Patient Outcomes With Endovascular Embolectomy Therapy for Acute Ischemic Stroke
A Study of the National Inpatient Sample: 2006 to 2008

Waleed Brinjikji, BS; Alejandro A. Rabinstein, MD; David F. Kallmes, MD; Harry J. Cloft, MD, PhD

Background and Purpose—Maturing techniques have spurred widespread implementation of endovascular embolectomy therapy for ischemic stroke. We evaluated a large administrative database to determine outcomes in patients treated with endovascular embolectomy in the general population.

Methods—Using the National Inpatient Sample, we evaluated outcomes of patients treated for acute ischemic stroke in the United States from 2006 to 2008. Patients who had an ischemic stroke and underwent endovascular clot retrieval were identified. Morbidity, defined as “discharge to long-term facility,” and mortality were evaluated as a function of patient age and of concomitant thrombolytic agent administration.

Results—For 2006 to 2008, a total of 3864 patients received endovascular clot retrieval with 266 (6.9%) patients in 2006, 800 (20.7) patients in 2007, and 2798 (72.4%) patients in 2008. The discharge to a long-term facility rate was 51.3% (1983 of 3864). The in-hospital mortality rate was 24.3% (940 of 3864). For patients <65 years old, the rate of in-hospital death was 17.1% (283 of 1658) as compared with a rate of 29.7% (656 of 2206) for patients ≥65 years old (P<0.0001). The rate of discharge to a long-term facility was 47.6% (789 of 1658) for patients <65 years old and 54.1% (1193 of 2206) for patients ≥65 years old (P<0.0001). The rate of intracranial hemorrhage was 15.5% without concomitant thrombolysis and 20.0% with concomitant thrombolysis (P=0.0009).

Conclusions—Rates of morbidity and mortality remain high for patients with acute stroke, even in the setting of endovascular embolectomy. Advanced age portends a worse outcome and patients treated with concomitant use of thrombolytic agent had higher rates of intracranial hemorrhage than those without such therapy. (Stroke. 2011;42:1648-1652.)

Key Words: acute stroke • endovascular treatment • interventional neuroradiology • outcomes • thrombolysis

The first endovascular clot retrieval device for acute ischemic stroke was approved by the US Food and Drug Administration in August 2004. Since that time, endovascular clot retrieval has been evaluated in published trials1–3 and has become a widely accepted treatment for a select group of patients with acute ischemic stroke. The US National Inpatient Sample (NIS) has been used previously to study outcomes of patients treated for acute ischemic stroke with intra-arterial thrombolysis4 and provides outcome data that can be used to evaluate outcomes in patients who undergo this therapy. The International Classification of Diseases, 9th Revision (ICD-9) procedure code 39.74, endovascular removal of obstruction from the head and neck, was first introduced into the NIS database in 2006, rendering it possible to identify patients treated with such treatment since that time in the NIS. In the current study, we evaluated the NIS data from 2006 to 2008 to determine outcomes in patients treated with endovascular clot retrieval in the general population and compare data across age strata and between patients treated with and without concomitant thrombolytic therapy.

Methods

Patient Population
We purchased the NIS hospital discharge database for the period 2006 to 2008 from the Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality, Rockville, MD. The NIS is a hospital discharge database that represents 20% of all inpatient admissions to nonfederal hospitals in the United States.

Patients who had an ischemic stroke were identified using ICD-9 codes 433, 434, 436, 437.0, and 437.1. Patients undergoing endovascular clot retrieval were identified using the ICD-9 procedure code 39.74, “endovascular removal of obstruction from the head and neck,” which was first introduced into the NIS database in 2006. We stratified patients into 2 groups: (1) patients receiving endovascular clot retrieval only; and (2) patients receiving endovascular clot retrieval and infusion of thrombolytics. The coding system does not allow differentiation between patients who received intravenous thrombolytic therapy from those who received intra-arterial thrombolytic therapy. We stratified patients into 3 age groups, including (1) patients <65 years old; (2) patients 65 years old to 79 years old; and (3) patients ≥80 years old. The Charlson Comorbidity Index was calculated for each patient.5

End Points
The two primary end points examined in this study were discharge to a long-term facility and in-hospital mortality. Discharge status was studied by using the Healthcare Cost and Utilization Project (HCUP) variable name DISPUNIFORM. In-hospital mortality was studied by using the binary HCUP variable name DIED. Length of stay was a secondary end point and was studied by using the continuous variable “LOS” from the NIS. Additional secondary end points included intracranial hemorrhage (ICD-9 diagnosis codes 430 to 432.9), gastrointestinal bleeding (ICD-9 diagnosis codes 578 to 578.9), performance of a gastrostomy (ICD-9 procedure codes 43.11 to 43.19), and performance of a tracheostomy (ICD-9 procedure codes 31.1 to 31.29).

Statistical Analysis
For the purposes of statistical analysis, we summed the data from 2006 to 2008. Chi-square testing was used to compare categorical variables and the Student t test was used to compare continuous variables. To obtain national estimates, proper weights were applied as indicated in the HCUP–NIS Calculating NIS Variances Guide. All statistical analysis was performed using the SAS-based statistical package JMP (www.jmp.com). A multivariate logistic regression analysis was performed to determine predictors of poor outcomes. Independent variables studied included tissue plasminogen activator administration, Charlson Comorbidity Index, age group, gender, and race (white versus nonwhite).

Results
Patient Demographics
For 2006 to 2008, a total of 3864 patients received endovascular clot retrieval with 266 (6.9%) patients in 2006, 800 (20.7%) patients in 2007, and 2798 (72.4%) patients in 2008. Of these patients, 2362 (61.1%) received endovascular clot retrieval only and 1502 patients (38.9%) received endovascular clot retrieval with thrombolysis. There was no significant difference in the average age, gender distribution, or proportion of white patients between the 2 groups. The mean Charlson Comorbidity Index score between the 2 groups was similar (P=0.27). These data are summarized in Table 1.

Primary Outcomes
For all patients treated from 2006 to 2008, the rate of discharge to a long-term facility was 51.3% (1983 of 2206) for patients aged 65 to 79 years old. These data are summarized in Table 2. The two primary end points examined in this study were discharge to a long-term facility and in-hospital mortality. Discharge status was studied by using the Healthcare Cost and Utilization Project (HCUP) variable name DISPUNIFORM. In-hospital mortality was studied by using the binary HCUP variable name DIED. Length of stay was a secondary end point and was studied by using the continuous variable “LOS” from the NIS. Additional secondary end points included intracranial hemorrhage (ICD-9 diagnosis codes 430 to 432.9), gastrointestinal bleeding (ICD-9 diagnosis codes 578 to 578.9), performance of a gastrostomy (ICD-9 procedure codes 43.11 to 43.19), and performance of a tracheostomy (ICD-9 procedure codes 31.1 to 31.29).

Secondary Outcomes
The mean days±SD length of hospital stay for patients undergoing endovascular clot retrieval was 10.0±17.8 and 10.9±21.5 for patients receiving clot retrieval plus thrombolysis (P=0.03). In-hospital mortality rates were 23.7% (560 of 2362) for endovascular clot retrieval alone and 49.1% (737 of 1502) for endovascular clot retrieval plus thrombolysis (P=0.0009). The 2 groups had similar rates of gastrointestinal hemorrhage (P=0.55), gastrostomy (P=0.054), and tracheostomy (P=0.25). These data are summarized in Table 1.

Age and Primary Outcomes
For all patients treated with clot retrieval (with and without thrombolysis) from 2006 to 2008, the rate of in-hospital mortality was 17.1% (283 of 1658) for patients <65 years old and 29.7% (656 of 2206) for patients ≥65 years old (P<0.0001). The rate of discharge to a long-term facility was 47.6% (789 of 1658) for patients <65 years old and 54.1% (1193 of 2206) for patients ≥65 years old (P<0.0001). These data are summarized in the Figure and Table 2.

Age and Secondary Outcomes
For patients receiving clot retrieval without thrombolysis, the mean length of stay did not differ among the 3 age groups and neither did the rate of intracranial hemorrhage or gastrointestinal hemorrhage. Patients ages 65 to 79 years old had a slightly increased probability of undergoing a gastrostomy (P=0.008) relative to patients <65 years old, but patients aged ≥80 years old were less likely to undergo gastrostomy (P=0.016) or tracheostomy (P=0.003) than those ages 65 to 79 years old. These data are summarized in Table 2.

Multivariate Analysis
On multivariate analysis, significant predictors of morbidity included increasing age (P<0.0001), male gender (P=0.0006), and Charlson Comorbidity Index (P<0.0001). Race and tissue plasminogen activator administration were not significant predictors of mortality (P=0.96). On multivariate analysis, significant predictors of any morbidity or mortality included increasing age (P=0.0001), male gender (P=0.0008), and Charlson Comorbidity Index (P=0.0001). Race and tissue plasminogen activator administration were not significant predictors of any morbidity or mortality (P=0.93).

Table 1. Outcomes

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Endovascular Clot Retrieval</th>
<th>Endovascular Clot Retrieval + Thrombolysis</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>2362</td>
<td>1502</td>
<td></td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>64.8 (34.2)</td>
<td>66.1 (35.4)</td>
<td>0.25</td>
</tr>
<tr>
<td>No. (%) female</td>
<td>1226 (51.9)</td>
<td>796 (53.0)</td>
<td>0.51</td>
</tr>
<tr>
<td>Percent white</td>
<td>76.8</td>
<td>73.9</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Table 2. Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Endovascular Clot Retrieval</th>
<th>Endovascular Clot Retrieval + Thrombolysis</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discharge to long-term care, no. (%)</td>
<td>1246 (52.7)</td>
<td>737 (49.1)</td>
<td>0.03</td>
</tr>
<tr>
<td>In-hospital death, no. (%)</td>
<td>560 (23.7)</td>
<td>380 (25.3)</td>
<td>0.25</td>
</tr>
<tr>
<td>Morbidity and mortality, no. (%)</td>
<td>1806 (76.4)</td>
<td>1117 (74.4)</td>
<td>0.14</td>
</tr>
<tr>
<td>Mean length of stay (SD)</td>
<td>10.0 (17.8)</td>
<td>10.9 (21.5)</td>
<td>0.15</td>
</tr>
<tr>
<td>Intracranial hemorrhage, no. (%)</td>
<td>366 (15.5)</td>
<td>300 (20.0)</td>
<td>0.0009</td>
</tr>
<tr>
<td>Gastrointestinal hemorrhage, no. (%)</td>
<td>68 (2.9)</td>
<td>39 (2.6)</td>
<td>0.55</td>
</tr>
<tr>
<td>Gastrostomy, no. (%)</td>
<td>360 (15.3)</td>
<td>195 (13.0)</td>
<td>0.05</td>
</tr>
<tr>
<td>Tracheostomy, no. (%)</td>
<td>184 (7.8)</td>
<td>134 (8.9)</td>
<td>0.25</td>
</tr>
<tr>
<td>Mean Charlson Comorbidity Index (SD)</td>
<td>5.3 (5.2)</td>
<td>5.2 (5.2)</td>
<td>0.27</td>
</tr>
</tbody>
</table>
predictors of morbidity. Significant predictors of mortality included age group \( (P = 0.0002) \), nonwhite race \( (P = 0.009) \), and Charlson Comorbidity Index \( (P = 0.03) \). These data are summarized in Table 3.

**Discussion**

The NIS provides data on outcomes for patients treated with endovascular clot retrieval across the United States, perhaps reflecting “real-world” practice. Our findings demonstrated a relatively high rate of poor outcomes with nearly three fourths of patients being discharged to long-term facilities or dying in the hospital. Rates of morbidity and mortality remain extremely high, even with clot removal. Unfortunately, these disappointing outcomes have been seen in multiple, recent studies of endovascular clot retrieval for stroke, suggesting that substantial work remains to be done to improve outcome in patients presenting with severe, acute stroke.

When comparing outcomes across the 3 age strata, we found that older patients who undergo endovascular clot retrieval for acute ischemic stroke generally have markedly higher rates of morbidity and mortality than their younger counterparts. However, in-hospital mortality was actually slightly lower for patients \( \geq 80 \) years old relative to those 65 to 79 years old. That might be due to selection bias with aggressive endovascular treatment being withheld from patients \( \geq 80 \) years old unless they were deemed to be quite healthy. Similarly, decreased rates of gastrostomy and tracheostomy procedures in patients \( \geq 80 \) years old probably reflect a bias toward withdrawing care in severely neurologically disabled elderly patients rather than pursuing aggressive measures.

A number of studies have examined the effect of age on outcomes of intra-arterial management of acute stroke. With regard to age and overall outcomes, a number of studies have found that age is associated with worse outcomes after intra-arterial therapy. One study demonstrated that “futile recanalization” was more common in patients \( > 70 \) years of age.\(^6\) Loh et al\(^7\) reported increased mortality in patients \( \geq 80 \) years old (48% versus 15%) but no increase in morbidity among survivors (38% versus 40%). Several studies have examined pooled results of the Mechanical Embolus Removal in Cerebral Ischemia (MERCI) and Multi MERCI trials and have demonstrated that increasing age is associated

| Table 2. Outcomes for Endovascular Clot Retrieval Stratified by Age |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
|                             | <65 Y | 65–79 Y | P (<65 vs 65–79 Y) | 80 Y | P (65–79 Y vs 80 Y) |
| Number of patients          | 1658  | 1505   |                 | 701   |                   |
| Mean (SD) Charlson Comorbidity | 3.7 (4.4) | 6.1 (4.0) | <0.0001 | 7.3 (3.8) | <0.0001 |
| Outcomes                    |       |       |                 |       |                   |
| Discharge to long-term care, no. (%) | 789 (47.6) | 803 (53.4) | <0.0001 | 390 (55.6) | 0.69 |
| In-hospital death, no. (%)   | 283 (17.1) | 452 (30.0) | <0.0001 | 204 (29.1) | 0.99 |
| Morbidity and mortality, no. (%) | 1072 (64.7) | 1255 (83.4) | <0.0001 | 594 (84.7) | 0.46 |
| Intracranial hemorrhage, no. (%) | 320 (19.3) | 227 (15.1) | 0.002 | 118 (16.8) | 0.32 |
| Gastrointestinal hemorrhage, no. (%) | 43 (2.6) | 44 (2.9) | 0.65 | 20 (2.9) | 0.93 |
| Gastrostomy, no. (%)         | 219 (13.2) | 250 (16.6) | 0.008 | 88 (12.6) | 0.016 |
| Tracheostomy, no. (%)        | 150 (9.0) | 133 (8.8) | 0.89 | 36 (5.1) | 0.003 |
| Mean length of stay (SD)     | 10.7 (21.0) | 10.5 (19.1) | 0.86 | 9.1 (14.7) | 0.08 |
with worse overall outcomes and increased risk of mortality.\textsuperscript{8–10} These data corroborate our findings that age was associated with an increased risk of discharge to long-term facilities and increased risk of in-hospital mortality.

Although increasing age is associated with worse outcomes after intra-arterial therapy, our study confirms previous findings that the rate of intracranial hemorrhage is not primarily responsible for this difference. Three reports in the literature found that the risk of hemorrhage associated with intravenous thrombolysis does not increase with age.\textsuperscript{11–13} Furthermore, two studies found that older age was not associated with an increased risk of hemorrhagic complications after administration of intra-arterial thrombolysis.\textsuperscript{12,14}

The rate of symptomatic intracranial hemorrhage in published trials of endovascular clot retrieval is between 8\% and 11\%.\textsuperscript{2,3,15} The rate of intracranial hemorrhage in the NIS was 15.5\% without concomitant thrombolysis and 20.0\% with concomitant thrombolysis ($P=0.0009$). However, we cannot be certain whether the intracranial hemorrhages in these patients were symptomatic or asymptomatic, so it is difficult to compare with the rates of symptomatic hemorrhage that are routinely reported in other studies. Contrary to our findings showing a higher risk of hemorrhage in patients receiving concomitant thrombolytic agents, Smith et al\textsuperscript{15} reported lower rates of symptomatic hemorrhage, which were similar in patients undergoing clot retrieval with (6.7\%) concomitant thrombolysis and in those without (9.9\%) concomitant intravenous thrombolysis ($P>0.99$). The NIS results might be different from those reported by Smith et al\textsuperscript{15} because the NIS comprises a much larger population and could therefore be more sensitive for the detection of differences between subgroups. However, the increased rate of intracranial hemorrhage with concomitant thrombolytic agent identified in the NIS may be of little clinical significance because the associated rate of death was only slightly higher and the rate of discharge to long-term facilities was slightly lower in this subgroup.

One previous study also sought to estimate the nationwide use of intra-arterial thrombolysis. Qureshi et al\textsuperscript{4}examined the NIS between the years 1999 to 2001 and found a total of 1314 patients who were presumed to have undergone intra-arterial thrombolysis. They identified cases of intra-arterial thrombolysis by assuming that patients who received thrombolysis and underwent cerebral angiography were treated with intra-arterial lytic therapy.\textsuperscript{4} Unfortunately, this technique has not been validated and it is almost certainly not valid because it results in inclusion of many cases that received intravenous lytic only. Qureshi et al\textsuperscript{4} noted a mortality rate of 9.6\%, discharge to a long-term facility rate of 11.0\%, and an intracranial hemorrhage rate of 1.8\%, which are substantially better outcomes than those we found among patients undergoing clot retrieval in our study. It is likely that the cohort evaluated by Qureshi et al included a substantial proportion of patients who were not found to have large artery occlusion and thus would be expected to have a better prognosis. We decided not to use this case identification strategy because we feel it may not accurately represent patients treated with intra-arterial lytic therapy. Unfortunately, reasonably accurate counting of intra-arterial thrombolysis cases in an administrative database such as the NIS cases is not feasible with the currently available coding system.

The rapid increase in number of intra-arterially treated stroke cases from 2006 to 2008 could be due to true exponential rise in treated cases but might also be explained by the adoption of the new ICD-9 code by participating hospitals. The NIS data for 2008 shows approximately 2800 cases of endovascular clot retrieval performed that year in the United States. Although large artery occlusions make up a significant proportion of strokes, the number of cases of endovascular clot retrieval performed make up a small fraction of the approximately 700 000 strokes occurring each year in the United States.\textsuperscript{16,17} Inaccurate coding might lead to an underestimate of the number of cases, a likely possibility in the early period after introduction of a new ICD-9 code. Cases of intra-arterial thrombolysis without clot retrieval were not included in our study, which probably led to an underestimation of the overall number of stroke cases treated with an intra-arterial intervention. It is impossible to know exactly how many patients were treated with intra-arterial thrombolysis during 2006 to 2008, but we suspect that this number is lower than the actual number of endovascular clot retrieval cases because endovascular clot retrieval, since its introduction in 2004, seems to have become the strategy favored by most neurointerventionalists.

There are a number of limitations to the use of this database, largely stemming from the lack of important clinical data that could provide a more detailed explanation of outcomes. As mentioned, the NIS does not provide data in the form of modified Rankin Scale score, National Institutes of Health Stroke Scale, and 90-day mortality, so we cannot assess outcomes in the same way as is typically done in clinical trials and case series. Thus, we used discharge status as a measure of morbidity, because it has been used in previous studies.\textsuperscript{4} When assessing mortality, we cannot account for patients who received comfort care measures and may have died shortly after their hospitalization. Because of our inability to assess stroke severity, we are unable to account for the role of the natural history of the stroke itself on morbidity and mortality. Additionally, we cannot assess the appropriateness of the therapies used because there is no angiographic data or information on the timing of treatment. Coding errors are also a potential limitation of this study because they are with any study of a large administrative database.\textsuperscript{18}

### Conclusions

Endovascular clot retrieval can certainly be beneficial in the treatment of selected cases of acute ischemic stroke, but
patients undergoing these procedures still have frequent morbidity and mortality. Not more than 1 in 4 patients is discharged home or to a short-term rehabilitation facility after endovascular acute stroke therapy. Increasing age is associated with increased morbidity and mortality and concomitant use of thrombolytic agent was associated with a higher rate of intracranial hemorrhage.

Disclosures
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References
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