Management of intracranial aneurysms has greatly evolved over the past 2 decades. New evidence has prompted changes in multiple aspects of patient care including diagnosis, imaging surveillance, and indications and strategies for aneurysm obliteration. For patients presenting with aneurysmal subarachnoid hemorrhage (SAH), updated guidelines for the prevention of aneurysmal rerupture, management of delayed cerebral ischemia, hydrocephalus, and medical complications of SAH have been developed. Analyses of nationwide trends using Nationwide Inpatient Sample (NIS) data have demonstrated a marked increase in the usage of endovascular therapy for both ruptured and unruptured aneurysms. The usage of endovascular therapy has spread from large academic hospitals to smaller hospitals across all geographic regions and has become the procedure of choice in older patients.

Endovascular therapy has resulted in improved morbidity and mortality, fewer adverse events, and shorter mean length of hospital stay than surgical clipping. A key limitation of NIS studies is that the NIS database does not record important predictors of outcome including neurological status at presentation and the amount of subarachnoid blood. As such, it is unclear whether improved outcomes are because of increased usage of endovascular therapy in patients with less severe presentations. In addition, the impact of evolving aneurysm management strategies on outcomes for patients with different clinical risk factors has yet to be investigated.

Conclusions

We report significantly improved outcomes over time for overall aneurysm management and for multiple patient subgroups, associated with increased usage of endovascular therapy. (Stroke. 2016;47:708-712. DOI: 10.1161/STROKEAHA.115.011959.)

Key Words: endovascular techniques • Glasgow Outcome Scale • intracranial aneurysms • outcomes research • surgical instruments

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From the Neurosurgical Service, Beth Israel Deaconess Medical Center, Brain Aneurysm Institute, Harvard Medical School, Boston, MA (M.H.C., C.J.G., L.H., A.J.T., C.S.O.); and Department of Neurosurgery, Massachusetts General Hospital, Boston (C.J.S.).

Guest Editor for this article was Giuseppe Lanzino, MD.

Correspondence to Christopher S. Ogilvy, MD, 110 Francis St, Suite 3B, Boston, MA 02215. E-mail cogilvy@bidmc.harvard.edu

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This stratification was chosen as age $\geq$50 years has been associated with poorer outcomes in previous studies.\textsuperscript{6,12,13} Statistical analysis was performed using R version 3.1.1 (http://www.r-project.org). In univariable analysis, variables were compared between groups by the Pearson $\chi^2$ test. Statistical significance was defined as $P<0.025$ and $P<0.0125$ for unruptured and ruptured aneurysms, respectively, using the Bonferroni correction. Changes in outcome for surgical, endovascular, and overall treatment of unruptured and ruptured aneurysms were examined using multivariable logistic regression models, accounting for patient age, aneurysm size, location (anterior or posterior circulation), neurological status at admission (Hunt and Hess grade), and amount of subarachnoid blood (Fisher grade), which are recognized predictors of outcome.\textsuperscript{12,13} Aneurysm size was defined as the largest dimension of the aneurysm (dome, length, or height). The original Fisher scale was used in this study to permit inclusion of aneurysms treated before the publication of the modified Fisher scale because a majority of old imaging studies are not presently available. Although less discriminative than the modified Fisher scale, the original Fisher scale correlates with the development of symptomatic vasospasm and has high interobserver agreement.\textsuperscript{14} All variables were included in the models without the use of a stepwise or other formal variable selection process. As the incidence of our outcome of interest (low or moderate disability) was high ($>10\%$), relative risk was approximated from the logistic regression odds ratio as described by Zhang and Yu.\textsuperscript{15}

### Results

#### Patient Characteristics

Treatment was performed on 1094 aneurysms in 958 patients from 1998 to 2003 and on 1543 aneurysms in 1315 patients from 2007 to 2013. Clinical follow-up (26 months) was available for 1023 aneurysms (93.5\%) in 890 patients (92.9\%) and for 1499 aneurysms (97.1\%) in 1282 patients (97.5\%). For unruptured aneurysms, mean age at time of treatment was 52.9±11.5 years in 1998 to 2003 and 55.3±11.9 years in 2007 to 2013 and mean aneurysm size was 8.3±6.39 mm in 1998 to 2003 and 6.92±5.01 mm in 2007 to 2013. For ruptured aneurysms, mean age at time of treatment was 53.3±13.9 years in 1998 to 2003 and 53.8±13.3 years in 2007 to 2013 and mean aneurysm size was 8.18±5.18 mm in 1998 to 2003 and 6.49±3.58 in 2007 to 2013. Relatively more unruptured aneurysms in older patients ($>50$ years) were treated in 2007 to 2013 when compared with those treated in 1998 to 2003 (Table 1). For ruptured aneurysms, there were no differences in patient age and Hunt and Hess grade distribution between the 2 time periods. Relatively more SAHs with poor Fisher grade were treated in 2007 to 2013 (Table 1).

#### Treatment Characteristics

There was increased usage of endovascular therapy for the treatment of both unruptured ($P<0.0001$) and ruptured ($P=0.000371$) aneurysms in 2007 to 2013 when compared with 1998 to 2003 (Table 2). For unruptured aneurysms, there was increased usage of endovascular therapy for both younger ($\leq$50 years) ($P<0.0001$) and older ($>50$ years; $P<0.0001$) patients and for both anterior ($P<0.0001$) and posterior ($P<0.0001$) circulation aneurysms. For ruptured aneurysms, there was increased usage of endovascular therapy for older patients ($P<0.0001$), good grade aneurysms (Hunt and Hess, 1–3; $P<0.0001$; Fisher 1–2; $P=0.0018$), and anterior circulation aneurysms ($P<0.0001$).

### Discussion

We report significant improvements in clinical outcome for surgical, endovascular, and overall treatment of unruptured and ruptured aneurysms from 1998 to 2003 to 2007 to 2013 (Tables 3–5). These findings are highly encouraging as SAH has traditionally been associated with dismal prognosis.\textsuperscript{16–18} In our 2007 to 2013 cohort, the proportion of cases with low or moderate disability at 26 months post SAH was 75.6\% for surgical clipping and 76.6\% for endovascular therapy. Improved outcomes were associated with a general increase in usage of endovascular therapy (Table 2). However, conclusions on causation cannot be drawn as this is not a randomized controlled study.

Relatively more unruptured aneurysms in older patients ($>50$ years) were treated in 2007 to 2013 versus 1998 to 2003.

### Table 1. Patient and Aneurysm Characteristics From 1998 to 2003 and 2007 to 2013

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Unruptured</td>
<td>n=613</td>
<td>n=1050</td>
<td></td>
</tr>
<tr>
<td>Age $\leq$50 y</td>
<td>226 (36.9%)</td>
<td>319 (30.4%)</td>
<td>0.00771</td>
</tr>
<tr>
<td>Age $&gt;$50 y</td>
<td>387 (63.1%)</td>
<td>731 (69.6%)</td>
<td></td>
</tr>
<tr>
<td>Anterior circulation</td>
<td>538 (87.8%)</td>
<td>940 (89.5%)</td>
<td>0.308</td>
</tr>
<tr>
<td>Posterior circulation</td>
<td>75 (12.2%)</td>
<td>110 (10.5%)</td>
<td></td>
</tr>
<tr>
<td>Ruptured</td>
<td>n=410</td>
<td>n=449</td>
<td></td>
</tr>
<tr>
<td>Age $\leq$50 y</td>
<td>164 (40.0%)</td>
<td>171 (38.1%)</td>
<td>0.614</td>
</tr>
<tr>
<td>Age $&gt;$50 y</td>
<td>246 (60.0%)</td>
<td>278 (61.9%)</td>
<td></td>
</tr>
<tr>
<td>Hunt and Hess 1–3</td>
<td>280 (68.3%)</td>
<td>332 (73.9%)</td>
<td>0.0798</td>
</tr>
<tr>
<td>Hunt and Hess 4–5</td>
<td>130 (31.7%)</td>
<td>117 (26.1%)</td>
<td></td>
</tr>
<tr>
<td>Fisher 0–2</td>
<td>111 (27.1%)</td>
<td>74 (16.5%)</td>
<td>0.000225</td>
</tr>
<tr>
<td>Fisher 3–4</td>
<td>299 (72.9%)</td>
<td>375 (83.5%)</td>
<td></td>
</tr>
<tr>
<td>Anterior circulation</td>
<td>327 (79.8%)</td>
<td>383 (85.3%)</td>
<td>0.0400</td>
</tr>
<tr>
<td>Posterior circulation</td>
<td>83 (20.2%)</td>
<td>66 (14.7%)</td>
<td></td>
</tr>
</tbody>
</table>

Statistical significance was assessed at $P<0.025$ and $P<0.0125$ for unruptured and ruptured aneurysms, respectively, using the Bonferroni correction.
Table 3. Outcomes From Surgical, Endovascular, and Overall Treatment of Unruptured Aneurysms From 1998 to 2003 and 2007 to 2013

<table>
<thead>
<tr>
<th></th>
<th>Low or Moderate Disability, %*</th>
<th>1998–2003</th>
<th>2007–2013</th>
<th>Unadjusted OR (95% CI)</th>
<th>Unadjusted RR (95% CI)</th>
<th>P Value</th>
<th>C Statistic</th>
<th>Adjusted OR (95% CI)†</th>
<th>Adjusted RR (95% CI)†</th>
<th>P Value</th>
<th>C Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>94.7</td>
<td>97.7</td>
<td></td>
<td>2.35 (1.27–4.35)</td>
<td>1.03 (1.01–1.04)</td>
<td>0.0062</td>
<td>0.605</td>
<td>2.33 (1.23–4.41)</td>
<td>1.03 (1.01–1.04)</td>
<td>0.0091</td>
<td>0.730</td>
</tr>
<tr>
<td>Endovascular</td>
<td>93.3</td>
<td>98.1</td>
<td></td>
<td>3.83 (1.20–12.2)</td>
<td>1.05 (1.01–1.07)</td>
<td>0.0229</td>
<td>0.647</td>
<td>4.40 (1.18–16.3)</td>
<td>1.06 (1.01–1.07)</td>
<td>0.0271</td>
<td>0.742</td>
</tr>
<tr>
<td>Overall</td>
<td>94.5</td>
<td>97.8</td>
<td></td>
<td>2.62 (1.53–4.49)</td>
<td>1.04 (1.02–1.05)</td>
<td>0.0005</td>
<td>0.618</td>
<td>2.58 (1.48–4.49)</td>
<td>1.04 (1.02–1.05)</td>
<td>0.0008</td>
<td>0.725</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; OR, odds ratio; and RR, relative risk.

*Glasgow Outcome Scale score of 4 or 5 at ≥6 months post treatment.
†Adjusted for age (years), size (mm), and location (anterior or posterior circulation). Patient age and aneurysm size were modeled as continuous variables. RR was approximated from the logistic regression OR as described by Zhang and Yu.15
we did not find any statistically significant differences in outcome for surgical clipping versus endovascular therapy in the post-ISAT period. This raises the possibility that NIS findings may be because of increased usage of endovascular therapy in patients with less severe presentations and higher complication rates from surgical clipping in smaller neurovascular centers.

Our findings reflect the experience of a single, high-volume neurovascular center with a unique patient referral pattern, which certainly limits the generalizability of our data. Nevertheless, this is encouraging evidence that advancements in aneurysm management strategies are being translated into improved outcomes. For neurosurgeons providing counseling to patients and families, it is important to know that prognosis is improving. This study involved a retrospective analysis of previously recorded outcomes (at ≥6 months post treatment) from 1998 to 2003. For consistency, cases from 2007 to 2013 with <6 months of clinical follow-up were excluded as well. However, this is unlikely to have significantly affected our findings as the proportion of cases which were lost to follow-up from both time periods is low. In addition, we were able to capture neurological recovery, which has been documented at and beyond 6 months post treatment. As this is a retrospective cohort study, the possibility of residual confounding cannot be excluded. For example, we cannot describe how patient referral patterns have changed. Improved outcomes are likely because of a combination of factors including increased usage of endovascular therapy, improved ICU care, and better selection of patients for surgery versus endovascular therapy.

**Disclosures**

Dr Ajith Thomas serves on a Data Safety Monitoring Board of a Stryker Trial for brain aneurysm treatment. The other authors report no conflicts.

### Table 4. Outcomes From Surgical, Endovascular, and Overall Treatment of Ruptured Aneurysms From 1998 to 2003 and 2007 to 2013

|-------------------|-----------|-----------|---------|-----------|-----------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|         |
|                   | Unadjusted OR (95% CI) | Unadjusted RR (95% CI) | P Value | C Value | Statistic | Adjusted OR (95% CI)† | Adjusted RR (95% CI)† | P Value | C Value | Statistic |
| Surgical          |           |           |         |           |           |         |         |         |         |         |         |         |         |         |         |         |
|                   | 59.2      | 75.6      | 2.13 (1.50–3.03) | 1.28 (1.16–1.38) | <0.0001   | 0.593   | 3.18 (1.88–4.43) | 1.39 (1.24–1.46) | 0.0004   | 0.831    |
| Endovascular      | 42.6      | 76.6      | 4.41 (2.57–7.57) | 1.80 (1.54–1.99) | <0.0001   | 0.674   | 3.54 (1.84–6.81) | 1.70 (1.36–1.96) | 0.0001   | 0.826    |
| Overall           | 55.1      | 75.9      | 2.57 (1.92–3.44) | 1.38 (1.27–1.47) | <0.0001   | 0.616   | 3.11 (2.18–4.42) | 1.44 (1.32–1.53) | <0.0001  | 0.821    |

*Glasgow Outcome Scale score of 4 or 5 at ≥6 months post treatment.
†Adjusted for age (years), size (mm), location (anterior or posterior circulation), Hunt and Hess grade (0–3 vs 4–5), and Fisher grade (0–2 vs 3–4).

Outcomes are reported as number of patients with low or moderate disability (Glasgow Outcome Scale score of 4 or 5)/total number of patients in each risk category (proportion of patients with low or moderate disability). Statistical significance was assessed at P<0.025 and P<0.0125 for unruptured and ruptured aneurysms, respectively, using the Bonferroni correction.
References


Documentation of Improved Outcomes for Intracranial Aneurysm Management Over a 15-Year Interval
Michelle H. Chua, Christoph J. Griessenauer, Christopher J. Stapleton, Lucy He, Ajith J. Thomas and Christopher S. Ogilvy

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