Recent Trends in Electively Treated Unruptured Intracranial Aneurysms

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Background and Purpose: To determine recent treatment and outcome trends in patients undergoing elective surgical clipping (SC) or endovascular therapy (EVT) for unruptured intracranial aneurysms (UIAs) in the United States. *Methods:* Data were extracted and analyzed from the National Inpatient Sample, Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality for all patients admitted for elective EVT or SC of UIAs between 2011 and 2014. Treatment trends, in-hospital mortality, complication rates, length of stay (LOS) and total hospital costs were evaluated and analyzed. *Results:* A total of 31,070 patients with UIAs were included in our analysis, of which 14,411 and 16,659 underwent elective SC and EVT, respectively. There was no significant difference in in-hospital mortality rates between the 2 groups. EVT was associated with lower in-hospital complication rates, decreased median LOS (.8 days versus 3.3 days, $P \le .0001$), and an increased likelihood of discharge to home (92.9% versus 72.9%, $P = .0001$). Median total hospital charges were similar in both treatment cohorts. Independent predictors of mortality in the elective population were age over 40 years ($P \le .0001$), weekend treatment ($P \le .0001$), and high co-morbidity status ($P \le .0001$). *Conclusions:* In-hospital mortality rates were similar in elective EVT and SC UIA patients; however, EVT was associated with lower in-hospital complication rates and shorter LOS.

Key Words: Intracranial aneurysm—endovascular therapy—unruptured—clipping—coiling

Introduction

The prevalence of unruptured intracranial aneurysms (UIA) ranges from 3% to 5% worldwide.[1,2] Detection of UIAs has increased in recent years due to the availability and use of computed tomography and magnetic resonance imaging in everyday clinical practice.[3] Intracranial aneurysms have a variable lifetime risk of rupture[4] and treatment complication rates, making management of this condition particularly challenging.

UIAs are managed with routine serial imaging, surgical intervention, or endovascular treatment techniques; however, there is a paucity of real world data to guide clinical decisions regarding the need and optimal time of intervention in patients with UIAs. Ultimately, the decision to treat an aneurysm depends on multiple factors including, but not limited to, the age of the patient, previous history of subarachnoid hemorrhage, size, location, and morphology of aneurysm, risk factors including hypertension and smoking, availability of expertise, and patient preference.

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Multiple advancements in techniques and devices, such as neck remodeling and flow diversion devices, and the increased availability of experienced endovascular surgeons have expanded the population of aneurysms amenable to endovascular therapy (EVT) and reduced the risks associated with treatment. Reduced recovery time, shorter hospital stays,[5] and avoidance of "surgery" have been important influences in patient preference for EVT. Surgical treatment of cerebral aneurysms has also improved due to modern neurosurgical clips, improved surgical approaches,[6] and surgical planning due to advanced imaging modalities.[7] Refinement of surgical bypass techniques,[6] electrophysiological monitoring,[8] and intraoperative angiography[9,10] have reduced surgical complications and even allowed management of large complex intracranial aneurysms where parent vessel sacrifice may be needed. Surgical clipping (SC) of intracranial aneurysms resulted in higher obliteration rates and decreased the need for close follow-up.[11] Furthermore, SC is needed for management of aneurysms that have failed prior therapy. Lastly, advances in anesthesiology with techniques such as use of barbiturates to decrease brain metabolism have made modern surgical treatment safer.[12]

Previous studies have evaluated the short-term complications in patients undergoing SC or EVT.[5,13,14] The objective of our study was to provide an update on the number of patients undergoing elective SC or EVT of UIAs in the United States and also to understand the rates of short-term complications and mortality in this patient population.

Methods

The National Inpatient Sample (NIS) is a hospital discharge database maintained by the Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality and represents approximately 20% of all inpatient admissions to nonfederal hospitals in the United States.[15,16] NIS data from 2011 through 2014 were purchased from HCUP and analyzed for the purposes of this study. As per the data use agreement with HCUP, review by an institutional review board is not required for use of this limited data set.

Cohort Definition

The NIS database was analyzed for patients with a primary diagnosis of UIA (ICD-9-CM diagnostic code 437.3) who underwent elective SC (ICD-9-CM code 39.51) or EVT (ICD-9-CM codes 39.79, 39.72) from 2011 to 2014. Patients with a primary diagnosis of subarachnoid hemorrhage (ICD-9-CM code 430), secondary diagnosis indicating trauma (ICD-9-CM codes 852-852.59, 802-802.9, 873.0-973.9), injury to a vessel (ICD-9-CM codes 900-904) besides the radial (ICD-9-CM code 903.2) or common femoral artery (ICD-9-CM code 904.0), arteriovenous malformation (ICD-9-CM code 747.81), and cerebral arteritis (ICD-9-CM code 437.4) were excluded from the cohort. We also excluded patients who did not undergo any procedure during the hospital stay, underwent cerebral angiography (ICD-9-CM code 88.41) only, patients who had the procedure before the current admission (procedure day < 0), or if data regarding the procedure day was unavailable. Data for each year were extracted individually, and then combined into the final cohort.

Study Outcomes

The primary outcome was in-hospital mortality rate. Patients with unknown in-hospital mortality status were excluded from the analysis.

Secondary outcomes included in-hospital complications, specifically iatrogenic stroke, intracranial hemorrhage, treated hydrocephalus, cardiac arrest, status epilepticus/epilepsia partialis continua, any central nervous system complications, myocardial infarction, sepsis, shock, pulmonary complications, hematoma, and renal complications (See Supplemental Table 1 for ICD-9-CM codes).

Statistical Analysis

Baseline characteristics, in-hospital mortality and complication rates, discharge disposition, length of stay (LOS), and treatment costs were determined for EVT and SC groups.

The variables, age ($<$40, 40-59, 60-79, and $\geq$80) and ethnicity (White/Caucasian, Black/African American, Hispanic, other), were stratified into groups. The Charlson co-morbidity index, a weighted composite score of 19 chronic conditions used to predict 10-year mortality rates, was used to group comorbidity status into low (0-2), medium (3-4), and high (5 or greater).

The survey mean procedure of SAS was used to analyze interval data including age. The frequency procedure (PROC SURVEYFREQ statement) was used to assess categorical data representing gender, hospital bed size, race, elective admission, death, and in-hospital complications. As NIS is a weighted sample, we utilized weight variable (trendwt) to determine national estimates. Observations equal to or less than 10 were not reported as per the HCUP data-use agreement. Logistic regression (PROC LOGISTIC statement) using individual and hospital level factors was used to determine predictors of in-hospital mortality for years 2011-2014. For categorical data, we used chi-square and the student t test for comparing means.

Median total hospital charges and LOS were compared across small, medium, and large sized hospitals according to region of the US, the urban-rural designation of the hospital, and teaching status (https://www.hcup-us.ahrq.gov/db/vars/hosp_bedsize/nisnote.jsp). Hospital charges were adjusted for inflation based on June 2011 values using the Bureau of Labor Statistics Inflation calculator (https://www.bls.gov/data/inflation_calculator.htm).

A P value $<.05$ or a confidence interval which did not include the null value of 1 was considered significant. All

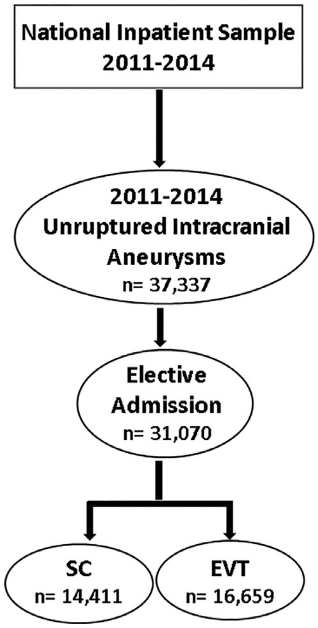

Figure 1. *Flowchart of the elective UIA population from 2011 to 2014.*

data were extracted and analyzed using the Statistical Analysis System (SAS) software.

Results

From 2011 to 2014, a total of 31,070 UIA patients were electively treated, of which 46.4% and 53.6% underwent SC and EVT, respectively (Fig 1). Overall treatment trends during the 4-year time period showed an increase in the number of UIAs undergoing elective treatment with EVT and a decline in the number of SC cases (Fig 2).

Table 1 summaries the baseline demographics of the SC and EVT populations. No difference was observed in race or co-morbidity index between the treatment groups; however, more females underwent EVT ($P = .02$; Table 1). Patients in the EVT cohort were older, with 47.3% ≥60 years of age compared to 39.1% in the SC group ($P \leq .0001$). In both the cohorts, the majority of patients were treated during the weekday. EVT patients were more likely to be discharged home (92.9% versus 72.9%, $P \leq .0001$), while SC patients had a higher rate of disposition to a skilled nursing facility (14.6% versus 3.5%).

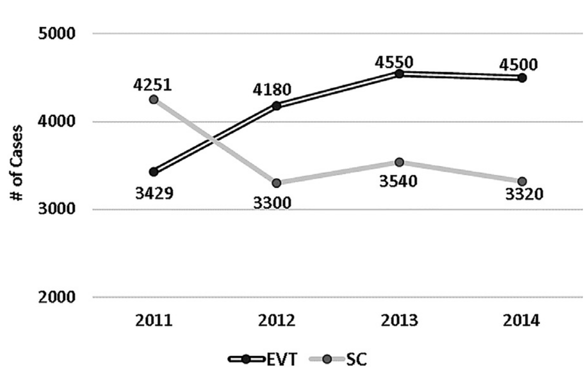

Figure 2. *Treatment trends of elective UIAs from 2011 to 2014.*

Table 1. *Baseline characteristics and discharge deposition in elective SC and EVT patients*

	SC (%)	EVT (%)	*P* value
Co-morbidity Index			
Low	59.8	62.5	.09
Medium	37.9	35.6	
High	2.2	2.0	
Race			
White	72.9	73.0	.41
Black	12.7	11.6	
Hispanic	8.6	8.9	
Other	5.8	6.5	
Age			
<40	7.8	7.3	**<.0001**
40-59	53.1	45.5	
60-79	38.6	44.5	
80+	.5	2.8	
Gender			
Female	75.6	78.1	**.02**
Discharge disposition			
Home	72.9	92.9	**<.0001**
Rehab	.4	.3	
Skilled nursing facility	14.6	3.5	
Home health care	11.7	2.8	
Hospital bed size			
Small	8.2	3.9	**<.0001**
Medium	15.0	16.8	
Large	76.8	79.3	
Median length of stay (days)	3.3	.8	**<.0001**
Median cost ($)	86,622	86,202	.91
Weekend Treatment	.6	.4	.15

Bold values indicates statistically significant values.

Complications

Table 2 summaries the in-hospital complication rates between SC and EVT groups. In-hospital complications were more common in SC patients, specifically acute renal failure (1.2% versus .62%, $P = .02$), cardiac arrest (.37% versus .09%, $P = .02$), any central nervous system complication (.87% versus .14%, $p \leq .0001$), iatrogenic stroke (5.9% versus 2.6%, $P \leq .0001$), intracranial hemorrhage (4.2% versus 1.3%, $p \leq .0001$), pulmonary complications (5.9% versus 2.3%, $p \leq .0001$), sepsis (.56% versus .12%, $P = .003$), and status epilepticus/epilepsia partialis continua (.52% versus .03%, $P = .0002$). Importantly, in-hospital mortality rates were similar ($P = .89$) between the SC (.41%) and EVT (.39%) cohorts.

LOS and Total Hospital Costs

EVT patients had an overall shorter median LOS (.8 days versus 3.3 days, $P \leq .0001$) compared to SC patients (Table 1). This trend remained consistent over the 4-year study period (Fig 3). When stratifying LOS

Table 2. *In-hospital complications in electively treated SC and EVT UIA patients*

	Elective		
	SC (%)	EVT (%)	*P* value
Acute renal failure	1.2	.62	**.02**
Cardiac arrest	.37	.09	**.02**
Central nervous system (any)	.87	.14	**<.0001**
Groin hematoma	.79	3.7	**<.0001**
Iatrogenic stroke	5.9	2.6	**<.0001**
Intracranial Hemorrhage	4.2	1.3	**<.0001**
Mortality	.41	039	.89
Myocardial infarction	.37	.15	.09
Pulmonary complications	5.9	2.3	**<.0001**
Sepsis	.56	.12	**.003**
Shock	.10	.24	.20
Status epilepticus or EPC	.52	.03	**.0002**
Treated hydrocephalus	.93	1.13	.43

Bold values indicates statistically significant values.
Abbreviation: EPC, epilepsia partialis continua.

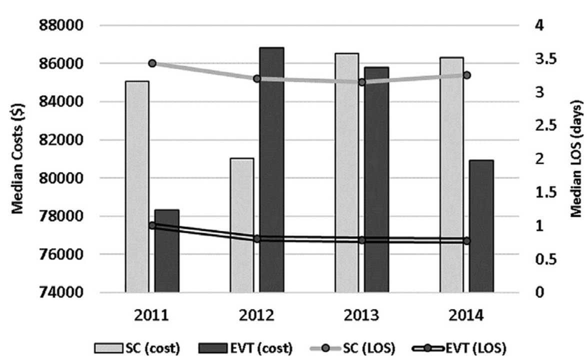

Figure 3. *Length of stay and total costs per year (2011-2014) in elective coiling and clipping patients.*

by hospital size, the median LOS was consistently lower in the EVT population regardless of hospital size (Table 3). In both treatment cohorts, LOS decreased with increasing hospital size, with LOS being the shortest in large hospitals.

Total median hospital costs were similar between SC ($86,622) and EVT ($86,202) patients (Table 1, Fig 3).

Table 3. *Length and cost of stay by hospital size*

	Elective		
	SC	EVT	*P* value
Hospital costs ($) (Median)			
Small	104,463	84,379	.24
Medium	82,689	79,444	.65
Large	86,528	87,308	.87
Length of Stay (days) (Median)			
Small	3.8	1.00	**<.0001**
Medium	3.3	.89	**<.0001**
Large	3.2	.78	**<.0001**

Bold values indicates statistically significant values.

Stratification of median costs by hospital size did not show any differences between the 2 cohorts (Table 3).

Predictors of Mortality

Multivariate logistic regression analysis was performed to evaluate predictors of in-hospital mortality. After adjusting for race, gender, treatment type, weekday/weekend treatment, hospital bed size, and co-morbidity status, independent predictors of in-hospital mortality in the elective population were age >40 years ($P = .0001$), high co-morbidity status ($P \leq .0001$), and treatment on weekends ($P \leq .0001$).

Discussion

In the present study, we found an upward trend in the number of elective cases undergoing EVT during the 4-year study period. Previous studies have also reported an upward trend in endovascular treatment of UIAs over time.[5,13,14,17,18] In a study examining clipping and coiling of UIAs in Medicare beneficiaries, the authors reported a ~15-fold increase in the rate of endovascular coiling from 2000 to 2010.[5] As the present study examines the time-frame from 2011 to 2014, our results demonstrated that this trend has continued through recent years. The increased incidental detection of UIAs, availability of new therapies and devices for treatment of aneurysms previously unamenable to endovascular approaches, and patient preference for “avoiding surgery” may have contributed to the higher rate of elective EVT seen in our study. Flow diversion with the pipeline embolization device increased the number of large anterior circulation cerebral aneurysms that can be approached with endovascular techniques.

In-hospital Complications

With the exception of myocardial infarction, shock, and treated hydrocephalus rates which were similar between the groups, lower in-hospital complication rates were seen in the EVT cohort in our study. Several studies have also demonstrated the association of endovascular coiling with lower rates of in-hospital complications in UIA patients.[5,13-14] A study by Jalbert et al demonstrated consistently lower in-hospital complication rates in the endovascular coiling group compared to SC in Medicare patients between 2000 and 2010.[5]

Iatrogenic Stroke

Previous studies evaluating short-term outcomes of treated UIAs from 1998 to 2008 have shown lower rates of stroke after endovascular treatment.[13,14,19] Our study found that the rate of iatrogenic stroke was significantly lower in the EVT group (2.6% versus 5.9%) throughout the study period. Modern endovascular techniques and improved device deployment are more likely to contribute to the lower rates of ischemic stroke in EVT patients. Endovascular treatment offers the benefit of real-time vessel imaging, which allows for the visualization of the aneurysm during and after device deployment. In surgical patients, improper placement of aneurysm clips may often be noticed only postoperatively when the patient has a change in neurological examination, which may result in ischemic injury prior to removal of the clip during emergent neurosurgery. However, increased use of intraoperative indocyanine green video angiography and hybrid intraoperative digital subtraction angiography suites may have resulted in lower rates of iatrogenic strokes compared to historical controls.

Intracranial Hemorrhage

Intracranial hemorrhage was also significantly lower in the EVT group (4.2% versus 1.3%, $P \leq .0001$). Alshekhlee et al separated complications into intracerebral hemorrhage and ischemic stroke and found a lower rate of hemorrhage in the endovascular group (2.38% versus 1.37%, $P = .0002$). Higher rates of intracerebral hemorrhage during neurosurgery may be related to traversing more planes and vessels during dissection as well as the difficulty of identifying small and slow bleeding sources during surgery.

Acute Renal Failure, Pulmonary, and Cardiac

Rates of acute renal failure from the NIS database were captured for the purposes of this study, as contrast-induced nephropathy is not associated with a specific diagnostic code. We found a lower rate of acute renal failure in the EVT group. Recent studies have shown lower rates of contrast induced nephropathy in cerebral angiography than previously thought, possibly related to low osmolar contrast mediums and other systemic factors.[20,21] Increased pulmonary and cardiac complications in the surgical group are possibly related to prolonged intubation and hemodynamic control during neurosurgery. Furthermore, vascular neurosurgery has been shown to have higher rates of surgical complications compared to tumor and other neurosurgical subspecialties.[22]

Mortality and Disposition

In the present study, in-hospital mortality rates were similar between the 2 treatment groups. This is in contrast to previous studies which reported lower rates of in-hospital mortality in patients treated with EVT.[19,23-25] Brinjiki et al reported on NIS UIA data from 2001 to 2008 and found lower rates of in-hospital mortality in coiled (.6%) versus clipped (1.2%) patients.[14] Importantly, data from our study reveal that mortality rates in both the SC and EVT cohorts continue to improve from historical rates in past years. The similar rates of in-hospital mortality in this study could be attributed to the improvement of surgical and endovascular techniques over time.

Independent predictors of in-hospital mortality in our elective cohort included weekend effect, high co-morbidity status, and age greater than 40. Previous studies evaluating treatment of UIAs from 1996 to 2000 found that age and medical co-morbidity were significant predictors of death.[26] The weekend effect as a predictor of mortality has been demonstrated in other surgical procedures as well.[27] Procedures performed electively over the weekend may have fewer technicians and nurses available, and when complications do occur, fewer physicians may be available.

Jalbert et al showed that in-hospital complications and discharge to long-term facilities were consistently lower in the endovascular group between 2000 and 2010. Similarly, our study shows a higher rate of discharge home after endovascular procedures which may be related to shorter procedure times, less blood loss and incision size, and earlier mobilization after endovascular treatments.

Length and Cost of Stay

Our analysis revealed similar total hospital charges between the 2 groups, although LOS was significantly shorter in the EVT group. After adjusting for hospital size, there continued to be no difference in median total hospital charges between the 2 groups (Table 3). Our study did find a trend of shorter hospital stays with increasing hospital size. Studies comparing length of hospital stay compared to hospital size and volume have found conflicting reports. A study between 2002 and 2006 evaluating UIAs found shorter LOS and lower costs in relation to hospital size and volume than with SC.[28] Increased hospital volumes were associated with decreased LOS and cost of hospital stay in a NIS study evaluating EVT between 1996 and 2000.[29] Another study by Johnston et al evaluating UIAs between 1990 and 1998 did not show any correlation between LOS and hospital volume.[24]

Limitations

Although our study has many advantages, including data derived from a large, prospective, random sample from nonfederal US hospitals diverse in hospital size and region (which minimizes selection bias at individual and institutional levels), several limitations exist. Our data represent trends in elective treatment and cannot account for individualized care which takes into consideration individual aneurysm characteristics including aneurysm number, location, size, and morphology, patient history, and preference of treatment. Since our data are extracted from the NIS database, conclusions of this study are only as strong as the data entry from each statewide database and any errors in ICD coding may affect these results.[30] Complication rates were recorded from physician records, and thus a systematic difference between physicians performing surgical and endovascular treatments in the ability to detect subtle neurological deficits may exist. Furthermore, our study did not exclude patients who were treated for multiple aneurysms during a single hospital admission. Patients who were readmitted for treatment of incompletely obliterated aneurysms were analyzed as new patients. Therefore, the proportion of patients treated in this study (Fig 1) may over-represent the true proportion of patients selected for treatment with EVT and likely under-represents the overall mortality and morbidity of patients undergoing multiple treatments for aneurysm obliteration. A meta-analysis evaluating endovascular embolization in unruptured aneurysms found that overall aneurysm obliteration rates were 86.1%, recurrence rate of 24%, retreatment rates of 9.1%, and an annual rupture risk of .2%. However, this study was limited by a short follow-up period, with 76.7% of patients being followed for only 6 months.[31] A recent study with a median follow-up of 12 years reported retreatment rates of 4.8% in 184 patients with UIAs treated with endovascular coiling.[32]

Our study primarily evaluated safety endpoints as opposed to efficacy which may impact long-term aneurysm rupture risk. Lastly, as our data evaluated patients from an in-hospital database which did not include long-term outcome, we could not report on ongoing serious adverse effects, functional outcome, or complications. Although we did not evaluate postprocedural modified Rankin scale or other dependency scores, discharge disposition may have a correlation with long-term outcomes and may be an indirect marker of mortality.

Despite these limitations, results of this study are likely generalizable as it included data from a large sample extracted from multiple centers, and different hospital sizes throughout the US.

Conclusions

Our study revealed UIA treatment trends between 2011 and 2014 that were comparable to previous studies examining SC and EVT, with EVT being the preferred therapy in the elective population. In-hospital complication rates were lower with EVT; however, in-hospital mortality rates were similar between treatment groups and lower than historical rates. LOS was shorter with EVT, although no difference was observed in total hospital costs between the treatments.

Supplementary materials

Supplementary data to this article can be found online at doi:10.1016/j.jstrokecerebrovasdis.2019.03.010.

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