“Awake” clipping of cerebral aneurysms: report of initial series

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OBJECTIVE Risk of ischemia during aneurysm surgery is significantly related to temporary clipping time and final clipping that might incorporate a perforator. In this study, the authors attempted to assess the potential added benefit to patient outcomes of “awake” neurological testing when compared with standard neurophysiological testing performed under general anesthesia. The procedure is performed after the induction of conscious sedation, and for the neurological testing, the patient is fully awake.

METHODS The authors conducted an institutional review board–approved prospective study of clipping unruptured intracranial aneurysms (UIAs) in 30 consecutive adult patients who underwent awake clipping. The end points were the incidence of stroke/cerebrovascular accident (CVA), death, discharge to a long-term facility, length of stay, and 30-day modified Rankin Scale score. All clinical and neurophysiological intraoperative monitoring data were recorded.

RESULTS The median patient age was 52 years (range 27–63 years); 19 (63%) female and 11 (37%) male patients were included. Twenty-seven (90%) aneurysms were anterior, and 3 (10%) were posterior circulation aneurysms. Five (17%) had been coiled previously, 3 (10%) had been clipped previously, 2 (7%) were partially calcified, and 2 (7%) were fusiform aneurysms. Three patients developed synchronous clinical neurological and neurophysiological changes during temporary clipping with consequent removal of the temporary clip and reversal of those clinical and neurophysiological changes. Three patients developed asynchronous clinical neurological and neurophysiological changes. These 3 patients developed hemiparesis without changes in neurophysiological monitoring results. One patient developed linked clinical neurological and neurophysiological changes during final clipping that were not reversed by reapplication of the clip, and the patient had a CVA. Four patients with internal carotid artery ophthalmic segment aneurysms underwent visual testing with final clipping, and 1 of these patients required repositioning of the clip. Three patients who required permanent occlusion of a vessel as part of their aneurysm treatment underwent a 10-minute intraoperative clinical respective-vessel test occlusion. The median length of stay was 3 days (range 1–5 days). The median modified Rankin Scale score was 1 (range 0–3). All of the patients were discharged to home from the hospital except for 1 who developed a CVA and was discharged to a rehabilitation facility. There were no deaths in this series.

CONCLUSIONS The 3 patients who developed neurological deterioration without a concomitant neurophysiological finding during temporary clipping revealed a potential advantage of awake aneurysm surgery (i.e., in decreasing the risk of ischemic injury).

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KEY WORDS awake craniotomy; cerebral aneurysms; aneurysm treatment outcomes; basilar artery aneurysm; temporary occlusion testing; vascular disorders

ABBREVIATIONS ACoA = anterior communicating artery; CVA = cerebrovascular accident; EEG = electroencephalography; ICA = internal carotid artery; LOS = length of stay; MCA = middle cerebral artery; MEP = motor evoked potential; mRS = modified Rankin Scale; NIS = National Inpatient Sample; SSEP = somatosensory evoked potential; UIA = unruptured intracranial aneurysm; VA = vertebral artery.

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AWAKE craniotomy (defined based on 1 of 2 protocols, initiated with the patient undergoing standard mechanical ventilation and then conversion to conscious sedation for neurological testing or initiated after induction of conscious sedation and then awakening the patient for neurological testing) is not a new concept; it has widely been used for glioma resection and functional procedures for neurological monitoring of eloquent cortical and subcortical areas.^{7,9,10,11,12,14,16,20,21,23,25,27,29,30,32,33,34,36,37,39}

Awake procedures have also been used in cerebrovascular surgery, specifically carotid endarterectomy.^{13,24,40} Awake craniotomy for aneurysm surgery has been presented in the literature in case report format. Lüders et al.²⁶ reported 3 cases of distal vessel occlusion for awake testing of patients with mycotic aneurysms. Chen et al.⁸ reported the clipping of an ophthalmic artery aneurysm performed with the patient awake for visual testing. Passacantilli et al.³¹ reported trapping a giant fusiform middle cerebral artery (MCA) aneurysm with testing performed with the patient awake. Suzuki et al.³⁵ reported the clipping of 4 aneurysms involving the anterior choroidal artery with testing performed while the patient was awake.⁴

During microsurgical clipping of cerebral aneurysms, the 2 steps at which patients are most at risk for neurological morbidity are as follows: 1) temporary clipping time and 2) permanent clipping of the aneurysm with an incorporated perforator(s). Despite detailed neurophysiological monitoring, morbidity and death as a result of these 2 steps are well documented in the literature. Moreover, there is essentially no established neurophysiological monitoring for temporal clipping of the basilar artery or visual function associated with clipping of ophthalmic artery aneurysms. The National (Nationwide) Inpatient Sample (NIS) has been used to deduce estimations of outcomes from clipping of unruptured intracranial aneurysms (UIAs).³⁸ From this database, morbidity rates ranging from 13.5% to 27.6% and mortality rates ranging from 0.7% to 3.5% have been reported.^{2,3,4,5,6,15,18,19,22,28,41}

The objective of this institutional review board–approved prospective study was to assess the feasibility and efficacy of the addition of direct neurological testing during both temporary and permanent clipping of UIAs.

Methods

The standard protocol for awake craniotomy was developed and approved by the Saint Louis University institutional review board for a prospective clinical consecutive 12-month study of UIAs. The specific end points were stroke/cerebrovascular accident (CVA), discharge to a long-term facility, length of stay (LOS), 30-day modified Rankin Scale (mRS) score, and death. The mRS evaluation was performed on postoperative Day 30 (undertaken by an independent hospital-based provider specially trained in administering outcome scales). The discharge data, LOS, and mortality data were prospectively provided by the hospital information systems office. Intraoperative clinical and neurophysiological monitoring data were also collected prospectively.

The surgical procedure was performed under monitored anesthesia care. Spontaneous respirations were maintained

throughout the procedure with dexmedetomidine (0.2–1.0 µg/kg per hour) and remifentanyl (0.05–2 µg/kg per min) infusions. Monitoring with electroencephalography (EEG) was used to help gauge the appropriate depth of anesthesia. A scalp block with 0.5% ropivacaine was performed to anesthetize the appropriate scalp region. Before the awake phase of the surgery, the dexmedetomidine infusion was discontinued.

Intraoperative electrophysiological monitoring included EEG, somatosensory evoked potentials (SSEPs), and motor evoked potentials (MEPs). All interpretations of the electrophysiological monitoring results were made by a specially trained neurologist in the operating room.

When approaching the required neurological testing, the dexmedetomidine and remifentanyl drips are halted, and the patient is brought into a fully awake stage. Intraoperative awake neurological testing included motor examination, speech examination, visual acuity testing, and field examination respective to the vascular territory tested. The visual examination was performed using the iPad-based Vision Test App 2.11 (Rocktime Ltd.).

Results

A total of 30 consecutive patients (19 female [63%] and 11 male [37%]) were included in this study. The median age was 52 years (range 27–63 years). Twenty-seven (90%) aneurysms were anterior, and 3 (10%) were posterior circulation aneurysms. Five (17%) had been coiled previously, 3 (10%) had been clipped previously, 2 (7%) were partially calcified, and 2 (6.7%) were fusiform aneurysms. More detailed patient and aneurysm features are provided in Fig. 1.

Four patients were excluded during the preoperative assessment visits; 2 declined the option of awake craniotomy, and 2 were excluded by the anesthesia team during the pre-anesthesia assessment (1 because of sleep apnea and 1 because of history of difficult intubation).

All 30 patients underwent the awake-craniotomy protocol (Fig. 2). No patient needed endotracheal intubation intraoperatively or postoperatively. During dural closure, 1 patient developed an intraoperative seizure that was treated with iced saline, and the patient was kept sedated throughout the remainder of the procedure. There were no postoperative complications in this patient.

Three patients developed synchronous clinical neurological and neurophysiological findings. One patient developed contralateral hemiparesis during temporary M₁ segment clipping. The temporary clip was removed immediately, and clipping of the MCA aneurysm was continued without the temporary clip. One patient developed contralateral arm weakness only during temporary M₁ clipping; the temporary clip was removed immediately, and clipping of the MCA aneurysm was continued without the temporary clip. One patient developed contralateral leg weakness during the temporary clipping of the A₁ segment; the temporary clip was removed immediately, and clipping of the anterior communicating artery (ACoA) aneurysm was continued without the temporary clip.

Three patients developed asynchronous (discrepant) voluntary motor-neurophysiological changes. These 3 patients

FIG. 1. Location (A), size (B), and special features (C) of aneurysms in the study patients. ACA = anterior cerebral artery; BA = basilar artery.

developed hemiparesis without changes in neurophysiological monitoring results. One patient with a dominant A_1 segment temporary clip occlusion developed immediate bilateral lower-extremity weakness without synchronous EEG or SSEP changes. No decline in the amplitudes of the MEPs was detected. The temporary clip was removed immediately, and the clipping of the ACoA aneurysm was completed without a temporary clip. No postoperative CVA was detected. One patient developed immediate contralateral hemiparesis after a temporary clip was placed on the internal carotid artery (ICA) without synchronous EEG or SSEP changes. No decline in the amplitudes of the MEPs was detected. The temporary clip was removed immediately, and clipping of the ICA aneurysm was completed without a temporary clip. No postoperative CVA

was detected. One patient developed immediate contralateral arm weakness after placement of a clip on the distal M_1 segment without synchronous EEG or SSEP changes. No decline in the amplitudes of the MEPs was detected (Fig. 3). The temporary clip was removed immediately, and clipping of the MCA aneurysm was completed without a temporary clip. Twenty minutes after placement of the initial temporary clip and during dural closure, a decline in the SSEPs was detected without a concomitant change in voluntary motor function. The dural closure was halted, and reinspection under a microscope followed by repeat indocyanine green angiography revealed no new changes. Results of the awake motor examination remained normal, and the SSEP changes reverted back to normal within 10 minutes. No postoperative CVA was detected.

One patient developed linked clinical-neurophysiological changes during final clipping that were not reversed by reapplication of the clip, and the patient had developed a small capsular stroke. This patient had the longest LOS in the hospital (5 days) and was discharged to a rehabilitation institution. Thirty days after surgery, the patient had an mRS score of 3.

Four patients with an ICA aneurysm at the ophthalmic segment underwent control (precraniotomy) visual testing as the final clip was being applied. Three patients had normal (same as control) visual examination results at final awake clipping. One patient developed immediate blurring of vision in the ipsilateral eye after final clip placement. The clip was readjusted, and, within 1 minute, the patient reported resolution of the blurring and passed the iPad-based visual testing to equal control preclipping testing results. All 4 patients had normal postoperative visual examination results.

Two patients with a basilar apex aneurysm underwent level-of-consciousness testing during temporary clipping of the basilar artery. Both of them remained at the same level of consciousness as a control (just before placement of a temporary clip). The temporary clipping time was 7 minutes in the first case (Fig. 4) and 3 minutes in the second case. In both cases, multimodality (motor, speech, cranial nerve, and vision) awake testing and level-of-consciousness testing were performed during temporary clipping of the basilar artery.

Three patients who required permanent occlusion of a vessel as part of their aneurysm treatment underwent 10-minute intraoperative clinical respective-vessel test occlusion. After intraoperative inspection of 1 patient with a large partially calcified A_1 – A_2 aneurysm, we felt that direct clipping was not advisable because of the high risk of embolic phenomena from the calcification. Ten-minute distal A_1 segment occlusion testing was performed. No voluntary motor or electrophysiological changes were detected. Permanent occlusion was performed, and the patient did not develop a CVA postoperatively (Fig. 5). After inspection, 1 patient with a vertebral artery (VA) aneurysm was found to have more of a dissecting-type aneurysm. Ten-minute VA occlusion testing was performed. No voluntary motor, speech, cranial nerve, visual, or electrophysiological changes were detected. Permanent occlusion was performed, and the patient did not develop a CVA postoperatively. One patient with a P_2 – P_3 fusiform aneu-

FIG. 2. Follow-up digital subtraction angiography (DSA) performed 12 months after surgery in a 61-year-old man who underwent stent placement plus coiling of a wide-neck ICA aneurysm (at the level of the posterior communicating artery [PCoA]) revealed coil compaction. **A:** Anteroposterior (AP) view. **B:** Lateral view. The key concern in the clipping of this aneurysm was the origin of the anterior choroidal artery. **C:** Intraoperative photograph showing clip placement coupled with direct neurological motor examination. The patient was discharged to home on the 2nd postoperative day; he had an mRS score of 0 at the 1-month follow-up visit.

rysm underwent a 10-minute distal P₂ segment occlusion test. No voluntary motor, visual, or electrophysiological changes were detected. The patient did not develop a CVA after surgery.

In this series (n = 30), the median LOS was 3 days (range 1–5 days). The median mRS score was 1 (range 0–3). All patients were discharged home except for one, who developed a CVA and was discharged to a rehabilitation facility. There were no deaths in this series.

Discussion

The neurosurgical concept of awake craniotomy has been well established in glioma surgery and functional procedures. Awake carotid endarterectomy, which enables neurological testing, is also well established. Aneurysm surgery involves microsurgical manipulations (temporary or permanent clipping) for specific vascular territories. Therefore, awake aneurysm microsurgery fits well with the aforementioned concept. Awake craniotomy in the

treatment of aneurysms has been reported in the literature in case-report format.^{1,8,26,31,35} Suzuki et al.³⁵ reported a discrepancy between MEP amplitudes and voluntary movements in 2 craniotomies performed to treat anterior choroidal artery aneurysms; in both cases, there was an immediate decline in voluntary motor movements without a concomitant change in neurophysiological monitoring after inadvertent occlusion of the anterior choroidal artery during aneurysm clipping.⁴

In our series (n = 30), we detected 3 (10%) patients with false-negative neurophysiological monitoring results, and all 3 developed specific respective testing deficits without concomitant neurophysiological changes while under the effects of conscious sedation. It is possible that these 3 patients would have developed a CVA if these procedures had not been performed with the awake-testing model. These initial data (n = 30) are too limited for any definitive conclusions to be made.

The conscious-sedation model for awake aneurysm

FIG. 3. **A:** 3D reconstruction of DSA images of the left ICA (AP view) in a 46-year-old man with an unruptured left MCA aneurysm. **B:** Intraoperative photograph showing placement of a temporary clip on distal M₁ segment. **C:** Within seconds of placement of the temporary clip, the patient lost voluntary motor movement in his right upper extremity. **D:** Electrophysiological monitoring data during the loss of motor function in the right upper extremity (*left column*) showing SSEPs of the upper extremities (the top screen shows data from the left side, and the bottom screen shows data from the right side). The *middle column* shows SSEPs of the lower extremities (the top screen shows data from the left side, and the bottom screen shows data from the right side). The *right column* shows MEPs of the abductor pollicis brevis, adductor hallucis, and tibialis anterior of both the right and left sides. No EEG, SSEP, or MEP changes detected during the clinical motor loss were observed during the temporary clipping of the M₁ segment. **E:** The temporary clip was removed, and the patient immediately recovered all voluntary movement of the right upper extremity. **F:** Final clipping was then performed without a temporary clip. The patient was discharged home on postoperative Day 3; he had an mRS score of 1 at the 1-month follow-up visit.

FIG. 4. **A:** 3D DSA image of a 45-year-old woman with a fusiform basilar apex aneurysm showing a smaller-sized left P_1 segment (yellow arrow) arising from the dome of the aneurysm. **B:** DSA image of the left ICA showing fetal PCoA (red arrow). **C:** Lateral DSA image of the right ICA lateral injection showing nonfetal PCoA (red arrow). **D:** 3D DSA image of a basilar aneurysm with the proposed awake plan: test occlusion of the left P_1 segment (yellow line) and, if passed safely, permanent occlusion of the left P_1 segment and clip occlusion of the aneurysm (green line). **E:** Intraoperative photograph showing awake occlusion test of the left P_1 segment (temporary clipping of P_1). **F:** Screen print of the iPad-based Vision Test App 2.11, used to perform a 10-minute concomitant motor and visual examination. The patient passed the test, which was followed by permanent occlusion and cutting of the P_1 segment. Next, temporary clipping of the basilar artery was performed (**G**), with continuous conversation with and motor examination of the patient (**H**). **I:** Finally, permanent clipping of the aneurysm was performed using 2 clips. **J:** Postoperative DSA image (AP view) of vertebral injection: 2 clips used for aneurysm occlusion (red arrow) and a clip occluding the left P_1 segment (green arrow) are shown. **K:** DSA image of the left ICA (AP view) showing posterior cerebral artery territory blood flow (yellow arrow) from the left PCoA. The patient had no postoperative neurological deficits. The length of hospital stay was 3 days; her mRS score 1 month after surgery was 1.

surgery in this series also gave us the ability to test the feasibility of evaluating functions that we cannot routinely test after the induction of general anesthesia. Four patients underwent visual testing for the clipping of an ophthalmic segment-based aneurysm, and 2 patients with a basilar apex aneurysm underwent multimodality (consciousness level, motor, speech, cranial nerve, and vision) testing during temporary clipping of their basilar artery. We also introduced the concept of “awake clip test occlusion,” akin to the balloon test occlusion used via an endovascular technique. Three patients underwent clip test occlusion (A_1 segment, VA, or P_3 segment) for 10 minutes with a hypotensive challenge while we tested the respective neurological functions.

During the modern era of microsurgical clipping including neurophysiological monitoring, there has been a number of large reviews, including meta-analyses, that specifically examined the outcomes outlined in Table 1. Given the small sample ($n = 30$) in our study, it is not pos-

sible to make any comparisons or to draw any concrete conclusions. Larger series of awake aneurysm surgery might validate the potential benefit of this technique when compared with standard microsurgical clipping of cerebral aneurysms.

This study was designed to be prospective. To add a framework for the outcomes of this team, we performed a retrospective review of our database to define a cohort of patients who underwent surgery for a UIA by the same neurosurgical anesthesia teams. The 2 inclusion criteria for defining the most recent retrospective computer-matched control group were aneurysm location and patient age (within 5 years). The outcome variables were exactly the same as those for the study group except for the 30-day mRS score, which was not available for the retrospective cohort. The results are shown in Table 2 (which also includes a comparison with the study-group outcomes). We provide these data purely to establish a general framework for the outcomes of patients treated by this specific team.

FIG. 5. Awake clip test occlusion in a 57-year-old woman who presented to an outside hospital with hydrocephalus as a result of a large partially calcified right A₁-A₂ junction aneurysm. **A:** The patient underwent placement of a ventriculoperitoneal shunt at an outside institution (axial CT image without contrast). **B:** DSA image of the right ICA showing slight filling of the aneurysm from the right A₁ segment. **C:** DSA image of the left ICA revealed filling of only the left A₂ segment and not the aneurysm. **D:** The intraoperative finding of calcifications in the right ICA and the A₁ segment led us to abort the plan to perform an in situ bypass from the right A₁ segment to the right A₂ segment. **E:** Permanent occlusion of the A₁ segment was considered. **F:** Ten minutes of temporary occlusion with a hypotensive challenge and clinical motor testing, along with neurophysiological testing (EEG, SSEPs, and MEPs), was performed. After induction of the conscious-sedation awake protocol, the patient passed intraoperative distal A₁ segment occlusion testing (both clinical and neurophysiological parameters). **G:** Permanent occlusion of the distal A₁ segment was performed. The patient was discharged home on postoperative Day 3; her mRS score 1 month after surgery was 2.

These data show that in the LOS, discharge to a facility other than home, and risk of stroke variables, the outcomes were better for the patients who underwent awake clipping of a UIA than for those who underwent this treatment after the induction of general anesthesia. However, no definitive conclusions can be made, because the study group was prospective and the control group was retrospective.

Conclusions

The 3 patients who developed neurological changes without a concomitant neurophysiological finding during temporary clipping revealed a potential advantage of awake aneurysm surgery in decreasing the risk of ischemic injury. In addition, this study revealed the feasibility of testing functions that are not currently testable using

TABLE 1. Contemporary (neurophysiological monitoring era) outcomes from clipping of UIAs

Authors & Year	Data Source/Study Design	No. of Patients	LOS (days)*	Discharged to a Facility (not home)†	No. of CVAs (%)	mRS Score (median)	Deaths†
Barker et al., 2003	NIS database/retrospective	3498	NA	565 (16.1)	NA	NA	73 (2.1)
Barker et al., 2004	NIS database/retrospective	3498	5	565 (16.1)	274 (7.8)	NA	73 (2.1)
Higashida et al., 2007	Health Economics and Outcomes Research Group of Boston Scientific Database/retrospective	1881	7.4	NA	249 (13.2)	NA	2.50
Alshekhlee et al., 2010	NIS database/retrospective	3738	4	NA	340 (9)	NA	60 (1.6)
Hoh et al., 2010	NIS/retrospective	4700	8.9 ± 10.1	NA	NA	NA	
Kotowski et al., 2013	60 published studies, meta-analysis/retrospective	9845	NA	NA	692 (7.0)	NA	157 (1.6)
McDonald et al., 2013	Premier Inc. Perspective database/retrospective	1380	NA	232 (17)	194 (14)	NA	10 (0.7)
Jalbert et al., 2015	Medicare provider analysis & review research identifiable files/retrospective	4357	7.1–9.2	(41.9–45.2)	NA	NA	NA
Present study	Single center/prospective	30	3	1 (3)	1 (3)	1	0

NA = not applicable.

* Values are median, mean ± SD, or range.

† Values are number (%) or percent range.

TABLE 2. Comparison of the outcome of the study group with a retrospective control cohort matched for aneurysm location and patient age

Group	No. of Patients	Median Age (yrs)	Median LOS (days)	No. Discharged to a Facility (not home) (%)	No. of CVAs (%)	mRS Score (median)	No. of Deaths
Retrospective (control)	30	55	5	3 (10)	3 (10)	NA	0
Prospective (study)	30	52	3	1 (3)	1 (3)	1	0

neurophysiological monitoring (vision, level of consciousness during temporary basilar artery clipping, and speech). The sample size (30 patients) is too small to make conclusive remarks, and additional studies are needed to study this concept further.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Conception and design: Abdulrauf, Vuong, Patel, Dryden. Acquisition of data: Abdulrauf, Vuong, Patel, Sampath, Ashour, Germany, Lebovitz, Brunson, Nijjar, Dryden, Khan, Stefan, Wiley, Cleary, Reis, Walsh. Analysis and interpretation of data: Abdulrauf, Patel, Germany, Dryden, Buchanan. Drafting the article: Abdulrauf, Ashour. Critically revising the article: Abdulrauf, Khan. Reviewed submitted version of manuscript: Abdulrauf, Vuong, Patel, Sampath, Ashour, Germany, Lebovitz, Brunson, Nijjar, Dryden, Khan, Stefan, Wiley, Cleary, Reis, Buchanan. Approved the final version of the manuscript on behalf of all authors: Abdulrauf. Statistical analysis: Buchanan. Study supervision: Abdulrauf.

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