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ORIGINAL RESEARCH

Trends of Ruptured and Unruptured Aneurysms Treatment in the United States in Post-ISAT Era: A National Inpatient Sample Analysis

Mohamed M. Salem, MD, MPH; Georgios A. Maragkos, MD; Santiago Gomez-Paz, MD; Luis C. Ascanio, MD; Long H. Ngo, PhD; Christopher S. Ogilvy, MD; Ajith J. Thomas, MD; Justin M. Moore, MD, PhD

BACKGROUND: The ISAT (International Subarachnoid Aneurysm Trial) has generated a paradigm shift towards endovascular treatment for intracranial aneurysms but remains unclear if this has led to a true reduction in the risk for aneurysmal subarachnoid hemorrhage (aSAH). We sought to study the association between the treatment burden of unruptured and ruptured aneurysms in the post-ISAT era.

METHODS AND RESULTS: Admissions data from the National Inpatient Sample (2004–2014) were extracted, including patients with a primary diagnosis of aSAH or unruptured intracranial aneurysms treated by clipping or coiling. Within each year, this combined group was randomly matched to non-aneurysmal control group, based on age, sex, and Elixhauser comorbidity index. Multinomial regression was performed to calculate the relative risk ratio of undergoing treatment for either ruptured or unruptured aneurysms in comparison with the reference control group, adjusted for time. After adjusting for National Inpatient Sample sampling effects, 243 754 patients with aneurysm were identified, 174 580 (71.6%) were women; mean age, 55.4±13.2 years. A total of 121 882 (50.01%) patients were treated for unruptured aneurysms, 79 627 (65.3%) endovascularly and 42 256 (34.7%) surgically. A total of 121 872 (49.99%) patients underwent procedures for aSAH, 68 921 (56.6%) endovascular, and 52 951 (43.5%) surgically. Multinomial regression revealed a significant year-to-year decrease in aSAH procedures compared with the control group of non-aneurysmal hospitalizations (relative risk ratio, 0.963 per year; $P<0.001$), while there was no statistical significance for unruptured aneurysms procedures (relative risk ratio, 1.012 per year; $P=0.35$).

CONCLUSIONS: With each passing year, there is a significant decrease in relative risk ratio of undergoing treatment for aSAH, concomitant with a stable annual risk of undergoing treatment for unruptured intracranial aneurysms.

Key Words: incidence ■ mortality ■ subarachnoid hemorrhage ■ unruptured aneurysms

Spontaneous subarachnoid hemorrhage (SAH) is a devastating condition after which approximately one third of patients die and another third become severely disabled.[1] Intracranial aneurysm rupture (aSAH), accounting for ≈80% of cases,[1] is the most common cause. Increased access to high-quality intracranial imaging has resulted in an exponential increase in the rate of diagnosis of incidental unruptured aneurysms. Recently, techniques for treating both unruptured and ruptured aneurysms have undergone a paradigm shift with the publication of the results of the ISAT (International Subarachnoid Aneurysm Trial), which supported the use of novel endovascular procedures for the treatment of ruptured aneurysms, demonstrating that coiling for ruptured aneurysms decreased the relative risk of dependence/death when compared with aneurysmal clipping by 7.4% at 1-year follow-up.[2] Previous

Correspondence to: Justin M. Moore, MD, PhD, Neurosurgical Service, Beth Israel Deaconess Medical Center 110 Francis Street, Suite 3B., Boston, MA 02215-5501. E-mail: jmoore4@bidmc.harvard.edu

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CLINICAL PERSPECTIVE

What Is New?

- Using the National Inpatient Sample database, we found that over 2004 to 2014, there was a significant decrease in the per-year relative risk of undergoing treatment for ruptured intracranial aneurysm, concomitantly with a stable annual risk of undergoing treatment for unruptured intracranial aneurysms, when compared with a similar matched non-aneurysmal control group, admitted for other reasons and controlling for potential confounders, suggesting current effective targeting of high-risk unruptured intracranial aneurysms to undergo preventive treatment.
- We show the temporal trends of progressive increased use of endovascular modalities over time as the modality of choice for intracranial aneurysms, with two thirds of unruptured cases and three fourths of ruptured cases treated endovascularly by 2014.

What Are the Clinical Implications?

- Maintaining hypervigilance for proper identification of "high-risk" unruptured aneurysms to undergo preemptive preventive treatment, and critically managing ruptured aneurysms through adequate anticipation and prevention of secondary complications is of paramount importance to further optimize intracranial aneurysms management protocols.

Nonstandard Abbreviations and Acronyms

aSAH	aneurysmal subarachnoid hemorrhage
HCUP	Health Cost Utilization Project
ISAT	International Subarachnoid Aneurysm Trial
NIS	National Inpatient Sample
RRR	relative risk ratio
UIA	unruptured intracranial aneurysm

data using the National Inpatient Sample (NIS) found that between 1998 and 2007, there was a significant increase in the number of interventions being performed on unruptured aneurysms, while the rate of ruptured aneurysms treated remained stable.[3] While this work has not recently been updated, it is likely that this trend has continued with further technological advancements in radiological imaging and endovascular interventions.

The indications and method of treatment depend on a variety of well-documented factors including aneurysm angioarchitecture (size, morphology, and location), age, comorbidities, family history, and previous rupture. Nevertheless, to date, only generic guidelines are available to inform surgeons, leading to significant intra-institutional protocol variations. It is unclear whether the increase in unruptured aneurysm treatment has led to a reduction in aSAH, the primary aim of such treatment, whether unruptured aneurysms are being overtreated, and whether patients are exposed to unnecessary procedural risk. Our study aims to simultaneously quantify rates of intervention for unruptured cerebral aneurysms and aSAH presentation over an 11-year period, to provide an indication on the association between the treatment burden of unruptured and ruptured aneurysms in the post-ISAT era.

METHODS

Data Availability Statement

The data that support the findings of this study are available upon reasonable request. All the analyses were conducted using the NIS publicly available data set, which can be accessed at https://www.hcup-us.ahrq.gov/db/nation/nis/nisdbdocumentation.jsp

Data Source

Data were obtained from the NIS, which is a component of the Health Cost Utilization Project (HCUP) administered by the Agency of Healthcare Research and Quality and the United States Department of Health and Human Services. The NIS, a nationally representative database, contains information on ≈8 million discharges per year from >4000 hospitals each year (since 2012) and covers ≈96% of the US population. Since 2012, the NIS represents approximately a 20% systematic sample of discharges from all hospitals participating in HCUP. These data were weighted according to HCUP standard procedures to provide national estimates and used appropriate trend weighting for the period according to published HCUP protocols. Studies using the NIS are exempt from Institutional Review Board approval at our institution. Patient consent was waived because of the retrospective nature of the study and data anonymization in the NIS.

Study Population

International Classification of Diseases, Ninth Revision, Clinical Modification (*ICD-9-CM*) codes were used to construct cohorts. Records from January 1, 2004 to December 30, 2014 were obtained from the HCUP central distributor (Rockville, Maryland) and analyzed.

Inclusion Criteria

Adults (aged ≥18 years) were included in the ruptured cerebral aneurysm cohort, if they had *ICD-9-CM* diagnosis codes for SAH (430.0) or intracerebral hemorrhage (431.0, 432.9) and specific cerebral aneurysm procedure codes for both microsurgical clipping (39.51) or endovascular treatment (3972, 3975, 3976, 3979, and 3952) in any position, in an effort to minimize sample contamination with traumatic subarachnoid hemorrhage.[3] Adults were included in the unruptured cerebral aneurysm cohort if they had *ICD-9-CM* diagnosis codes for unruptured cerebral aneurysm code (4373) with specific cerebral aneurysm procedures codes for both microsurgical clipping (39.51) or endovascular treatment (3972, 3975, 3976, 3979, and 3952) in any position. Patients who had a diagnosis of both ruptured and unruptured were included in the ruptured group. The reason for placing patients with ruptured and unruptured aneurysms in the ruptured group is related to the inherent limitations in the NIS data as each row in the database constitutes a single discharge (with no data on follow-ups). So, patients who have both codes of ruptured and unruptured aneurysm almost certainly presented with the ruptured aneurysm and an additional unruptured aneurysm was found at that time, which is not uncommon (or alternatively an unruptured aneurysm ruptured in the hospital, this would be a rare occurrence). However, either way, their entire clinical course is essentially driven by the aSAH, with the unruptured aneurysm representing an incidental finding and thus were classified in the ruptured category. Similarly, with patients who got clipped and coiled, the longer length of stay would be primarily driven by the clipping rather than the coiling, given the known difference in the invasiveness and immediate post-procedural morbidity. This approach was used in prior NIS studies.[3]

Exclusion Criteria

Records containing codes for cerebrovascular arterial malformation (747.81), syphilitic aneurysms (094.87), and cerebral arteritis (437.4) were excluded for the previously defined cohorts, as were records containing procedure codes for arteriovenous malformation repair (39.53) or stereotactic radiosurgery (923, 9231, 9232, 9233, 9239) to minimize contamination of the cohort with causes of SAH other than aSAH.

Covariates and Analysis

Continuous variables are presented as mean±SD, while categorical variables are reported as proportions. Baseline demographics included age, sex, race, household income quartile, and comorbidity score (Elixhauser index[4]; in addition, hospital bed size, and teaching hospital status were assessed, as well). Patients with a primary diagnosis of aSAH or unruptured intracranial aneurysm (UIA) treated by either clipping or coiling were included. Baseline covariates between the unruptured and ruptured cohort were compared using standardized difference. This was used instead of standard *P* values because of the large sample size of both cohorts which made any comparisons prone to detecting statistical significance for small differences in absolute numbers (type I error) without clinical relevance. We calculated the Cohen delta value to estimate effect size, independent of the sample size, for both continuous and categorical variables. The delta value was calculated using the mean and pooled standard deviation of both groups for continuous variables and proportions for categorical variables; those with a value >0.5 are considered medium to large standardized differences.[5] A standardized difference >0.5 implies that there is ≥33% of non-overlap between groups (unruptured versus ruptured) and that >60% of the cases have observations with values that are greater than more than half of the control group values. In simple terms, effect size indices of 0.2 represent a small effect size, while >0.5 correspond to a medium effect size and >0.8 is considered a large effect size.[5] All statistical analyses were performed using the STATA 15 software (StataCorp, TX, USA).

Within each year, the combined group of patients with and without rupture was randomly matched to a non-aneurysmal control group, based on 3 specific matching factors: age, sex, and Elixhauser comorbidity index. Following the extraction of the sample of interest within each year of the NIS, controls with age outside the range of ±1 SD of the total cohort (ie, ruptured and unruptured) mean were eliminated from the matching pool. Similarly, controls with a composite Elixhauser comorbidity score outside the range of ±1 SD of the cohort mean were also eliminated. Finally, an algorithm matched the cases in a random fashion to the remaining eligible controls to have a similar sex distribution to the cases. Multinomial logistic regression was performed to calculate the relative risk ratio (RRR) of undergoing treatment for either ruptured or unruptured aneurysms, in comparison with the selected controls (reference group) adjusted for time (primary independent variable of interest) and controlling for other potential confounders (eg, for hospital size, region, and type). Finally, graphs showing the total numbers of ruptured and unruptured aneurysmal cases treated were graphed and plotted across the years. Numbers were adjusted for the NIS survey analysis design to infer national estimates.

RESULTS

Results of Matching Process

In total, 121 882 and 121 872 subjects in the NIS underwent clipping or coiling procedures for unruptured and ruptured aneurysms, respectively, after adjustment for Agency for Healthcare Research and Quality standard weights in the period between 2004 and 2014. An additional 241 658 subjects with other diagnoses were selected from the database within the same time period as controls. The success of the matching process is presented in Table 1. Since matching was performed before accounting for Agency for Healthcare Research and Quality standard weights, Table 1 shows unadjusted values for the matched variables. Using Chi-square testing, there was no statistically significant difference between the sample (ruptured and unruptured) and the control group about patient sex. However, statistical significance using Mann-Whitney *U* was detected on patient age, which was 55.7±13.1 for the study group and 56.5±7.5 for controls, and Elixhauser comorbidity index, which was 3.6±7.8 for the study group and 1.9±3.9 for controls. The differences in absolute numbers were found to be acceptable in terms of matching, considering the existence of 2 different patient groups (unruptured and ruptured aneurysms) which had to be merged and matched to a single control group, and the large number of patients, which made any comparisons prone to detecting statistical significance for small differences in absolute numbers (type I error). Therefore, the matching process was considered adequate and accepted for further analysis.

Patient Demographic and Clinical Characteristics

The mean age of the unruptured aneurysm population was 56.7±11.9 years and 54.8±13.5 for the patients with ruptured aneurysm. Both cohorts had a majority of female patients (75.2% and 68%, respectively). A total of 588 (0.5%) patients (399 women; 67.8%) died during their index hospitalization in the unruptured aneurysm cohort, compared with 15 510 (12.7%) (10 680 women; 68.9%) who died in the ruptured aneurysm cohort. Among the patients with unruptured aneurysm, 79 627 (65.3%) had an endovascular procedure, while this was true for 68 921 (56.6%) of the patients with ruptured aneurysm. The rest of the patients included had open surgical procedures (ie, aneurysm clipping). Total charges incurred during index hospitalization amounted to a mean of $93 406±76 634 for unruptured and $255 707±214 959 for ruptured aneurysms. The mean length of stay was 4.0±5.6 days for unruptured and 18.6±14.1 days for ruptured aneurysms. Using standardized difference for effect-size interpretation, large effect size was noted in terms of the ruptured cohort distribution according to the hospital teaching status with an expected gravitation towards receiving care in urban teaching hospital compared with the unruptured cohort. Moreover, longer length of stay and more expensive hospital course was observed in the ruptured cohort (large effect size), with higher in-hospital mortality in the ruptured group compared with the unruptured cohort (medium effect size). Baseline demographic and clinical characteristics of the patient cohorts are presented in detail in Table 2.

Clipping Versus Coiling Trends

The 11-year cohort shows a progressive increase in the use of endovascular modalities for both ruptured and unruptured aneurysms, increasing from 37% of ruptured aneurysms treatments in 2004 to 68% at 2014 (Figure 1). Similar trends were observed in unruptured aneurysms, with endovascular procedures performed in around 52% of procedures in 2004, increasing to 73% by the end of 2014 (Figure 2). Overall, 60.9% of the total 11-year cohort (ruptured and unruptured aneurysms) were treated endovascularly.

Table 1. Matching Quality (Analysis Not Adjusted for Survey Design)

Variables	Control	Sample	Total	Matched
Total	50 342 (50)	50 342 (50)	100 684 (100)	
Sex, n (%)				Yes
Men	14 135 (28.08)	14 285 (28.39)	28 420 (28.23)	
Women	36 207 (71.92)	36 057 (71.62)	72 264 (71.77)	
Mortality, n (%)				No
Alive	49 773 (98.87)	46 997 (93.36)	96 770 (96.11)	
Dead	569 (1.13)	3345 (6.64)	3914 (3.89)	
Intervention				
Surgical	0 (0)	19 731 (39.19)	19 731 (19.6)	No
Endovascular	0 (0)	30 611 (60.81)	30 611 (30.4)	No
Age (mean, SD)	56.5±7.5	55.7±13.1	56.1±10.7	Yes
Total charges, USD (mean, SD)	35 678±48 383	173 697±183 469	104 688±150 874	No
Length of stay, d (mean, SD)	4.4±6	11.3±13.3	7.9±10.9	No
Elixhauser comorbidity index (mean, SD)	1.9±3.9	3.6±7.8	2.7±6.3	Yes

Sample includes unruptured and ruptured aneurysm cases. Chi-square used for categorical variables, Mann-Whitney *U* test for continuous.

Table 2. Univariable Frequencies, Percentages, and Comparisons Over Ruptured and Unruptured Aneurysms, Adjusted for the NIS Survey Design

Variable	Unruptured (n=121 882)	Ruptured (n=121 872)	Standardized Difference*
Age, mean (SD)	56.7±11.9	54.8±13.5	0.15
Sex, n (%)			0.16
Men	30 208 (24.8)	38 967 (32)	
Women	91 675 (75.2)	82 905 (68)	
Intervention			0.18
Surgical	42 256 (34.7)	52 951 (43.5)	
Endovascular	79 627 (65.3)	68 921 (56.6)	
Hospital bed size, n (%)			0.2
Small	16 251 (13.3)	5876 (4.9)	
Medium	30 755 (25.2)	17 179 (14.2)	
Large	74 876 (61.4)	98 188 (81)	
Hospital region, n (%)			0.04
Northeast	24 255 (19.9)	22 997 (18.9)	
Midwest	27 302 (22.4)	30 285 (24.9)	
South	48 143 (39.5)	42 223 (34.6)	
West	22 182 (18.2)	26 367 (21.6)	
Hospital location and teaching status, n (%)			0.98
Rural	13 894 (11.4)	1106 (0.9)	
Urban nonteaching	48 022 (39.4)	11 326 (9.3)	
Urban teaching	59 966 (49.2)	108 811 (89.8)	
Mortality, n (%)			0.51
Dead	588 (0.5)	15 510 (12.7)	
Alive	121 294 (99.5)	106 362 (87.3)	
Sex mortality, n (%)			0.024
Women	399 (67.8)	10 680 (68.9)	
Total charges, USD (mean, SD)	93 406±76 634	255 707±214 959	15.27
Length of stay, d (mean, SD)	4.0±5.6	18.6±14.1	1.36

In these comparisons, 150 observations with missing sex were imputed as men, 43 missing mortality as alive, 51 missing age as being 55 years old, 2049 missing charges as $45 364, and 1 missing length of stay as 3 days. NIS indicates National Inpatient Sample.

*>0.5 is considered medium to large difference.

Length of Stay and Regionalization to Large Academic Centers

The average length of stay for patients treated for UIA was 4 days, and 19 days for patients with aSAH. The gravitation of care towards teaching hospitals was more pronounced in ruptured cases, with almost 90% of cases managed in a teaching hospital, compared with 50% in unruptured aneurysms. Similar trends were observed in terms of the hospital bed-size, with around 81% of ruptured cases and 61% of unruptured aneurysms receiving care in large bed-sized hospitals.

Multivariable Trends in Aneurysm Hospitalizations

Table 3 presents the multivariable RRR per each year passed after 2004, for hospitalizations for unruptured or ruptured aneurysms against matched controls

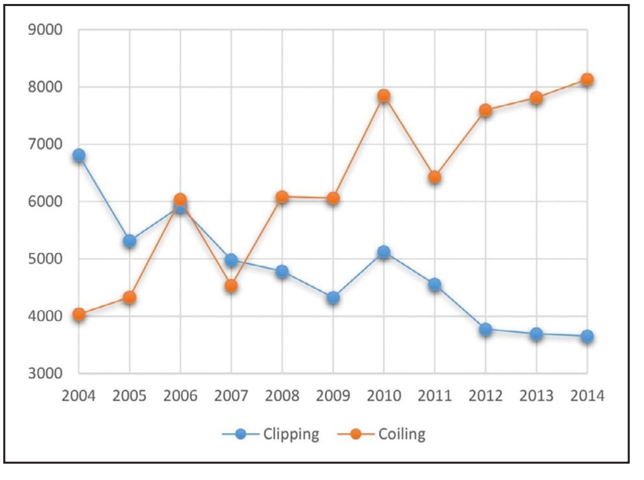

Figure 1. The 2004 to 2014 trends of use of clipping and endovascular modalities for ruptured intracranial aneurysms.

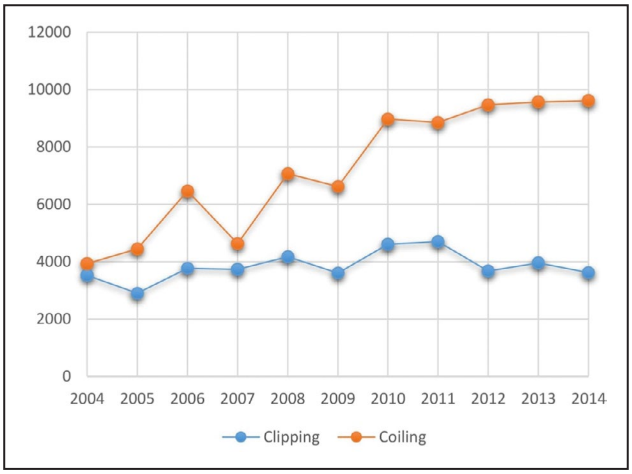

Figure 2. The 2004 to 2014 trends of use of clipping and endovascular modalities for unruptured intracranial aneurysms.

hospitalized for other causes, controlling for hospital size, region, and type. The ratio identified was between consecutive years. The RRR represents the ratio of the risk of being hospitalized for unruptured or ruptured aneurysms, respectively, versus being hospitalized for a different cause. The RRR for ruptured aneurysms was 0.963 (0.944–0.982, *P*<0.001), <1, demonstrating a statistical significance, denoting that for each year passing after 2004 there was a significant decrease in the risk of being hospitalized for a ruptured intracranial aneurysm, compared with being hospitalized for any other cause when controlling for hospital size, region, and type (Figure 3A). The RRR for unruptured aneurysms was 1.012 per passing year (95% CI, 0.987–1.037; *P*=0.35), >1, yet was not significant, denoting that each year passing after 2004 brought a non-significant increase in the risk of being hospitalized for unruptured aneurysm treatment when compared for any other cause, controlling for hospital size, region, and type (Figure 3B). These analyses were adjusted to consider the NIS sampling design. One stratum was omitted because it contained no subpopulation members.

Table 3. Multivariable Relative Risk Ratio Per Year Passed After 2004, for Hospitalizations Regarding Unruptured or Ruptured Aneurysms Against Matched Controls Hospitalized for Other Causes, Controlling for Hospital Size, Region and Type. For Hospital Size, Region and Type

Relative Risk Ratio Against Matched Controls	RRR	95% CI	*P* Value
Unruptured aneurysms			
Per year after 2004	1.012	0.987–1.037	0.35
Hospital bed size			
Small	Reference group		
Medium	1.685	1.008–2.817	0.047
Large	4.246	2.65–6.802	<0.001
Hospital region			
Northeast	Reference group		
Midwest	1.35	1.005–1.813	0.046
South	1.332	1.02–1.74	0.035
West	1.809	1.304–2.51	<0.001
Hospital type			
Rural	Reference group		
Urban, non-teaching	2.889	0.97–8.61	0.057
Urban, teaching	24.654	8.243–73.735	<0.001
Ruptured aneurysms			
Per year after 2004	0.963	0.944–0.982	<0.001
Hospital bed size			
Small	Reference group		
Medium	2.098	1.413–3.115	<0.001
Large	5.479	3.819–7.86	<0.001
Hospital region			
Northeast	Reference group		
Midwest	1.259	0.974–1.628	0.078
South	1.457	1.147–1.851	0.002
West	2.142	1.642–2.793	<0.001
Hospital type			
Rural	Reference group		
Urban, non-teaching	3.211	1.117–9.233	0.03
Urban, teaching	23.744	8.211–68.656	<0.001

The RRR represents the ratio of the risk of being hospitalized for unruptured or ruptured aneurysms, respectively, vs being hospitalized for a different cause. This analysis is adjusted to consider the National Inpatient Sample sampling design. One stratum was omitted because it contained no subpopulation members. RRR indicates relative risk ratio.

DISCUSSION

Standard of Care

Patients with aSAH are usually admitted to the intensive care unit for close neurological monitoring. Following the identification of source of bleeding on vessel imaging (eg, head computed tomography angiography , or angiogram), the patient is taken for definitive treatment to secure the offending aneurysm, either by coiling or clipping depending on factors such as aneurysmal location, size and morphology, as well as overall health status and comorbidity burden of the patient. Postoperatively, patients are monitored in the intensive care unit for an average of 2 to 3 weeks, with a special emphasis on preventing secondary complications, such as hydrocephalus and to monitor vasospasm which can occur at any time 3 to 21 days after ictus.[6] In patients who survive the initial insult, delayed cerebral ischemia is a known complication that occurs in one third of the patients and is thought to be primarily attributable to vasospasm. Delayed cerebral ischemia is the

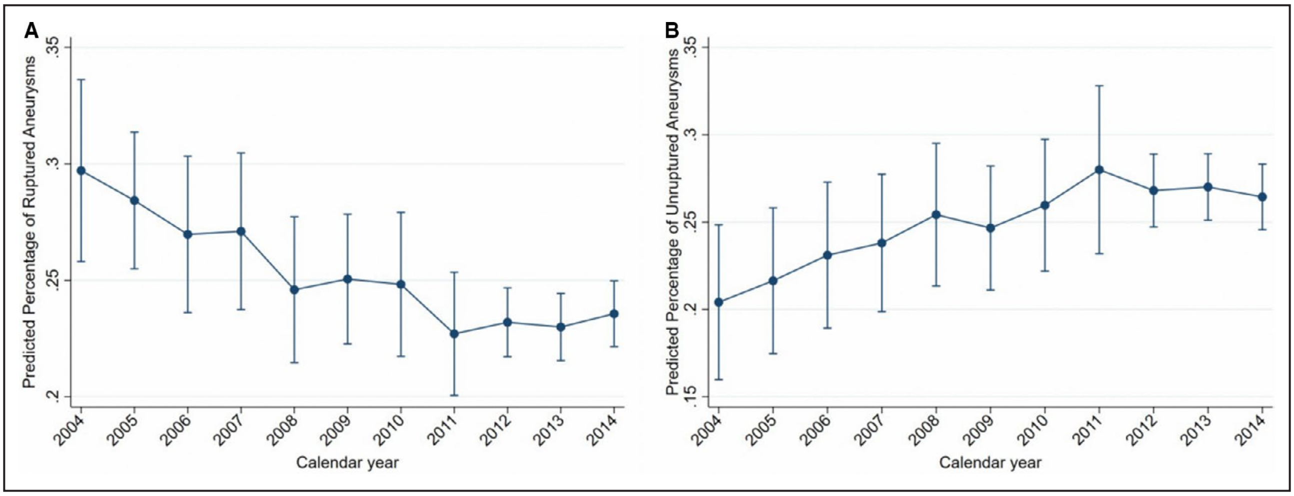

Figure 3. Predicted percentages of patients hospitalized for ruptured (A) and unruptured (B) intracranial aneurysms, compared with matched control of patients hospitalized for other indications, over the period of 2004 to 2014.
Predictions were made using univariable logistic regression for the relative risk ratio of each aneurysm hospitalization category against the matched control, and the margin plots were derived using predicted probabilities. Analyses were adjusted for the National Inpatient Sample survey design.

strongest predictor of poor patient outcomes after an aSAH.[6] Adequate fluid resuscitation along with close neurological monitoring are key components of active surveillance for early delayed cerebral ischemia detection and intervention.

Decreasing in the Relative Risk of Ruptured Aneurysms Treatment

Based on the results of this NIS cohort, there is a significant national decrease in the annual relative risk of hospitalization for treated aSAH, spanning an 11-year-interval from 2004. Secondly, we observed a non-significant trend towards the increased intervention of unruptured aneurysms. This is an important finding and while direct causality cannot be confirmed, these findings suggest that the decrease in treated aSAH is potentially the result of selective targeting of the "high-risk" unruptured aneurysms population to undergo treatment and thus potentially preventing their progression towards rupturing. This decrease corresponds with a higher incidence of unruptured aneurysm procedures over the past years and may be an indirect indication of the effectiveness of such procedures. These findings must be interpreted with caution, given the nature of the NIS data and their inherent limitations, however, our data are consistent with the underlying clinical assumption, that treating unruptured aneurysm ultimately will reduce the risk of aSAH. Despite the low risk for aSAH, the associated risk of severe disability and mortality ranges from 30% to 45% in the first month, and of the patients who do survive, the quality of life in almost two thirds of the patients is significantly reduced.[7]

Our findings confirm a significantly high mortality rate during the index hospital admission for aSAH (12.7% versus 0.5%). This is particularly important as many of the survivors are relatively young and represent a significant social, physical, and economic burden on the community. Our findings represent the first study to identify a significant decrease in the rate of treated aSAH over time and also identify the concurrent trend in unruptured aneurysm treatment. Secondly, indirect corollaries can be drawn about the national economic burden of aSAH, which are reflected by the 3-fold increase in hospitalization costs in patients undergoing treatment for an aSAH when compared with the unruptured aneurysm cohort, highlighting the complex care aSAH requires. A previous study by Hoh et al demonstrated a higher economic burden that patients with aSAH face when compared with patients being treated for unruptured intracranial aneurysms.[8] The economic impact of aSAH goes far beyond hospitalization, as one third of those who survive suffer from major neurological sequelae, preventing a return to work.[9] Previous studies have shown that treatment of UIA has been steadily increasing over the last 2 decades,[10] owing to improved detection and technological developments, which have led to less invasive and more effective treatments to secure aneurysms while achieving better clinical outcomes.[11] While we identified an increased probability of being hospitalized for UIA treatment, this did not reach significance. Our study also suggests improved patient selection and safety in treating patients with UIA. Lin et al found an overall mortality rate of 1.19% for the treatment (both endovascular and open procedures) of aneurysms 1998 to 2007, in contrast, our study mortality was less than half of that (0.5%).

Impact of the ISAT on Clipping and Coiling Trends

The ISAT set the ground for the current aSAH treatment paradigm currently used. Essentially, it demonstrated that coiling ruptured aneurysms decreased the relative risk of dependence or death when compared with aneurysmal clipping by 7.4% at 1-year follow-up.[2,12] These results lead to a paradigm shift in treatment. Lin et al quantified how this impact in the United States using NIS years 1998 to 2007. Before 2002, 90.7% of ruptured aneurysms were clipped. After 2002, the number decreased to 57.1%. This shift was even more pronounced for unruptured aneurysms, where the number of clippings went from 79.4% before 2002 to 38.3% after 2002.[3]

Prior NIS data in the peri-ISAT era (1997–2003) revealed a significant increase in the number of endovascular treatment hospitalization with a concurrent decrease in clipping-related hospitalizations.[9] We sought to extend upon prior studies assessing national trends in aneurysm treatment.[3,13] The latest year in our cohort (2014) shows that nationally, around two thirds and three fourths of ruptured and unruptured aneurysms, respectively, are treated via endovascular techniques (Figures 2 and 3, respectively). Such findings warrant further discussion and debate about its long-term implications and its impact on the practice, providers, and health outcomes. Ultimately, this change in practice may result in a generation of neurosurgeons less familiar with open surgery,[14] and strategies must be developed to maintain training and proficiency in open surgery aneurysm treatments. Of note, the ISAT long-term results showed similar 10-year overall outcomes between the intervention groups.[15] Nonetheless, the appeal of endovascular treatment continues to grow, especially with the constant introduction of new endovascular device modalities such as flow diversion. Currently, it is not clear whether the long-term ISAT results will dampen the enthusiasm for endovascular technique treatment and future studies will be illuminating in this regard.

Sex Differences in SAH

Aneurysmal SAH is a disease of sex differential patterns that has been consistently reported in the literature, including differences in aneurysmal location and prevalence. The cause of this disparity is yet to be elucidated; however, several theories have been postulated. The drop in hormonal estrogen protection has been proposed as a mechanism for increased occurrence of aneurysms in women, supported by the increased prevalence in peri and post-menopausal women.[16] In terms of location, anterior cerebral artery aneurysms are more commonly encountered in men, while other internal carotid artery aneurysms are more common in women.[17] Conflicting studies have been reported on the difference in clinical outcomes following aSAH between men and women, with reportedly worse outcomes in women. This has been hypothesized to be because of worse vasospasm in women, despite not being consistent in all studies.[16,18,19]

In line with prior reports and over the span of the 11 years of this cohort, women constituted around three fourths of the unruptured aneurysms cohort (75.2%) while accounting for 67.8% of inpatient mortality in this group. Similarly, there was a clear sex-differential in terms of the ruptured aneurysms, with women comprising 68% of the unruptured cohort, and 68.9% of inpatient hospital mortality of the ruptured cases. There were no significant differences in sex mortality distribution between the unruptured and the ruptured cohort (67.8% versus 68.9%, respectively). Further comparisons of sex differences in relationship to aneurysmal locations and functional outcomes are not possible because of lack of longitudinal follow-up and unavailability of key prognostic clinical details in NIS data.

Length of Stay Trends in Ruptured and Unruptured Intracranial Aneurysms

Interestingly, the average hospital length of stay seems to have increased over time in the setting of increased endovascular treatment. From 1998 to 2003, the average length of stay was 3.5 days for patients being treated for UIA, while the average length of stay for patients being treated for aSAH was 16 days.[13] In contrast, the average length of stay for patients in the following decade who were treated for UIA was 4 days, and 19 days for patients with aSAH. There is a trend for an overall increase in the length of stay for the last decade. This proportionate rise in length of stay (3.5–4 days in the unruptured [14% increase] versus 16–19 in the ruptured group [19% increase]) is relatively higher in the ruptured group. This could be explained by the increased complexity of medical care for patients with aSAH relative to the unruptured group, higher intensity of care and more rigorous surveillance of patients in the setting of a dedicated neuro-intensive care unit and overall, more specialized management directed towards early detection and delayed cerebral ischemia prevention.

Regionalization to Large Academic Centers

As reported by Andaluz et al, the trends of mortality rates based on the teaching status of the hospital have been around 6.5% to 13% for non-teaching centers and from 6% to 8% for teaching centers.[10] These findings were further consolidated with data from Pandey et al evaluating inpatient mortality based on hospital patient volume, in which a dramatic 50% reduction in inpatient mortality was observed when comparing hospitals in the 5 quintile versus the 1 quintile (52% versus 22.5% inpatient mortality).[20] In this 11-year report and in line with previous findings, 90% of ruptured aneurysms were managed in a teaching hospital, underscoring the complex multidisciplinary high-level care required for treating such critically-ill patients.

Strengths and Limitations

The NIS includes patients admitted to hospitals from across the United States including academic and community medical centers, which enhances its generalizability. The size of the database enables large sample sizes. The disease entity of aSAH has a clear clinical definition and the *ICD-9-CM* codes are well-validated. However, directly testing the assumption that the treatment of UIA will ultimately reduce aSAH is not currently possible, nevertheless, our data provide a novel method to indirectly test this assumption. Moreover, the *ICD-9 CM* code for SAH is not specific for aSAH and thus required refinement with the addition of procedural codes for aneurysmal repair procedures. While this method reduces sample contamination (with patients with traumatic SAH for example), it also excludes patients who suffered aSAH and did not undergo a repair procedure (often patients with extremely poor prognoses) and patients who expired with aSAH before arriving at the hospital and so were not admitted. Secondly, information bias secondary to coding errors may be present. Thirdly, the NIS lacks granularity about important clinical factors such as aneurysm size. Moreover, the study is retrospective in nature and while codes were determined and collected before analysis, it is still vulnerable to the potential bias associated with such a design.

It's also conceivable that the increased frequency of radiological imaging leading to increased detection of asymptomatic aneurysms and their subsequent treatment could be a contributing factor to the decreased RRR of ruptured case admissions. However, there are several parameters in the design of this study that limits this type of confounding effect, which was specifically considered in the study design and statistical plan before data retrieval. Patients with unruptured aneurysms who did not undergo any treatment (ie, clipping or coiling) were not included. Therefore, we only included unruptured aneurysms which underwent treatment during the hospitalization and therefore were deemed of considerable risk of rupture. Additionally, we matched cases to controls in a random fashion based on age and sex, which are two known confounders for aneurysms rupture risk. We also attempted to homogenize the cases and control pool as much as possible by matching from a group within 1 SD range of the Elixhauser comorbidity index to capture a control group of a similar comorbidity burden.

CONCLUSIONS

With each passing year, there is a significant decrease in RRR of undergoing treatment for aSAH, concomitant with a stable annual risk of undergoing treatment for UIA, when compared with a similar matched non-aneurysmal control group, admitted for other reasons. This is consistent with the fundamental assumption that treating unruptured aneurysms will lead to a reduction in aSAH. Our study also identified a significant decline in the mortality associated with the treatment of unruptured aneurysms. Further optimization of intracranial aneurysms management protocols is warranted to enhance the quality of care delivery to this subpopulation of patients. This includes maintaining hypervigilance for proper identification of "high-risk" aneurysms to undergo prompt treatment, and critically managing ruptured aneurysms through adequate anticipation and prevention of secondary complications which are detrimental to patients' clinical outcomes.

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Affiliations

From the Neurosurgery Service (M.M.S., G.A.M., S.G.-P., L.C.A., C.S.O., A.J.T., J.M.M.) and Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA (L.H.N.).

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