Craniotomy for Treatment of Unruptured Aneurysms Is Not Associated With Long-Term Cognitive Dysfunction

Elizabeth Tuffiash, BS; Rafael J. Tamargo, MD; Argye E. Hillis, MD

Background and Purpose—Many studies have reported frequent cognitive deficits associated with subarachnoid hemorrhage (SAH) and aneurysm repair. One study found more severe cognitive deficits after clipping than coiling of aneurysms, raising the possibility that deficits are due to surgery instead of SAH itself. This possibility was directly addressed by evaluating the cognitive effects of surgery without SAH. The goal of this study was to identify changes in cognitive function associated with surgical clipping of unruptured intracerebral aneurysms.

Methods—A consecutive series of 25 patients who underwent surgical clipping of ≥1 unruptured intracerebral aneurysm were tested within 1 week preoperatively and again postoperatively (before hospital discharge and at 3-month follow-up if they had deficits at discharge) on a neuropsychological battery. Different forms of each test were used preoperatively and postoperatively to reduce practice effects. Paired t tests were used to examine differences between preoperative and postoperative test scores across individuals.

Results—On most tests, there was no significant change between preoperative and postoperative scores. A significant decline in accuracy before hospital discharge was found only in figure copying (P < 0.04) and associative learning (P < 0.01), and significant slowing was found on 1 test (P < 0.01). Even on these tests, only 3 of 25 patients showed significant deterioration. All but 1 patient returned to baseline by the 3-month follow-up.

Conclusions—We found no evidence of subtle cognitive deficits resulting from aneurysm clipping alone, suggesting that the common impairments after surgery for ruptured aneurysms are due to SAH itself, complications of SAH such as vasospasm or hydrocephalus, or perioperative stroke. (Stroke. 2003;34:2195-2199.)

Key Words: cerebral aneurysm ■ craniotomy ■ outcome
In studies of patients with SAH and aneurysm clipping, it is difficult to determine what proportion of impaired cognition is a consequence of SAH or craniotomy and perioperative management, including associated general anesthesia and complications of surgery. The dominant view is that cognitive impairment results from the SAH itself.\textsuperscript{4,9,11} However, some authors have reported that patients with traumatic SAH in whom no aneurysm is identified have a lesser degree of cognitive impairment than those patients who undergo surgery for aneurysmal SAH.\textsuperscript{2,13}

Another limitation of neuropsychological studies after craniotomy for aneurysmal repair is that neuropsychological tests are administered only postoperatively. Without a preoperative neuropsychological evaluation, it is difficult to isolate the effect of craniotomy and associated perioperative management on cognitive function. In any population administered a battery of neuropsychological tests, a certain number of individuals will show impaired performance on some tests. In support of this assumption, the few studies that have reported performance on neuropsychological tests before craniotomy for unruptured aneurysm have found that most subjects showed baseline deficits on $\geq$ 1 cognitive tests.\textsuperscript{14,15}

In this study, we report the results of detailed preoperative and postoperative neuropsychological testing in a prospective series of patients who underwent surgery for repair of unruptured aneurysms. By excluding patients with ruptured aneurysms, we eliminate the confounding effects of SAH on cognitive function; by comparing preoperative and postoperative testing in each patient, we account for premorbid cognitive disorders.

Materials and Methods

Experimental Design

The subjects of this prospective study were drawn from 51 patients with unruptured aneurysms operated on by 1 neurosurgeon over 45 months. Although attempts were made to enroll all 51 patients in the study, only 25 enrolled and underwent full neuropsychological evaluations as described below. These 25 patients are referred to as the study group. Statistics for both the included and excluded patients are presented in Table 1. Aneurysm locations for the study group are shown in Table 2.

Subjects

Between February 1998 and October 2001, 51 patients underwent craniotomy for repair of unruptured aneurysms by 1 neurosurgeon (R.J.T.). Although attempts were made to recruit all patients into this prospective study, 26 patients were excluded. The reasons for exclusion included patient refusal to participate, difficulty in scheduling the preoperative neuropsychological testing sessions in patients from outside the Baltimore area, inability to speak or read English, and refusal to complete the postoperative tests. Short-term and long-term postoperative follow-up was obtained for the entire group. The entire group included 8 men (16%) and 43 women (84%). Of the aneurysms treated, 49 (96%) were in the anterior circulation, and 2 (4%) in the posterior circulation. The average size of the treated aneurysms was 9.4 mm, and 10% were giant (≥25 mm). Of the 51 patients, 13 (25%) had multiple aneurysms. Detailed statistics for the entire group and for the patients included in and excluded from the study are presented in Table 1. Aneurysm locations for the study group are shown in Table 2.

Neuropsychological Tests and Outcome Measures

Neuropsychological evaluations were completed within 1 week before surgery, 1 week after surgery (before discharge), and 3 to 6 months after surgery if a significant decline was documented in the second evaluation. The evaluation included the following tests: (1) Weschler Memory Scale-Revised Test,\textsuperscript{16} which tests orientation, recall of current information, recall of passages, sustained attention, digit span, and new learning of associative word pairs; (2) Rey-Osterreith Complex Figure Test,\textsuperscript{17} a copy and delayed recall test that assesses planning, perceptual, motor, and visual memory functions; (3) Trail Making Test,\textsuperscript{18} which tests rapid visual search and executive functions such as visuospatial sequencing and cognitive set shifting; (4) Grooved Pegboard Test (Psychological Assessment Resources, Inc 1999), which tests manual dexterity and motor speed; and (5) Controlled Word Association Test,\textsuperscript{19} which tests verbal association fluency. Patients were evaluated postoperatively with the

| TABLE 1. Clinical Characteristics of Entire Group and Study Group |
|--------------------------|--------------------------|--------------------------|
| Age, y                    | Excluded Group | Study Group |
| Range                    | 28–71          | 32–67         |
| Mean                     | 53.2           | 49.8          |
| Sex, n (%)               | Male           | Male           |
| Female                   | 22 (85)        | 21 (84)       |
| Male                     | 4 (16)         | 4 (16)        |
| Aneurysm size, mm        | Range          | 2–40          |
| Mean                     | 6.9            | 11.9          |

<table>
<thead>
<tr>
<th>TABLE 2. Aneurysm Locations for the Study Group</th>
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<tbody>
<tr>
<td>Aneurysm Location</td>
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<tr>
<td>Single aneurysms</td>
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<tr>
<td>Left PCom</td>
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<tr>
<td>Right PCom</td>
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<tr>
<td>Left MCA</td>
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<tr>
<td>Right MCA</td>
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<td>Left ICA</td>
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<td>Right ICA</td>
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<tr>
<td>Right ACA</td>
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<tr>
<td>Basilar artery</td>
</tr>
<tr>
<td>Multiple aneurysms</td>
</tr>
<tr>
<td>Bilateral superior hypophysael artery</td>
</tr>
<tr>
<td>Bilateral ICA</td>
</tr>
<tr>
<td>Left PCom and left ACA</td>
</tr>
<tr>
<td>Ophthalmic and anterior choroidal, ICA</td>
</tr>
<tr>
<td>Right MCA and right PCom</td>
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<tr>
<td>2 Right MCA and left ACom</td>
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<tr>
<td>Right PCom and left ophthalmic</td>
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PCom indicates posterior communicating artery; ICA, internal carotid artery; ACA, anterior cerebral artery; and ACom, anterior communicating artery.
same battery of tests but different forms to minimize practice effects. Patients who demonstrated a significant decline in cognitive performance were tested 3 to 6 months after surgery. In addition, standard outcome measures such as mortality, major or minor strokes, transient deficits, and Glasgow Outcome Scale (GOS; 5=inactive; 4=mild disability; 3=severe disability, 2=moderate disability, 1=death) were documented for all 51 patients. Major stroke was defined as a complete or severe deficit (eg, plegia or aphasia) and/or imaging evidence of stroke in the distribution of a first- or second-order vessel (eg, internal carotid artery, M1, M2). Minor stroke was defined as partial or mild deficits only (eg, three-fifths to four-fifths strength) associated with imaging evidence of stroke in a smaller branch. Transient deficits were defined as minor sensory or motor deficits that resolved 2 to 3 days after surgery and were attributed to transient edema or retraction.

**Surgical Procedures**

Of the 51 patients, 49 underwent frontosphenotemporal (pterional) craniotomies, 2 underwent combined frontosphenotemporal/subtemporal craniotomies for basilar artery apex aneurysms, and 4 underwent contralateral approaches through frontosphenotemporal craniotomies for repair of bilateral supratentorial aneurysms. The surgical approach involved a curvilinear frontotemporal incision, subfascial dissection of the temporalis muscle, burr hole craniotomy with the Gigli saw, curvilinear dural opening, brain protection with Telfa and Bicol strips, and reversal of mechanical vasospasm with the use of dexamethasone intravenously immediately before, during, and 24 hours after surgery; and anticonvulsants (phenytoin) for 4 to 5 days after surgery. Of the 51 patients, 23 underwent temporary clipping. Of the 25 study group patients, 8 underwent temporary clipping.

**Data Analysis**

Paired Student’s t tests were used to assess the differences between preoperative and postoperative neuropsychological test scores. Values of P<0.05 were considered significant.

**Results**

The outcome measures for study group and the excluded patients were very similar (Table 3). In the study group, 1 patient had a major stroke, 1 had a minor stroke, and 1 had a transient deficit. The patient with the major stroke had presented originally with a left frontotemporal stroke from a middle cerebral artery (MCA) embolus and was found at the time to have an incidental left posterior communicating artery aneurysm. She had, however, a benign neurological examination at the time of admission for aneurysm surgery. Postoperatively, although she did well initially, she developed a delayed hemorrhage into the area of the previous stroke and a new watershed stroke in the left MCA/posterior cerebral artery distribution that required a second craniotomy for evacuation of the intraparenchymal hematoma and a limited anterior frontal lobectomy. She was discharged with a nonfluent aphasia and right hemiparesis. The patient with the minor stroke had a proximal MCA aneurysm and suffered a limited lenticulostriate perforator stroke that resulted in an isolated mild right hemiparesis.

Neuropsychological testing at the time of discharge showed that only 4 subjects showed decline on any of the tests. Three patients (12%) showed a significant decline in the Rey-Osterreith Complex Figure Test (resulting in a significant decline from preoperative to postoperative scores for the group; df=21, P<0.04), and 2 patients (8%) showed a significant decline in the Grooved Pegboard Test (also resulting in a significant decline from preoperative to postoperative scores for the group; df=16, P<0.01). These 2 test groups had only 1 patient in common who showed a significant decline in both of these tests. At the time of discharge, although there was no significant difference in the overall Weschler Memory Scale-Revised Test scores, there was a significant decline in the Associative Learning subtest for the group (df=21, P<0.01), which reflected decline in 3 patients. However, there was also a significant improvement for the group in the Logical Memory subtest (df=23, P<0.05). These results are summarized in Table 4.

Neuropsychological testing at 3 to 6 months after surgery showed that only 1 patient of 25 in the study group (4%) remained with significantly lower cognitive scores. Not surprisingly, this was the patient who suffered a major stroke as described above. That is, 3 to 6 months after surgery, all patients who demonstrated significant decline in scores in the immediate postoperative period had returned to baseline except for the 1 patient with major stroke.

At 3 to 6 months, no hidden neuropsychological deficits were identified in patients with GOS scores of 5. Of the 2 patients in the study group with GOS of 4 at 3 to 6 months, the patient with major stroke had documented neuropsychological deficits, but the patient with minor lenticulostriate perforator stroke did not. Of the other 2 patients who had cognitive deficits at the time of discharge, both returned to baseline neuropsychological performance and GOS of 5 at 3 to 6 months after surgery.

**Discussion**

In this study, craniotomy for repair of unruptured aneurysms was associated with a 4% incidence (1 of 25) of cognitive dysfunction, as documented by detailed neuropsychological testing, 3 to 6 months after surgery. This patient had suffered a perioperative stroke resulting in aphasia and right hemiparesis and at 3 to 6 months after surgery remained with a GOS score of 4. At 3 to 6 months after surgery, no patients with GOS scores of 5 demonstrated any cognitive deficits. These
results indicate that craniotomy for aneurysm clipping and the associated perioperative care (eg, general anesthesia), at least under our protocol, do not result in subtle or hidden neurocognitive deficits.

Our outcomes are comparable to those of larger series of surgical treatment of unruptured aneurysms, which suggests that our results could be generalized to most patients with unruptured aneurysms. In a large series of 202 consecutive operations for unruptured aneurysms, Solomon and colleagues reported a 3% mortality, a 7% incidence of major complications, and an 88% incidence of excellent outcomes. In another series of 72 patients treated surgically for unruptured aneurysms, a 25% incidence of postoperative neurologic deficit, and an 88% incidence of excellent outcomes.

We suspect that the higher proportion of postoperative complications in our series may be due to the lack of neuropsychological testing 6 months after early aneurysm repair after SAH, most patients had “marked disability” on a complex reaction time test, 53% had impaired short-term memory, and 10% had aphasia. The only factors associated with cognitive impairment at 6 months were patient age and size of the hemorrhage. These results suggest that it may be the SAH itself that results in the “hidden” cognitive impairment that was not reflected in the GOS, although older patients may also have slow cognitive recovery after any surgery with general anesthesia. However, because all patients in this study had both surgery and SAH, it is impossible to clearly distinguish the effects of each.

To the best of our knowledge, only 2 studies, each with a small number of patients, have attempted to separate the cognitive impact of the SAH from that of the surgical intervention. One small study of unruptured aneurysm repair concluded that there was deterioration in cognitive scores after surgery compared with before surgery. However, only 3 tests were administered preoperatively and postoperatively: the Mini-Mental State Examination, a letter-search task, and a maze test. On the Mini-Mental State Examination, 10 cases showed a decrease in scores, but 11 showed an increase in scores postoperatively. Similarly, on the letter-searching test, scores of 17 patients decreased, but scores of 11 patients increased. In fact, there were no statistically significant changes in cognitive functioning documented, so the conclusion that there was cognitive deterioration is unwarranted. An earlier study at our institution compared 2 groups of patients who underwent aneurysm clipping, those with SAH and those with unruptured aneurysms. Patients who had surgical clipping of ruptured aneurysms performed significantly worse than patients who underwent surgical clipping of unruptured aneurysms on tests of memory. Furthermore, most patients with unruptured aneurysms showed no decline between preoperative treatment and postoperative cognitive scores. The present study, with a larger patient population, confirms these findings.
In our study, only patients with complications (stroke) who had GOS scores of ≤4, showed deterioration from preoperative performance on neuropsychological tests. The only patient with long-term deficits had a hemorrhage into an old infarct postoperatively, requiring a second craniotomy and limited anterior lobectomy, which likely contributed to her persistent deficits. Therefore, aneurysm surgery alone (and associated perioperative management) did not cause the types of mild cognitive deficits not reflected in the GOS that have been reported after SAH. A few patients showed decline in copying, in the Grooved Pegboard (perhaps because of mild weakness), or in associative learning at the time of hospital discharge but showed no significant change from preoperative scores at the 3-month follow-up. The clinical significance of these temporary deficits is unclear; they may have been due to pain medications.

In conclusion, craniotomy for aneurysm repair and associated perioperative care and complications do not result in subtle or hidden cognitive dysfunction in patients with good outcomes, as determined by standard outcomes scales such as the GOS.

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References
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