headache frequencies measured as total headache days per month in the study cohort were compared using  $\chi^2$  analysis and statistical significance was not reached.

In our cohort, 57% experienced preexisting headaches which predated their present illness by years and fulfilled the ICHD-II criteria for TTH (42.1%), migraine (42.1%) or trigeminal autonomic cephalalgia (15.7%). Six percent reported migraine-related aura (visual, speech or sensory).

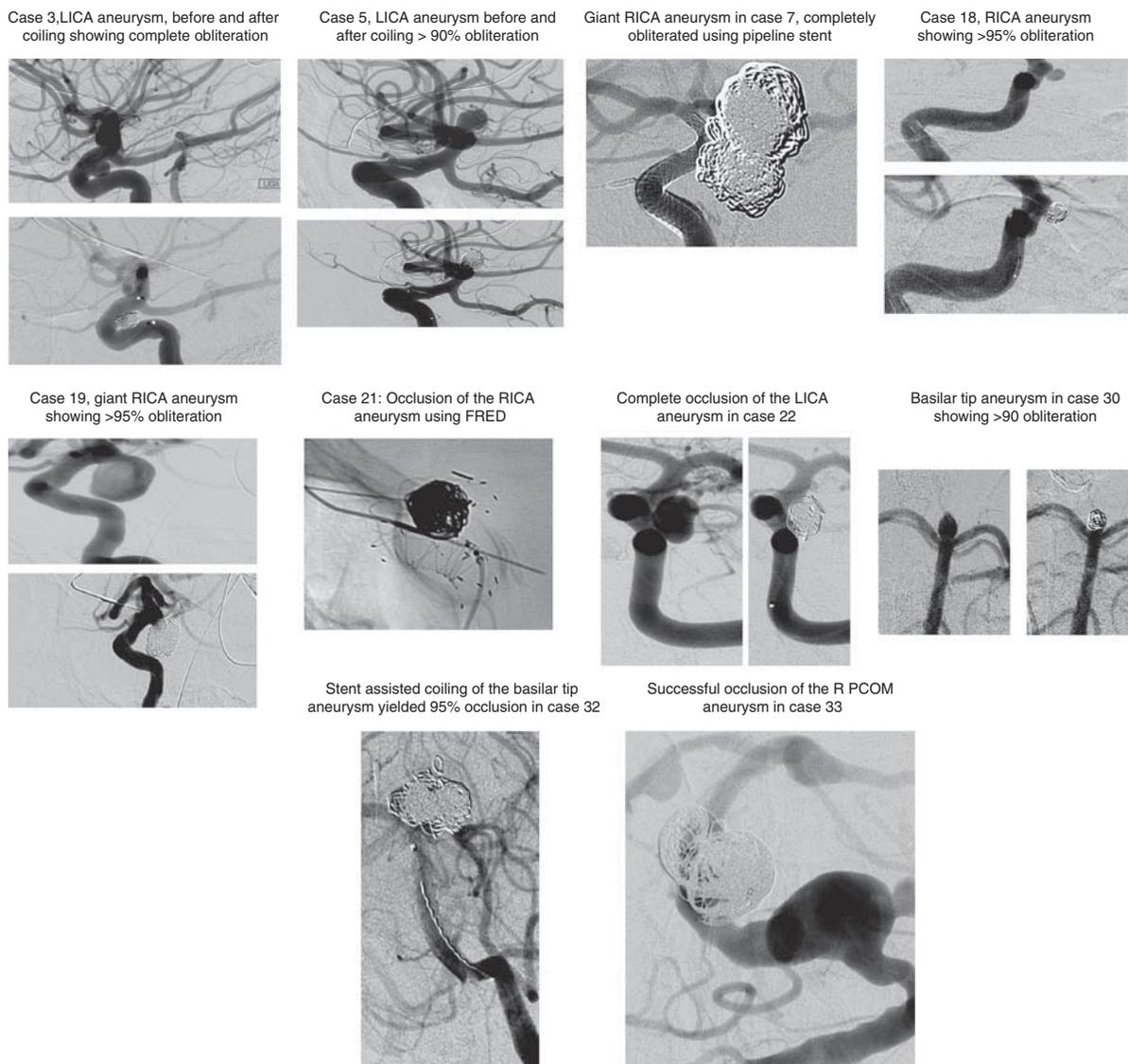
Using the data provided by the patients related to the age of onset of the preexisting headaches, we calculated the headaches-years for the cohort (mean = 29.9, SD = 17.1). For the 19 patients with long standing diagnosis of headaches, the HIT-6 scores at baseline were higher than the rest (58.9 vs. 43.6). In this group, the drop in the HIT-6 score was more significant (58.9 to 54.7, paired *t* test  $P < 0.07$ ) compared with the rest (43.6 to 42.6, paired *t* test  $P < 0.44$ ). It must be noted that although statistical significance was not reached due to the small sample size, the results are suggestive of a more robust response in individuals with preexisting headaches.

### DISCUSSION

Although headaches are often the presenting symptom leading to the imaging study and hence the diagnosis of aneurysms,<sup>1</sup> a clear causal relationship between the 2 conditions has not been established. Moreover, the effects of the endovascular treatment of aneurysms on patients' headaches have to be elucidated. There are numerous studies reporting the

**TABLE 1.** The Procedure Used in the Study Cohort

Procedure	Frequency	%
Flow redirection endoluminal device	3	9.09
Coil embolization	16	48.48
Pipeline stent	4	12.12
Stent-assisted coil embolization	10	30.30



**FIGURE 1.** Samples of imaging studies in our cohort at baseline and following the obliteration of the aneurysms. FRED indicates flow redirection endoluminal device; LICA, left internal carotid artery; RICA, right internal carotid artery.

safety and efficacy as well the technical details of these methods in patients with cerebral aneurysms.<sup>8-11</sup> For the most part, these papers focus on neurological outcomes pertaining to mortality and morbidity rather than headaches. There are few manuscripts that designate headaches as the primary outcome, however, the significant limitation on the sample size precludes us from extrapolating the results. Excluding these case reports, we have cited 2 papers<sup>1,12</sup> focusing on headache as the primary outcome measure after the endovascular treatment of aneurysms. Qureshi and colleagues report a retrospective survey of 32 cases which was performed years after the procedure. Gu and colleagues performed a prospective study of 52 elderly patients using an 11-point scale. Both authors concluded that the endovascular obliteration of the aneurysms resulted in an improvement in the headaches as measured by their semiquantitative questionnaires. They reported preexisting headaches in a large number of cases (38% and 72.2%, respectively) but did not investigate the age of onset or correlation with primary headache disorder diagnosis. Both

studies reported presence of migraine type manifestations such as nausea, vomiting, light or sound sensitivity and auras in large number of participants.

We have to concur with these authors that the endovascular treatment of the aneurysms may mitigate the headache-related disability. We expected to see a more robust effect in individuals with large aneurysms, however, were unable to reach statistical significance due to small sample size.

Our treatment approaches achieved grade 0 or 1 obliteration of the aneurysms in all cases, precluding us from evaluating the relation between the headache improvement and the treatment success.

Primary headache disorders are common among the general population. Given the accessibility of various brain imaging studies, cerebral aneurysms are recognized frequently in these individuals. As such, in individuals with preexisting headaches, the co-occurrence of the 2 conditions may be incidental and not indicative of a causal relation. Our data indicated that more than half of our cohort had preexisting

headaches which fulfilled the criteria for a primary headache disorder. These individuals showed a more robust response to the intervention compared with the remainder of the group, although the *P*-value per se is not considered statistically significant due to the small sample size.

To further investigate the relation between the preexisting headaches and the aneurysms, we calculated the headaches-years in these individuals (mean = 29.9, SD = 17.1). On average, the onset of headaches in these individuals predated their present illness by more than 1 decade, questioning any causal relation between the current headaches and the cerebral aneurysm in these cases. Our data did not confirm any significant recent changes in the headache characteristics.

In individuals with aneurysms, neither the exact cause of the headaches, nor the reasons for improvement following the obliteration of the aneurysms are clear. Qureshi et al<sup>1</sup> hypothesized that the improvement may be caused by reducing the pulsatile expansion of the aneurysm sac posttreatment. It is conceivable that the pulsation in the aneurysm may trigger the chemical cascade producing the headaches in individuals with primary headache disorders, hence better clinical response to the intervention.

In conclusion, clinicians should be cognizant of the presence of primary headache disorders and must discern the extent to which the headache may be attributed to these diagnoses based on patients' historical information. Offering an endovascular intervention should be determined based on the size of the aneurysm and the overall risk of bleeding not presence of headaches per se. Presence of a history of preexisting headache may be a predictor of headache outcome after the procedure and possibly yielding more improvement in the headaches.

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