Better Outcomes with Treatment by Coiling Relative to Clipping of Unruptured Intracranial Aneurysms in the United States, 2001–2008

BACKGROUND AND PURPOSE: Endovascular therapy has increasingly become an acceptable option for treatment of unruptured aneurysms. To better understand the recent trends in the use of and outcomes related to coiling compared with clipping for unruptured aneurysms in the United States, we evaluated the NIS.

MATERIALS AND METHODS: Hospitalizations for clipping or coiling of unruptured cerebral aneurysms from 2001 to 2008 were identified by cross-matching ICD codes for the diagnosis of unruptured aneurysm (437.3) with procedural codes for clipping (39.51) or coiling (39.52, 39.79, or 39.72) of cerebral aneurysms and excluding all patients with a diagnosis of subarachnoid hemorrhage (430) and intracerebral hemorrhage (431). Mortality and discharge to a long-term facility were evaluated for both clipping and coiling patient populations.

RESULTS: The fraction of unruptured aneurysms treated with coiling increased from 20% in 2001 to 63% in 2008. For surgical clipping, the percentage of patients discharged to long-term facilities was 14.0% (4184/29,918) compared with 4.9% (1655/34,125) of coiled patients (P < .0001). Clipped patients also had a higher mortality rate because 344 (1.2%) clipped patients died compared with 215 (0.6%) coiled patients (P < .0001). Between 2001 and 2008, the overall number of adverse outcomes from treatment had decreased from 14.8% to 7.6%.

CONCLUSIONS: The use of endovascular coiling relative to surgical clipping of unruptured intracranial aneurysms is associated with decreasing periprocedural morbidity and mortality among patients treated in the United States from 2001 to 2008.

ABBRVIATIONS: HCUP = Healthcare Cost and Utilization Project; ICD-9-CM = International Classification of Diseases, 9th Revision, Clinical Modification; ISAT = International Subarachnoid Aneurysm Trial; ISUIA = International Study of Unruptured Intracranial Aneurysms; NIS = National Inpatient Sample; VP = ventriculoperitoneal

Physicians are able to choose among surgery, endovascular treatment, and no treatment for each patient who presents with an unruptured intracranial aneurysm. Because the risk of subarachnoid hemorrhage resulting from an unruptured aneurysm is relatively low, the risks associated with either surgical or endovascular treatment must be even lower for treat-ment to be justified. The treatment strategies for unruptured aneurysms are rapidly evolving, mainly due to an increasing role of endovascular therapy. It is, therefore, important to monitor recent trends in patient treatment and outcomes so that we can assess whether evolving therapies for these patients are having a positive effect on patient outcome. Given its comprehensive nature and the massive amount of clinical data it provides, the NIS has been used previously to study outcomes of patients treated for unruptured cerebral aneurysms.1-3 In the current study, we applied the NIS data from 2001 to 2008 to correlate the recent national trends in treatment strategy with the outcomes among patients treated with clipping and coiling for unruptured cerebral aneurysms.

Materials and Methods

Patient Population

We purchased the NIS hospital discharge data base for 2001–2008 from the HCUP of the Agency for Healthcare Research and Quality, Rockville, Maryland. The NIS is a hospital discharge data base that represents 20% of all inpatient admissions to nonfederal hospitals in the United States.

All patients included in this study carried a primary diagnosis of unruptured aneurysm (code 437.3 in the ICD-9-CM) and a primary ICD-9-CM procedural code of “clipping of aneurysm” (ICD-9-CM code 39.51) or of coiling of aneurysm, which included “other repair of aneurysm” (ICD-9-CM code 39.52), “endovascular repair or occlu-
Between the years 2001 and 2008, a total of 64,043 unruptured intracranial aneurysms were treated with surgical clipping or endovascular coiling; 34,125 cases (53%) were treated with endovascular coiling and 29,918 cases (47%) were treated with surgical clipping. The average age of patients being coiled and clipped was 56.1 ± 29.4 and 53.2 ± 25.7 years, respectively (P < .0001).

### Primary End Points
For patients treated with surgical clipping, the percentage of patients discharged to long-term facilities was 14.0% (4184/29,918) compared with 4.9% (1655/34,125) of coiled patients. There was a statistically significant difference in the discharge-to-long-term-facility rate between clipped and coiled patients (P < .0001). Clipped patients also had a higher in-hospital mortality rate; 345 (1.2%) clipped patients died in the hospital compared with 219 (0.6%) coiled patients (P < .0001). These data are summarized in Table 1.

### Secondary End Points
Data comparing rates of secondary end points between clipped and coiled patients are summarized in Table 1. Except for headache and hydrocephalus not requiring ventriculostomy, the rate of secondary end points was significantly greater in clipped patients than in coiled patients (P < .0001 for all complications).

### Trends in Treatment of Unruptured Aneurysms
Between 2001 and 2008, there has been a steady increase in the proportion of unruptured aneurysms being treated with endovascular therapy. In 2001, only 19.8% of unruptured aneurysms were treated endovascularly compared with 63.3% in 2008. This trend peaked in 2006, when 63.8% of unruptured aneurysms were treated with coil embolization. Theses trends are illustrated in Fig 1.

Because the fraction of unruptured aneurysms treated with coil embolization increased from 2001 to 2008, the percentage of adverse outcomes from treatment decreased from 14.8% (683/4620) to a nadir of 7.6% (899/11,825) in 2008 (P < .0001). These data are summarized in Table 2.

### Discussion
In this sample of patients treated in the United States from 2001 to 2008, we have found that endovascular coiling of unruptured intracranial aneurysms was associated with a lower chance of discharge to a long-term facility compared with surgical clipping. Additionally, surgical clipping was associated with a higher in-hospital mortality rate compared with endovascular coiling. These findings highlight the importance of considering both the technical and clinical outcomes when choosing the appropriate treatment for unruptured aneurysms.
raptured intracranial aneurysms was associated with significantly less morbidity and mortality than surgical clipping. While we cannot know for any individual case in our study the relative merits of endovascular therapy versus open surgery versus observation, the results from the NIS data base suggest that patients treated in the United States with surgery generally face a significantly higher risk of adverse outcome than patients treated with endovascular therapy. This trend does not necessarily imply that all the patients treated with surgery should have been offered endovascular therapy, because for many of these patients, endovascular therapy may have been an inadequate option. While some have recommended that in treating unruptured cerebral aneurysms, “microsurgical clipping rather than endovascular clipping should be the first treatment choice in low-risk cases,” our study offers compelling data that surgical treatment is being performed at a higher periprocedural risk of morbidity and mortality than coiling, with the lowest morbidity for all patients occurring in 2006 when the fraction of coiled patients was highest. Of course, the patients in the NIS data base represent the entire spectrum of cerebral aneurysms, and some patients in the sample were undoubtedly better candidates for clipping than for coiling. However, the data from the NIS sample clearly show that the increasing adoption of endovascular coiling is strongly associated with a decreasing risk of morbidity and mortality. This finding would support an argument for coiling as the first-line therapy for unruptured aneurysms in patients who are considered good candidates for both forms of treatment.

It might be true that many patients with a low risk for clipping are increasingly being treated with coiling, which would lead to a gradual shift toward a higher risk population among clipping patients. If this trend was the explanation for our findings, it would follow that greater attention should be paid to patient selection for clipping. The ISUIA\(^5\) showed that risk factors for adverse surgical outcomes included increasing age, increasing size of aneurysm, location of aneurysm in the posterior circulation, history of ischemic cerebrovascular disease, and the presence of aneurysmal symptoms other than rupture. Such risk factors should be adequately integrated into practice.

Because risk of rupture is related to aneurysm size, the acceptable risk for therapy is also related to aneurysm size. The American Heart Association recommendations\(^6\) note that treatment of small unruptured cerebral aneurysms cannot generally be advocated. ISUIA\(^5\) showed that the size of an intracranial aneurysm is a key determinant in assessing the risk of future rupture. Based on ISUIA, the risk of rupture of small (<7 mm) anterior circulation aneurysms is quite low and would not justify the risks of treatment with clipping or coiling observed in our study. Information about the size and location of aneurysms treated in the NIS is not available, so we cannot ascertain the relative risk of rupture in this population according to the natural history data from ISUIA. However, in the general population, most aneurysms are <7 mm and are located in the anterior circulation,\(^7\) so it is reasonable to suspect that a significant fraction of patients treated in the NIS population had small anterior circulation aneurysms.

The NIS results in our study show higher morbidity and mortality for clipping than is typically reported in single-center series, which was reported to be 7.9% on average. The difference could be explained by publication bias (ie, a greater tendency among centers with the best results to publish their findings). It is also possible that the single-center series reported by surgeons might be less accurate in reporting their outcomes. With carotid endarterectomy, adverse event rates tend to be significantly lower when assessed by the treating surgeon than when they are evaluated by a neurologist following surgery.\(^5\)\(^,\)\(^10\) The NIS data used in our study are somewhat

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**Table 2: Morbidity and mortality associated with treatment of unruptured aneurysms from 2001 to 2008**

<table>
<thead>
<tr>
<th>Year</th>
<th>% Cases Coiled per Year</th>
<th>All Patients</th>
<th>Coiled Patients</th>
<th>Clipped Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>19.8</td>
<td>14.8</td>
<td>6.2</td>
<td>16.9</td>
</tr>
<tr>
<td>2002</td>
<td>31.4</td>
<td>13.3</td>
<td>7.1</td>
<td>16.2</td>
</tr>
<tr>
<td>2003</td>
<td>46.6</td>
<td>11.2</td>
<td>6.7</td>
<td>15.2</td>
</tr>
<tr>
<td>2004</td>
<td>53.5</td>
<td>10.1</td>
<td>5.1</td>
<td>15.9</td>
</tr>
<tr>
<td>2005</td>
<td>61.3</td>
<td>9.2</td>
<td>5.3</td>
<td>15.6</td>
</tr>
<tr>
<td>2006</td>
<td>63.8</td>
<td>8.0</td>
<td>5.0</td>
<td>13.2</td>
</tr>
<tr>
<td>2007</td>
<td>55.8</td>
<td>10.6</td>
<td>6.9</td>
<td>15.3</td>
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<tr>
<td>2008</td>
<td>63.3</td>
<td>7.6</td>
<td>4.3</td>
<td>13.2</td>
</tr>
</tbody>
</table>
free from such biases because the coding process is rather objective.

The number of unruptured aneurysms treated in the United States increased steadily from 2001 to 2008 (Fig 1). This change is probably due to expanded use of CT and MR imaging leading to the discovery of increasing numbers of incidental unruptured aneurysms. All increases in the number of treated aneurysms are accounted for by an increase in the coiling procedures, because from 2001 to 2008, the rate of coiling increased by a factor of 10, whereas surgical clipping rates remained rather constant (Fig 1). The marked increase in the number of treated unruptured aneurysms occurred despite the report of fairly benign natural history data in USUIA. Thus, ISUIA apparently has had little impact on decisions regarding treatment of unruptured aneurysms in the United States, perhaps due to criticisms raised about the trial methods.11 A randomized study may be indicated to definitively assess the efficacy of treatment of unruptured cerebral aneurysms.12

A recent study of the NIS from 2000 to 2006 showed less morbidity and mortality with coiling of unruptured aneurysms than with surgical clipping.13 Our study includes data from 2007 and 2008 and further confirms the decreased morbidity with coiling by showing that the morbidity and mortality increased in 2007 in association with an increase in the rate of surgical clipping and then fell again in 2008 in association with a decrease in the rate of surgical clipping (Table 2).

Our study updates previous evaluations of the NIS that took place before the use of endovascular therapy was widespread. Treatment with clipping was uncommon from 1996 to 2000 compared with 2001–2008 (421 cases in the NIS for 1996–20001 versus 34,125 cases for 2001–2008); therefore, the sample of coiling patients in our study is much larger than that in previous reports. Mortality for coiling decreased from 1.7% in 1996–20001 to 0.6% in 2001–2008. Mortality for clipping decreased from 2.1% in 1996–20002 to 1.2% in 2001–2008. The morbidity associated with clipping decreased from 7.6% in 1996–20002 to 4.9% in 2001–2008, and the morbidity associated with clipping decreased from 16.1% in 1996–20003 to 14.0% in 2001–2008. The decrease in morbidity and mortality associated with clipping between these time periods is likely due to advances in endovascular techniques. Because the technique of surgical clipping has not changed recently, this argument is less likely to be applicable to open surgical cases, which saw a relatively smaller decrease in morbidity and mortality compared with coiling.

Limitations

Our study is retrospective, and patients were not treated in a randomized manner. Therefore, there is significant potential for selection bias that might affect outcomes of clipping or coiling. ISAT was a randomized trial, and it showed that 23.7% of patients with subarachnoid hemorrhage treated with endovascular therapy were dependent or dead at 1 year compared with 30.6% in the surgical group. It is not unreasonable to expect that the benefit with endovascular therapy that ISAT showed in patients with subarachnoid hemorrhage would also be seen in patients with unruptured cerebral aneurysms and that this would be reflected in the NIS data base.

Long-term outcomes cannot be measured in the NIS, but it is reasonable to assume that discharge status has significant correlation with long-term outcome. In addition, discharge to a long-term facility is not a perfect surrogate for calculating morbidity. In ISUIA,3 30-day morbidity and mortality were 13.7% with surgery and 9.3% with endovascular therapy, whereas at 1 year, they were 12.6% and 9.8%, respectively. It might also be argued that the higher recurrence rate associated with clipping than with coiling could lead to hemorrhages that negate some of the better periprocedural outcomes. ISAT14 and cerebral aneurysm rerupture after treatment (CARAT)15 showed that the risk of rehemorrhage of ruptured aneurysms following coiling was only slightly increased with coiling as opposed to clipping, and it is reasonable to expect that coiling would offer a similar relative efficacy for preventing hemorrhage from unruptured aneurysms. In comparing long-term outcomes for unruptured aneurysms treated with clipping versus coiling, small differences in hemorrhage rates for a period of years are unlikely to overcome the relatively large differences in periprocedural morbidity and mortality. We acknowledge that some coding inaccuracies undoubtedly occur, which can affect the retrospective evaluation of an administrative data base.16,17 This potential limitation is no different from that in other studies of cerebral aneurysms using such data bases.1–3,18–23

Conclusions

In the NIS from 2001 to 2008, endovascular coiling of unruptured intracranial aneurysms was associated with significantly less morbidity and mortality than surgical clipping. The increasing use of endovascular coiling of unruptured intracranial aneurysms was associated with decreasing periprocedural morbidity and mortality in the population of patients treated in the United States from 2001 to 2008.

References