ORIGINAL RESEARCH

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

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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.

ABBREVIATIONS: 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 treatment 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.

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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-

Table 1: Complications associated with clipping and coiling of unruptured aneurysms

Complications	Coiled (Total Patients = 34,125)	Coiled (%)	Clipped (Total Patients = 29,918)	Clipped (%)	*P*
Primary outcomes					
Death	215	0.6	345	1.2	<.0001
Discharge to long-term facility	1655	4.9	4184	14.0	<.0001
Secondary outcomes					
Headache	1434	4.2	1058	3.5	<.0001
Aphasia	372	1.0	800	2.7	<.0001
Hemiplegia/paresis	582	1.7	1163	3.9	<.0001
Hydrocephalus	431	1.3	414	1.4	.48
Ventriculostomy	185	0.5	402	1.3	<.0001
VP shunt surgery	97	0.2	216	0.7	<.0001
Cerebral artery occlusion	852	2.5	981	3.3	<.0001
Cardiac complications	165	0.5	494	1.7	<.0001
Tracheostomy	148	0.4	359	1.2	<.0001
Endotracheal tube	483	1.4	1010	3.4	<.0001
Postoperative surgical complications	547	1.6	997	3.3	<.0001
Postoperative neurologic complications	775	2.3	2340	7.8	<.0001

sion of head and neck vessels" (ICD-9-CM code 39.72), and "other endovascular repair (of aneurysm) of other vessels" (ICD-9-CM code 39.79). We excluded all patients with a diagnosis of "subarachnoid hemorrhage" (ICD-9-CM code 430) and "intracerebral hemorrhage" (ICD-9-CM code 431).

End Points

The 2 primary end points examined in this study were the following: 1) discharge to a long-term facility, and 2) in-hospital mortality. Discharge to a long-term facility was studied by using the HCUP variable name "DISPUNIFORM." In-hospital mortality was studied by using the binary HCUP variable name "DIED" and calculating the number of patients who had died during their hospital stay.

Other secondary end points included headache (ICD-9-CM code 784.0), aphasia (ICD-9-CM code 784.3), hemiplegia/paresis (ICD-9-CM codes 342.0–342.9), hydrocephalus (ICD-9-CM codes 331.3–331.4), cerebral artery occlusion (ICD-9-CM codes 434.0–434.9), postoperative cardiac complications (ICD-9-CM code 997.1), other surgical complications/postoperative infection (ICD-9-CM codes 99.72–99.75, 998.2, 998.59, and 998.0), postoperative neurologic complications (ICD-9-CM codes 997.00–997.09), performance of tracheostomy (ICD-9-CM codes 31.1–31.29), placement of an endotracheal tube (ICD-9-CM code 96.04), performance of ventriculostomy (ICD-9-CM code 02.2), and ventriculoperitoneal shunt surgery (ICD-9-CM code 02.34).

Statistical Analysis

For the purposes of statistical analysis, we summed the data from 2001 to 2008. χ^2 tests were used to compare categoric variables, and *t* testing was used to compare continuous variables. To obtain national estimates, we applied proper weights as indicated in the HCUP-NIS "Variance Calculations" guide (http://www.hcup-us.ahrq.gov/db/nation/nis/NIS_Introduction_2006.jsp#variance). All statistical analysis was performed by using the SAS-based statistical package JMP (www.jmp.com).

Results

Patients

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 coiling 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 un-

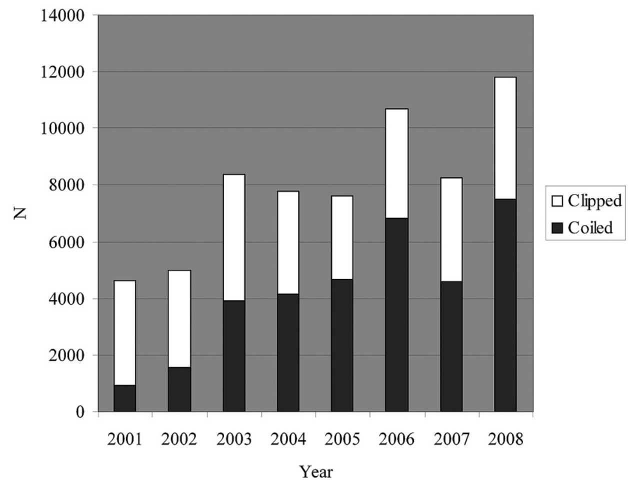

Fig 1. Trends in the treatment of unruptured aneurysms from 2001 to 2008.

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

		Morbidity and Mortality		
Year	% Cases Coiled per Year	All Patients	Coiled Patients	Clipped Patients
2001	19.8	14.8	6.2	16.9
2002	31.4	13.3	7.1	16.2
2003	46.6	11.2	6.7	15.2
2004	53.5	10.1	5.1	15.9
2005	61.3	9.2	5.3	15.6
2006	63.8	8.0	5.0	13.2
2007	55.8	10.6	6.9	15.3
2008	63.3	7.6	4.3	13.2

ruptured 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 coiling should be the first treatment choice in low-risk cases,"[4] our study offers compelling data that surgical treatment is being performed at a higher periprocedural risk of morbidity and mortality than coiling for a great number of patients in the United States.

According to Cowan et al,[3] the percentage of unruptured aneurysms treated by endovascular therapy increased from 11% in 1998% to 43% in 2003. Our study shows that the percentage increased to a high of 63.8% in 2006 and then fell to 55.8% by 2007, for unknown reasons, rising again in 2008 to 63.2%. Since 2004, a greater percentage of patients with unruptured aneurysms has been treated with coiling than with clipping. As coiling has become more available and refined, it is reasonable to expect that treating centers are becoming more adept at recognizing patients who can be expected to have a better outcome with coiling. Surgical outcomes might also improve if higher risk surgical patients, such as those with basilar aneurysms, are increasingly directed toward endovascular therapy. However, the NIS data do not show any trend of improving outcomes with either clipping or coiling individually. Rather, they show an improvement in outcomes correlated with a higher fraction of patients being treated with 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.[8] 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.[9,10] The NIS data used in our study are somewhat 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 trial 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 coiling was uncommon from 1996 to 2000 compared with 2001–2008 (421 cases in the NIS for 1996–2000[1] 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 1996–2000[1] to 0.6% in 2001–2008. Mortality for clipping decreased from 2.1% in 1996–2000[2] to 1.2% in 2001–2008. The morbidity associated with coiling decreased from 7.6% in 1996–2000[1] to 4.9% in 2001–2008, and the morbidity associated with clipping decreased from 16.1% in 1996–2000[2] to 14.0% in 2001–2008. The decrease in morbidity and mortality associated with coiling 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,[5] 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 coiling than with clipping could lead to hemorrhages that negate some of the better periprocedural outcomes. ISAT[14] 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.

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