The Risk of Seizure After Surgery for Unruptured Intracranial Aneurysms: A Prospective Cohort Study

BACKGROUND: We aimed to identify a group of patients with a low risk of seizure after surgery for unruptured intracranial aneurysms (UIA).

OBJECTIVE: To determine the risk of seizure after discharge from surgery for UIA.

METHODS: A consecutive prospectively collected cohort database was interrogated for all surgical UIA cases. There were 726 cases of UIA (excluding cases proximal to the superior cerebellar artery on the vertebrobasilar system) identified and analyzed. Cox proportional hazards regression models and Kaplan-Meier life table analyses were generated assessing risk factors.

RESULTS: Preoperative seizure history and complication of aneurysm repair were the only risk factors found to be significant. The risk of first seizure after discharge from hospital following surgery for patients with neither preoperative seizure, treated middle cerebral artery aneurysm, nor postoperative complications (leading to a modified Rankin Scale score $\geq 1$) was $0.1\%$ and $1.1\%$ at 12 months and 7 years, respectively. The risk for those with preoperative seizures was $17.3\%$ and $66\%$ at 12 months and 7 years, respectively. The risk for seizures with either complications (leading to a modified Rankin Scale score $\geq 1$) from surgery or treated middle cerebral artery aneurysm was $1.4\%$ and $6.8\%$ at 12 months and 7 years, respectively. These differences in the 3 Kaplan-Meier curves were significant (log-rank $P < .001$).

CONCLUSION: The risk of seizures after discharge from hospital following surgery for UIA is very low when there is no preexisting history of seizures. If this result can be supported by other series, guidelines that restrict returning to driving because of the risk of postoperative seizures should be reconsidered.

KEY WORDS: Aneurysm, Brain, Cox regression, Kaplan-Meier, Seizure, Surgery

The risk of seizure after surgery for intracranial aneurysm has been reported to be $0\%$ to $15.7\%$.

A variety of characteristics have been cited as increasing the risk of seizure after surgery, including hemorrhagic events and low aneurysm-volume hospitals. Some factors relate to the number of aneurysms and others are related to the aneurysm repair itself. The risk of future hemorrhage has been associated with the increased risk of seizure. In an analysis of the literature, 2 factors were commonly associated with an increased risk of future seizure: multiple aneurysms and middle cerebral artery (MCA) location.

Understanding which factors are associated with an increased risk of postoperative seizure together with the cumulative risk of postoperative seizure will assist in advising individual patients of the risk of potential seizures, which will restrict activities and the ability to resume preoperative activities such as driving and work.

Driving after craniotomy for unruptured aneurysms is restricted for noncommercial drivers by some driving authorities for periods ranging from 3 to 6 months, although no restrictions are required depending on specific conditions by other authorities. For commercial drivers, restrictions on returning to driving range from 6 to 12 months. Restrictions on driving

ABBREVIATIONS: MCA, middle cerebral artery; mRS, modified Rankin Scale; UIA, unruptured intracranial aneurysms
after a seizure are prescribed in many driving authorities with diverse time periods.

Three case series, each of more than 100 patients, reported the incidence of seizures after surgery for unruptured intracranial aneurysms (UIA) to be between 0%9,11 and 4%23 during a mean follow-up period of 3 to 28 months. However, these studies were not performed with survival analysis methodologies. The overall rate of seizures for these amalgamated populations was 1.1% for an average 12 months of follow-up.

Our prospectively collected aneurysm database of the senior author (M.K.M.) was reviewed to examine which factors, of those identified by other authors, influence the risk of first seizure after surgery of an UIA. Excluded from our analysis were aneurysms proximal to the superior cerebellar artery on the vertebrobasilar system, as surgery that does not involve access via a supratentorial route is very unlikely to be associated with the development of seizures. Cox proportional hazards regression and Kaplan-Meier survival models are used. The purpose was to identify a group of patients that have a low risk of seizures after discharge from hospital.

METHODS

Patient Population

This study was approved by the Macquarie University Human Ethics Committee and was performed in accordance with institutional ethics committee guidelines. A prospectively collected database of the senior author (M.K.M.) containing consecutive patients from multiple treatment centers was retrospectively analyzed for the years 1989 to July 2014. The database contained demographic, clinical, radiological, and treatment-related information. Due to the legal requirement in Australia for postsurgical patients to not drive if they have had a seizure, screening occurred at each postoperative consultation by the surgeon. This information was entered into the database at the time of the consultation. Included in the records was correspondence referring to seizure events. Seizures could be either focal or generalized and considered to have occurred if reported as such by an emergency room physician, neurosurgeon, or neurologist or were considered to be by the senior author on review of history. Patients were included if they were confirmed to have been treated by surgery for UIA and was confined to aneurysms of the anterior circulation or located distal to the level of the superior cerebellar artery (ie, those in which surgical access was performed via a supratentorial approach) (Figure 1). These patients were not treated with anticonvulsants during the hospital admission for surgery or during the postoperative period unless they were previously prescribed anticonvulsants for seizures occurring before the hospital admission for surgery.

Patients were excluded if they had aneurysms that did not occupy and require access via the supratentorial space or were not typical berry aneurysms (infected, dissection, or traumatic aneurysms). UIA cases were excluded if they were surgically treated coincidentally with a ruptured aneurysm. UIA associated with brain arteriovenous malformations were excluded if they were surgically treated coincidentally with a ruptured aneurysms (infected, dissection, or traumatic aneurysms). UIA cases were excluded if they were surgically treated coincidentally with a ruptured aneurysms (infected, dissection, or traumatic aneurysms). UIA associated with brain arteriovenous malformations or its surgery. Seizures that occurred during the hospital admission for aneurysm surgery were not included, as the purpose of the study was to ascertain risks of seizures occurring after discharge from the hospital, and during the course of normal activities for patients and because of the difficulty in distinguishing these events from other neurological episodes at this time (eg, syncope from postural hypotension).

Variables Investigated

Eleven variables were selected for examination, based upon our literature review.5-7,11 These variables were aneurysm size, multiple craniotomies, sex, age (dichotomized for those less than 50 years of age and those 50 years or more), preexisting stroke, preexisting brain injury or brain tumor, past ruptured aneurysm (other site), preoperative seizure, symptomatic brain compression, multiple aneurysms repaired at 1 surgery, MCA aneurysm treated, and complication of aneurysm repair. Complication of aneurysm repair was aimed to identify stroke arising as a consequence of surgery. Because of artifact from clips, this was not possible to confirm in all cases (eg, medial basal frontal lobe or hypothalamus in the case of anterior communicating artery repair). Therefore, we used the presence of a new neurological deficit assigned at 6 weeks with a permanent neurological deficit persisting at 12 months (modified Rankin Scale [mRS] score >1). The patient assignment at the 6-week postoperative review (or if this did not occur, at the time of discharge from hospital), with the eventual mRS >1 for this complication not assigned until 12 months, allowed diplopia and eyelid
pros (that may be responsible for an mRS of 2) to resolve and thus, not be confused with infarction. Therefore, this clinical outcome variable was used as an independent variable.

**Outcome**

The outcome of the study was first seizure after discharge from surgery. This required confirmation by accident and emergency room physician, neurologist, or neurosurgeon. The seizure could be generalized or partial. Because of the difficulties ascribing unwitnessed events leading to alterations of consciousness in the immediate postoperative period (eg, narcotics, syncope, and seizure), and because our specific focus was on the impact upon driving restriction, seizures were not included during the perioperative hospital admission.

**Sensitivity Analysis**

To examine what impact cases excluded may have had on the outcome from primary analysis, a sensitivity analysis was performed. For this analysis, cases followed for less than 31 days with a postoperative mRS <2 excluded were modeled to have had a postoperative seizure and added to the actual number of included cases (of postoperative seizures) for the sensitivity analysis.

**Statistical Analysis**

Statistical analysis was performed using Prism (version 6; GraphPad Software Inc, La Jolla, California) and IBM SPSS Statistics (version 22; IBM Corporation, Armonk, New York). For the purpose of life table analysis (Kaplan-Meier estimates) and Cox regression, patients were included when reviewed on more than one occasion with the event being first seizure after discharge for UIA and censoring at last review.

The 2-tailed P value was determined using Fisher’s exact test to identify characteristics for further review by Cox regression and Kaplan-Meier curve analysis. Because of the low number of events (cases with first postoperative seizures), a limited number of variables were selected. Multivariate Cox regression was performed for 3 variables: (1) preoperative seizure, (2) MCA aneurysm treatment, and (3) complication of aneurysm repair with mRS >1 at 12 months. A statistical significance level of P < .05 was used throughout. MCA aneurysm treatment and complication of aneurysm repair with mRS >1 at 12 months were combined for Kaplan-Meier analysis because of the lack of difference between these curves on first Kaplan-Meier analysis (Figure 2).

**RESULTS**

A total of 777 cases of UIA treated by surgery with a supratentorial exposure were identified. From this total, 51 cases were not followed for a minimum of 30 days. Failure to follow these cases was due to death or poor neurological state in 20, distance to travel to follow-up (interstate or overseas) in 6, and lost to planned follow-up in 25 with a last mRS <4 (Figure 1). There were 17 cases with a mRS <2 lost to follow-up that were intended to be followed beyond 30 days. Data were collected and analyzed for the remaining 726 consecutive UIA (excluding posterior circulation aneurysms proximal to the superior cerebellar artery). The mean and median time interval between initial referral and censoring or first seizure was 1063 (SD 1292 days) and 525 days (upper and lower 25% quartile 200 and 1463 days), respectively.

The mean follow-up from referral to last follow-up is given in Table 1. Postoperative complications by the definition proposed in this study were thought to be due to infarction in all cases. Postoperative seizures occurred in 14 cases. Four of these 14 cases had a preoperative seizure history and 3 had postoperative complications resulting in a mRS >1 at 12 months (Table 2). Of the 12 variables examined by Fisher’s exact test, only preoperative seizure (P < .001), maximum size > 15 mm (P = .01), MCA treatment (P < .01), and complication of surgery (P = .07) were identified as potentially significant indicators of the increased risk of postoperative seizures (Table 1). Further investigation of these 4 variables by multivariate Cox regression showed preoperative seizures (P < .001, HR 17.8: 95% CI 4.5%-70.9%), MCA treatment (P < .005, HR 5.8: 95% CI 1.7%-19.6%), and complication of aneurysm repair with mRS >1 at 12 months (P = 0.04, HR 4.3: 95% CI 1.04%-17.4%) were identified as characteristics associated with significantly increasing the risk of first seizure after discharge from hospital (Table 3). The occurrence of both preoperative seizure and complication of repair with mRS >1 occurred in 2 cases. Neither of these cases was reported to have had a postoperative seizure. The occurrence of both preoperative seizures and MCA aneurysm treatment occurred in 8 cases, 4 of which developed postoperative seizures.

By Kaplan-Meier analysis the cumulative risk of first postoperative seizure for cases with neither preoperative seizures, MCA aneurysm treatment nor complications of surgery (leading to a mRS >1 at 12 months) was <0.1% and 1.1% at 12 months and 7 years, respectively (Figure 2). For cases with preoperative seizures, the cumulative rate of first postoperative seizure was 17% and 66% at 12 months and 7 years, respectively (Figure 2). For cases with either complications of surgery (leading to a mRS >1 at 12 months) or MCA aneurysm treatment, the cumulative risk of first postoperative seizure was 1.4% and 6.8% at 12 months and 7 years, respectively (Figure 2). The difference between these 3 groups was significant by the Kaplan-Meier curve analysis (log-rank [Mantel-Cox] P < .001) (Figure 2). There was no discernable difference by log-rank (Mantel-Cox) analysis between those with complications of surgery (leading to a mRS >1 at 12 months) and MCA aneurysm treatment, and these 2 were therefore combined for subsequent Kaplan-Meier analysis. Beyond 7 years, the number at risk decreased to less than 10%, making analysis beyond this time unreliable.

There was no change in the levels of significance found in the sensitivity analysis. No variable achieved a P value of <.05 after the inclusion of 17 excluded cases that were followed for less than 30 days with a last mRS <2.

**DISCUSSION**

The purpose of our investigation was to determine the level of risk of seizure after discharge from surgery for UIAs that may affect a person’s ability to return to normal activities, such as driving a motor vehicle. For the total cohort, we found that in the absence of preoperative seizure, MCA aneurysm treatment, or
FIGURE 2. Kaplan-Meier analysis for the cumulative percentage free of postoperative seizures for 726 cases after surgical repair of unruptured intracranial aneurysms requiring a supratentorial subarachnoid space access. 

A, represents the 4 categories of risk identified by Cox regression (preoperative seizures, middle cerebral artery [MCA] aneurysm, complication of surgery leading to a modified Rankin score [mRS] ≥ 1 at 12 months). In this graph, some cases are represented in more than a single curve. There is a difference in the curves by log-rank, but no difference between MCA aneurysm and complication of surgery leading to a mRS ≥ 1 at 12 months.

B, combines the curves of MCA aneurysm and complication of surgery leading to a mRS ≥ 1 at 12 months (excluding preoperative seizure cases). There are no cases represented in more than 1 curve. There is a difference between these curves.

Difference between curves: 

All 4 curves:
Log-rank (Mantel-Cox): p = 0.001
MCA aneurysm vs Complication of surgery leading to mRS ≥ 1 at 12 months (excluding preoperative seizures):
Log-rank (Mantel-Cox): p = 0.12
Hazard ratio (95% CI) = 2.9 (0.7 to 27.5)

Difference between curves:

All 3 curves:
Log-rank (Mantel-Cox): p = 0.001
2 curves excluding preoperative seizures:
Log-rank (Mantel-Cox): p = 0.008
Hazard ratio (95% CI) = 6.2 (1.6 to 19.7)

* = includes cases that may be in more than one curve
complications of aneurysm repair, the cumulative risk of seizures at 7 years was 1.1%. Furthermore, in the absence of preoperative seizure, but with either MCA aneurysm treatment or complications of aneurysm repair, the cumulative risk of seizures at 7 years was 6.8%.

In theory, because the aneurysm neck is located within the subarachnoid space, microsurgical repair should be possible without significant brain damage, thus avoiding the potential for seizure development. In practice, this potential for seizure development is difficult to avoid because of a number of events that may occur during surgery, such as surgical retraction causing brain injury, venous infarction occurring from ligation and division of veins, when the fundus of the aneurysm requires dissection from within the brain, infarction, or hemorrhage.

The risk of seizure after surgery for UIAs has important implications for driving. The paucity of evidence has made driving authorities rely on expert opinion to develop fitness to drive guidelines. In this cohort, no patient was commenced on anticonvulsants for UIA or treatment of UIA unless they had been treated for seizures prior to their admission. We excluded from analysis aneurysm cases that did not require a supratentorial approach, as these cases do not have an obvious reason for an increased risk of seizure. From the factors that we examined (aneurysm size, multiple craniotomies, sex, age, preexisting stroke, brain injury or brain tumor, past ruptured aneurysm, preoperative seizure, symptomatic brain compression, multiple aneurysms repaired at 1 surgery, and complication of aneurysm repair), we found preoperative seizure and complication of aneurysm repair to be discriminators of increased risk for the development of seizure.

Although it is difficult to compare this study with the natural history of seizures occurring in a similar population, it is worth noting that the annual rate of detection of unprovoked first seizure is 23 to 61 per 100 000 population. This is considerably lower than was found after surgery for UIA in our series. However, our findings do suggest patients who have no preoperative seizures, MCA aneurysm treatment, or complications due to surgery can be reassured that the risk for seizure development is very low and that it is unnecessary on this account to either be prescribed preventative anticonvulsant therapy or alter daily living activities in this cohort. This study has altered our routine practice from uniformly restricting driving for a minimum of 3 months after surgery. We continue to only recommend anticonvulsants for patients with preoperative seizures (including single seizures). We now suggest to patients that they may resume driving in the absence of preoperative seizures or complications of surgery at the time of their 6-week postoperative follow-up. For those with complications of surgery leading to stroke, we continue to restrict their return to driving until such time as their mRS <2. If this does not occur we suggest a restriction of driving or driving with anticonvulsants providing they pass a driver assessment test. In the event that there is a postoperative seizure, these patients are...

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**TABLE 1. Characteristics of 726 Patients Undergoing Surgery for UIA**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>% Cases With Characteristic in Column 1 (Number of Cases With Characteristic)</th>
<th>% Cases With Characteristic Identified in Column 1 Developing Postoperative Seizure; 95% CI (Number of Cases With Characteristic Developing Seizure)</th>
<th>Fisher's Exact or Mann-Whitney Tests Comparing Group With Postoperative Seizures With Those Without P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cases: %; 95% CI (number)</td>
<td>726</td>
<td>1.9; 1.1% to 3.2% (14)</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Characteristic examined</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>72 (525)</td>
<td>1.9; 1.0% to 3.5% (10)</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Age 50 years or more</td>
<td>62 (448)</td>
<td>2.0; 1.0% to 3.8% (9)</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Preoperative seizures</td>
<td>2.6 (19)</td>
<td>21; 4.0% to 44% (4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Previous craniotomy elsewhere</td>
<td>1.4 (10)</td>
<td>10; &lt;43% (1)</td>
<td>.18</td>
</tr>
<tr>
<td>Past stroke/brain injury/brain tumor</td>
<td>3.6 (26)</td>
<td>4; &lt;20% (1)</td>
<td>.40</td>
</tr>
<tr>
<td>Past ruptured aneurysm</td>
<td>3.0 (22)</td>
<td>5; &lt;24% (1)</td>
<td>.35</td>
</tr>
<tr>
<td>Presentation with symptomatic brain compression</td>
<td>1.0 (7)</td>
<td>14; &lt;53% (1)</td>
<td>.13</td>
</tr>
<tr>
<td>Maximum size (largest aneurysm) &gt;15 mm</td>
<td>25 (182)</td>
<td>4.4; 2.1% to 8.6% (8)</td>
<td>.01</td>
</tr>
<tr>
<td>Any MCA location (includes MCA aneurysms that are not primary target)</td>
<td>36 (263)</td>
<td>3.8; 2.0% to 7.0% (10)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Multiple aneurysms repaired</td>
<td>26 (190)</td>
<td>1.1; 0.04% to 4.0% (2)</td>
<td>.54</td>
</tr>
<tr>
<td>Multiple craniotomies</td>
<td>6.9 (50)</td>
<td>4; 0.3% to 14% (2)</td>
<td>.25</td>
</tr>
<tr>
<td>Complication of aneurysm repair with mRS &gt;1 at 12 month</td>
<td>6.9 (50)</td>
<td>6; 1.4% to 17% (3)</td>
<td>.07</td>
</tr>
<tr>
<td>Follow-up, d</td>
<td>1082; 1311 (534; 7625)</td>
<td>2007; 1654 (1445; 4988)</td>
<td>.015</td>
</tr>
</tbody>
</table>

*CI, confidence interval; MCA, middle cerebral artery; mRS, modified Rankin Scale score; SD, standard deviation; UIA, unruptured intracranial aneurysms.
### TABLE 2. Patients Experiencing First Seizure Undergoing Surgery for UIA Aneurysms

<table>
<thead>
<tr>
<th>Case</th>
<th>Age and Sex</th>
<th>Multiple Aneurysms Repaired</th>
<th>Aneurysm Size $&gt;15$ mm</th>
<th>Preoperative Neurological History</th>
<th>Neurological Condition at Discharge</th>
<th>Complications of Surgery Leading to mRS $&gt;1$ at 12 months</th>
<th>MCA Aneurysm Treated</th>
<th>Days Between Referral and First Seizure</th>
<th>Seizure Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>54 F</td>
<td>No</td>
<td>No</td>
<td>Normal</td>
<td>Hemiparesis</td>
<td>mRS = 2</td>
<td>No</td>
<td>697</td>
<td>Simple partial</td>
</tr>
<tr>
<td>2</td>
<td>64 F</td>
<td>No</td>
<td>Yes</td>
<td>Normal</td>
<td>Normal</td>
<td>mRS = 2</td>
<td>Yes</td>
<td>1954</td>
<td>Generalized</td>
</tr>
<tr>
<td>3</td>
<td>37 F</td>
<td>No</td>
<td>Yes</td>
<td>Normal</td>
<td>Dysphasia</td>
<td>mRS = 2</td>
<td>Yes</td>
<td>100</td>
<td>Generalized</td>
</tr>
<tr>
<td>4</td>
<td>54 F</td>
<td>No</td>
<td>Yes</td>
<td>Normal</td>
<td>Normal</td>
<td>Nil</td>
<td>Yes</td>
<td>367</td>
<td>Generalized</td>
</tr>
<tr>
<td>5</td>
<td>34 F</td>
<td>No</td>
<td>Yes</td>
<td>Normal</td>
<td>Normal</td>
<td>Nil</td>
<td>Yes</td>
<td>116</td>
<td>Generalized</td>
</tr>
<tr>
<td>6</td>
<td>41 F</td>
<td>Yes</td>
<td>No</td>
<td>Normal</td>
<td>Normal</td>
<td>Nil</td>
<td>Yes</td>
<td>2129</td>
<td>Generalized</td>
</tr>
<tr>
<td>7</td>
<td>46 M</td>
<td>No</td>
<td>No</td>
<td>Normal</td>
<td>Normal</td>
<td>Nil</td>
<td>No</td>
<td>585</td>
<td>Generalized</td>
</tr>
<tr>
<td>8</td>
<td>34 F</td>
<td>No</td>
<td>No</td>
<td>Normal</td>
<td>Normal</td>
<td>Nil</td>
<td>Yes</td>
<td>3465</td>
<td>Generalized</td>
</tr>
<tr>
<td>9</td>
<td>36 M</td>
<td>No</td>
<td>Yes</td>
<td>Normal</td>
<td>Normal</td>
<td>Nil</td>
<td>No</td>
<td>931</td>
<td>Generalized</td>
</tr>
<tr>
<td>10</td>
<td>16 F</td>
<td>No</td>
<td>No</td>
<td>Single generalized seizure</td>
<td>Normal</td>
<td>Nil</td>
<td>Yes</td>
<td>1884</td>
<td>Generalized</td>
</tr>
<tr>
<td>11</td>
<td>32 F</td>
<td>No</td>
<td>Yes</td>
<td>Multiple generalized seizure</td>
<td>Normal</td>
<td>Nil</td>
<td>Yes</td>
<td>61</td>
<td>Generalized</td>
</tr>
<tr>
<td>12</td>
<td>47 M</td>
<td>Yes</td>
<td>Yes</td>
<td>Single complex partial seizure</td>
<td>Normal</td>
<td>Nil</td>
<td>Yes</td>
<td>727</td>
<td>Complex partial</td>
</tr>
<tr>
<td>13</td>
<td>55 F</td>
<td>No</td>
<td>No</td>
<td>Nocturnal generalized seizures</td>
<td>Normal</td>
<td>Nil</td>
<td>Yes</td>
<td>307</td>
<td>Nocturnal generalized</td>
</tr>
<tr>
<td>14</td>
<td>52 M</td>
<td>No</td>
<td>Yes</td>
<td>Normal</td>
<td>Hemiparesis and dysphasia</td>
<td>mRS = 2</td>
<td>No</td>
<td>398</td>
<td>Generalized</td>
</tr>
</tbody>
</table>

All cases

Days: mean (SD) [median: 25% and 75% quartile]

980 (1004) [641: 259 and 1901]

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*MCA, middle cerebral artery; mRS, modified Rankin Scale; SD, standard deviation; UIA, unruptured intracranial aneurysms.*
A report of a US nationwide inpatient seizure rate after surgical repair of UIA of 9.2% is comparatively high as compared with our post discharge first seizure incidence. We have previously reported results from the Australian National Hospital Morbidity Database that identified an overall 2.7% incidence of perioperative seizures for UIA surgery between the years 1998 and 2008. For the Australian study, the incidence declined steadily from 4.2% in 1998 to 2.0% in 2008. The explanation for the comparatively high rate of perioperative seizures as compared with after discharge seizures reported from our cohort may well relate to greater exposure to temporary precipitants of seizure during the perioperative period that are unique to this period and not a manifestation of permanent changes of the brain that may predispose to ongoing seizures. The disconnect between early and late seizures may be similar to early seizures after stroke not predicting long-term development of seizures (unless associated with intracerebral hemorrhage). There are a number of possible temporary precipitants that can be suggested to increase the risk of seizure, particularly when several may be present at the same time. These include brain trauma, pneumocephalus, and brain shift (as for example can occur after chronic subdural hematoma drainage), hyponatremia, orthostatic hypotension, pharmacological interaction, blood loss at the time of surgery, anesthesia, fever, brain distortion, and complications of surgery such as subdural hemorrhage and stroke. These are well-recognized precipitating events for seizures, but may be only temporally associated with the perioperative period. Therefore, there is a reasonable expectation that for UIA, the explanation for seizures during the hospital administration may be significantly different from those resulting from permanent brain injury that will only be manifest after the acute phase has resolved and the time taken for gliosis or siderosis to commence inducing seizures. This may also account for the long delay between surgery and first seizures identified in our cohort. However, considering the literature, there is a paucity of seizure incidence data in articles reporting the outcomes of surgery for UIAs after discharge from surgery. Few cohort series report the incidence of seizures after discharge from hospital. Those cohort studies reporting an incidence of seizure for UIA surgery have not used survival analysis methodology in determining this incidence.

**Limitations**

The limitations of cohort studies are well known. There is the problem of whether the cohort treated by the authors reflects the general population of UIA. These results would need to be confirmed by others to accept these results as generalizable. In our study, patients were likely to include more surgically complex than simple aneurysms, reflecting referral bias to a center with expertise in cerebrovascular surgery. In addition, the grading of outcomes is not independent.

A specific limitation of this study was the use of the variable complication of surgery leading to a mRS >1 at 12 months. The use of a clinical outcome variable not determined before 1 year after surgery in the determination of seizure outcome may at first seem to be of limited use in assisting clinicians to determine the eligibility for return to driving after surgery. However, this clinical variable is a surrogate for stroke complicating surgery, the clinical determination of which is evident prior to discharge. The discrimination between neurological deficits responsible for outcomes with a mRS >1 caused by stroke and dissection...
may be made by computed tomographic scan or magnetic resonance imaging in the postoperative period. However, this cannot always be made because of clip artifact (eg, infarcts of the hypothalamus associated with anterior communicating artery aneurysm repair) and a mRS of 2 can be caused by prosis or diplopia (usually not caused by stroke) in the early postoperative period. Therefore, the clinical complication definition of this study was used as a surrogate for stroke caused by the surgery for aneurysm repair. As such, the determination of the advice regarding return to driving can reasonably be made early after surgery in most cases. Very few cases would require a protracted period before determining whether they fell within or outside the low risk group.

A limitation in analysis by multivariate Cox regression and Kaplan-Meier curve analysis is the low number of events (ie, postoperative seizures) occurring, limiting the number of variables that can be analyzed by these techniques. By choosing only 3 variables, there is a risk of missing variables that may be significant in a larger series.

**CONCLUSION**

Cases of UIA undergoing surgical repair with no history of preoperative seizure and no postoperative complication or treated MCA aneurysm had a low risk of subsequent seizure (approximately 1% during the first 7 years after surgery). If either MCA aneurysm treatment or postoperative complication has occurred, in the absence of preoperative seizures, the risk of first seizure is no greater than 1% per year.

**Disclosure**

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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