Endovascular revascularization is an effective therapy for acute ischemic stroke (AIS) secondary to large vessel occlusion.1–5 The number of hospitals across the country with endovascular capabilities remains relatively small,6–8 however. Consequently, endovascular interventions often take place at institutions with high procedural volume. Although the centralization of care has been associated with improved patient outcomes,6,9 it often currently necessitates transfer of endovascular candidates from the hospital of initial presentation to an endovascular center. Hospital transfer inevitably delays intervention,10 and there is evidence to suggest that prolonged travel times may blunt the benefit of treatment at specialized centers.11 For the optimal planning of endovascular treatment networks, data on whether the need for hospital transfer reduces the beneficial effect of centralization are needed. Herein, we compared the outcomes after revascularization of patients directly admitted to a low-volume center and those transferred to a high-volume center.

Methods—We searched a national database of hospital-reported outcomes for patients who underwent endovascular revascularization for acute ischemic stroke. Hospitals were categorized as low, medium, or high procedural volume hospitals. Outcomes of inpatient admissions were collected and compared on the basis of admission source and hospital procedural volume.

Results—A total of 118 institutions with 8533 patients were included. Mortality rate (14.9% versus 18.6%; P=0.049) and mortality index (1.1 versus 1.6; P=0.048) were significantly lower among directly admitted relative to transferred patients. For all patients, there were significant differences in institutional mortality rate (low: 19.7%, medium: 14.9%, high: 9.8%; P=0.003) and mortality index (low: 1.5, medium: 1.1, high: 0.8; P=0.004) between low-, medium-, and high-volume hospitals. For transferred patients to high-volume centers, both mortality rate (high: 10.0% versus low: 20.4%; P=0.005) and mortality index (high: 0.8 versus low: 1.5; P=0.034) were significantly lower than that observed for directly admitted patients to low-volume hospitals.

Conclusions—We report a beneficial effect of treatment at high-volume hospitals in spite of the detrimental effects of transfer. These findings argue for the centralization of care. (Stroke. 2017;48:1316-1321. DOI: 10.1161/STROKEAHA.116.016360.)

Key Words: cerebral hemorrhage ■ certification ■ female ■ morbidity ■ regression analysis
determined was the proportion of patients treated at each hospital aged 65 or older, the proportion of patients who were female, and the proportion of patients treated at each hospital who were transferred from another facility. The proportion of patients who received intravenous thrombolysis tPA (tissue-type plasminogen activator) while admitted to the endovascular center was determined using the ICD-9 code 9910 and ICD-10 codes E033.17 and E043.17. Information on patient and hospital characteristics was initially determined for all patients and then separately for patients directly admitted to the endovascular center and for those transferred from another hospital.

### Patient Outcomes
The primary outcome of interest was the institutional rate of mortality among patients admitted for endovascular treatment of AIS. The CDB/RM reports both observed and expected mortality, allowing the calculation of mortality index, which is the ratio of observed:expected mortality. Expected mortality is adjusted for patient demographics and comorbidities and is determined using validated risk prediction models. Secondary outcomes of interest included the rate of intracerebral hemorrhage, discharge to home, and discharge to a skilled nursing or hospice facility. Patients who suffered intracerebral hemorrhage were identified using the ICD-9 code 431 and ICD-10 codes I61, I610, I611, I612, I613, I614, I615, I616, I618, and I619.

### Determination of Low-, Medium-, and High-Volume Centers
Numeric cutoffs for the determination of low-, medium-, and high-volume centers were obtained using classification and regression tree analysis. For an independent variable, in this instance institutional procedural volume, classification and regression tree analysis determines natural cutoffs above and below which are observed the greatest differences in a dependent variable, in this case mortality index. Institutions were grouped together and defined as low-, medium-, or high-volume institutions on the basis of cutoff values determined by classification and regression tree analysis.

### Statistical Analysis
Descriptive statistics for continuous variables were reported as a mean, SD, and range. Comparisons of characteristics and outcomes of directly admitted and transferred patients treated at a given hospital were performed using the unpaired Student t test. The relationship between institutional procedural volume and mortality rate and index was performed using linear regression analysis. Comparison of patient characteristics and outcomes between low-, medium-, and high-volume centers was performed using 1-way ANOVA. Further comparison of mortality rate and index between low-, medium-, and high-volume centers was performed using the unpaired Student t test. Finally, comparison of mortality rate and index between directly admitted and transferred patients at low-, medium-, and high-volume centers was performed using the unpaired Student t test. All statistical tests were 2-sided with a 0.05 level set at 0.05 for statistical significance. Analyses were performed using commercially available software (SAS Institute Inc).

### Results

#### Baseline Characteristics
A total of 118 institutions reported outcomes from 8533 inpatient admissions for endovascular treatment of AIS that met our inclusion criteria. The mean number of cases reported by each institution was 72.3 (93.3 cases per year). The mean number of patients treated for acute stroke at each institution was 1620.8 (432.3 per year), with a mean institutional proportion of stroke cases treated with endovascular intervention of 4.5%. A majority of hospitals reporting outcomes were AAMC teaching hospitals (89.0%, 105/118). A lesser majority of institutions were certified as stroke centers (72.9%, 86/118) and had a helipad available to facilitate air transportation (73.7%, 87/118). The mean percentage of patients ≥65 years was 61.1%, whereas 49.1% were female. The mean percentage of cases of patients transferred from another facility was 36.1%. The mean percentage of patients who received intravenous tPA while admitted to the endovascular center was 34.7%. For comparison, the mean rate of intravenous tPA administration among all patients admitted for acute stroke was 6.7%. The mean rate of intracerebral hemorrhage was 18.9%. The mean mortality rate was 15.6%, whereas the mean mortality index was 1.2. The mean percentage of patients who were ultimately discharged to home was 17.2%, whereas the mean percentage of patient discharged to a skilled nursing facility or hospice was 20.2% (Table 1).

#### Transferred Versus Directly Admitted Patients
A total of 4908 patients were directly admitted, and 3625 patients were transferred. There were no differences between the frequency of patients ≥65 years (62.4% versus 58.7%; P=0.079) and female patients (48.8% versus 47.3%; P=0.554) between directly admitted and transferred patients. The percentage of directly admitted patients who received intravenous tPA at the endovascular center was significantly greater than the percentage of transferred patients (47.6% versus 17.1%; P<0.001). There was no difference in the rate of intracerebral hemorrhage between directly admitted and transferred patients (18.7% versus 17.2%; P=0.314). The rate of mortality (14.9% versus 18.6%; P=0.049) and mortality index (1.1 versus 1.6; P=0.048) was significantly lower among directly admitted relative to transferred patients. There was no difference in the rate of discharge to home between directly admitted and transferred patients (17.7% versus 16.7%; P=0.589). There was also no difference in the rate of discharge to a skilled nursing facility or hospice between directly admitted and transferred patients (21.2% versus 18.8%; P=0.227).

#### Hospital Volume and Outcomes
We observed a negative correlation between institutional procedural volume and mortality rate (r²=0.060; P=0.007) and mortality index (r²=0.043; P=0.025) on linear regression analysis. Given its significant relationship to procedural volume, mortality index was then used to divide reporting institutions into low-, medium-, and high-volume groups by means of classification and regression tree analysis. Numeric cutoffs for institutional procedural volume over the study period that yielded the greatest differences in mortality index were 27 (7.2 cases per year; ≤27=1.5 versus ≥27=1.1) and 132 cases (35.2 cases per year; ≥27<132=1.1 versus ≥132=0.8). Low-, medium-, and high-volume institutions were thus considered institutions with <27, ≥27<132, and ≥132 cases, respectively. Four-hundred and sixteen patients were treated at low-volume centers, 5616 patients were treated at medium-volume centers, and 2501 patients were treated at high-volume centers. Patient characteristics and outcomes were then compared between these groups using 1-way ANOVA (Table 2). High endovascular volume institutions had higher overall stroke volumes (low: 1015.7 cases, medium: 1699.4, high: 2632.0; P<0.001) and proportion of all stroke patients...
We observed significant differences in mortality rate (low: 19.7%, medium: 14.9%, high: 9.8%; \( P<0.003 \)) and mortality index (low: 1.5, medium: 1.1, high: 0.8; \( P=0.004 \)) across groups. In addition, significant differences existed in the rate of in-hospital intravenous tPA administration (low: 42.8%, medium: 34.8%, high: 26.4%; \( P=0.011 \)) and proportion of patients who were transferred from another hospital (low: 23.4%, medium: 38.4%, high: 51.3%; \( P=0.004 \)). The complete results of the comparisons between low-, medium-, and high-volume hospitals can be seen in Table 2.

We then further compared mortality rates and mortality indices between low-, medium-, and high-volume hospitals. Low-volume hospitals had significantly greater mortality rates and indices compared with both medium-volume (\( P=0.010; \) \( P=0.070 \)) and high-volume (\( P=0.001; \) \( P=0.003 \)) hospitals. Mortality rates and indices were not significantly different between medium- and high-volume hospitals (\( P=0.058; \) \( P=0.130; \) Table 3).

### Interaction of Volume and Transfer

Mortality rates and indices for directly admitted and transferred patients in different hospital volume groups can be seen in Table 4. Comparisons were then made between specific groups using the unpaired Student \( t \) test. The mortality rate for directly admitted patients to low-volume centers was significantly greater than the mortality rate for directly admitted patients to medium-volume centers (20.4% versus 14.2%; \( P=0.007 \)) and transferred patients to high-volume centers (20.4% versus 10.0%; \( P=0.005 \)) but was not significantly different from mortality rate for transferred patients to medium-volume centers (20.4% versus 16.8%; \( P=0.116 \)). Similarly, mortality index for directly admitted patients to low-volume centers was significantly greater than mortality index for directly admitted patients to medium-volume centers (1.5 versus 1.1; \( P=0.022 \)) and transferred patients to high-volume centers (0.9 versus 1.5; \( P=0.034 \); Table 4). In addition, mortality rate for directly admitted patients to medium-volume centers was significantly greater than that for transferred patients to high-volume centers (14.2% versus 10.0%; \( P=0.042 \)); however, there was not a significant difference in mortality index between these 2 groups (1.1 versus 0.9; \( P=0.113 \); Table 4).

To investigate the mechanism by which treatment at high-volume centers may reduce mortality, we examined the effect on mortality of certain hospital characteristics definable within the CDB/RM. We did not observe an effect of AAMC teaching hospital status (19.5% versus 15.8; \( P=0.552 \)), stroke center certification (18.7% versus 20.3%; \( P=0.713 \)), or availability of a helipad (19.5% versus 17.9%; \( P=0.726 \)) on overall mortality rate. However, there was a trend toward reduced mortality index at hospitals certified as stroke centers by the Joint Commission (1.4 versus 2.3; \( P=0.060 \), although this relationship was not statistically significant (Table 5). There was no trend toward decreased adjusted mortality at certified stroke centers when directly admitted and transferred patients were considered together (1.2 versus 1.2; \( P=0.797 \)). Of note, the proportion of high-volume hospitals that were certified stroke centers was higher than that among low-volume centers (81.8% versus 64.2%; Table 1).

### Discussion

In this study, we compared the outcomes of inpatient admissions for endovascular treatment of AIS of directly admitted and transferred patients treated at low, medium, and high procedural volume centers. Transfer from another hospital and increasing institutional procedural volume were found to be associated with...
increased and decreased mortality, respectively. Interestingly, however, we observed that patients transferred to high-volume centers had reduced mortality relative to patients directly admitted to low-volume centers, suggesting that the benefit of treatment at high-volume institutions may outweigh the detrimental effect of hospital transfer. These findings provide further evidence supporting the centralization of AIS therapy.

Previous work has found increased institutional procedural volume to be associated with reduced mortality. In addition, a study by Gupta et al found higher-volume centers to have faster times to treatment and higher reperfusion rates, translating into improved patient outcomes despite a greater proportion of patients transferring from another hospital. Although determinants of prompt reperfusion are myriad and vary on a case-by-case basis, many core policies have been consistently found to promote timely endovascular intervention. These include the routine use of computed tomographic angiography for patients presenting with symptoms above a predetermined threshold of stroke severity, the notification of the endovascular team as soon as an endovascular candidate is identified, the use of adjunctive imaging techniques, such as computed tomographic perfusion, to identify appropriate candidates in difficult cases, and the eschewing of general anesthesia for endovascular procedures. It is likely that high-volume centers implement these policies routinely and thus minimize delays to revascularization. These policies may also be particularly important for the care of transferred patients, as evidenced by the fact that stroke center certification seemed to have an effect on mortality that was evident for transferred patients only. Additional studies are needed to fully understand the benefit of treatment at high-volume centers.

We observed an increased adjusted rate of mortality among transferred patients relative to patients directly admitted to an endovascular center. Results of previous studies examining differences in outcome after revascularization between directly admitted and transferred patients have been mixed, with 2 studies alternatively detecting a slightly negative and no effect. Both studies reported longer times from stroke onset to intervention among transferred patients, which could explain a negative association between transfer and functional outcomes. Both were single-center studies, and thus their results were likely influenced by the breadth of the institutional catchment area and local protocols for the identification and transfer of patients with large vessel occlusion. While lacking the granularity of previous work, this study allows the gauging of the effect of transfer across a fairly large number

### Table 2. Comparison of Demographics and Outcome of Low-, Medium-, and High-Volume Centers

<table>
<thead>
<tr>
<th>Variable</th>
<th>Low</th>
<th>Medium</th>
<th>High</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (\geq 65), % (SD)</td>
<td>58.1 (18.0)</td>
<td>61.9 (8.7)</td>
<td>63.1 (8.6)</td>
<td>0.274</td>
</tr>
<tr>
<td>Female, % (SD)</td>
<td>49.4 (16.2)</td>
<td>48.7 (7.4)</td>
<td>50.4 (4.7)</td>
<td>0.849</td>
</tr>
<tr>
<td>Transfers, % (SD)</td>
<td>23.4 (24.3)</td>
<td>38.4 (24.3)</td>
<td>51.3 (25.8)</td>
<td>0.004</td>
</tr>
<tr>
<td>Total stroke volume, mean (SD)</td>
<td>1015.7 (504.8)</td>
<td>1699.4 (691.7)</td>
<td>2632.0 (815.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% endovascular, mean (SD)</td>
<td>1.9 (1.3)</td>
<td>4.8 (2.2)</td>
<td>8.9 (4.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>tPA, % (SD)</td>
<td>42.8 (19.8)</td>
<td>34.8 (15.0)</td>
<td>26.4 (13.0)</td>
<td>0.011</td>
</tr>
<tr>
<td>tPA among all strokes, % (SD)</td>
<td>6.8 (2.4)</td>
<td>6.7 (3.2)</td>
<td>6.1 (3.4)</td>
<td>0.804</td>
</tr>
<tr>
<td>Hemorrhage rate, % (SD)</td>
<td>18.3 (12.0)</td>
<td>18.9 (7.1)</td>
<td>18.2 (4.5)</td>
<td>0.924</td>
</tr>
<tr>
<td>Mortality rate, % (SD)</td>
<td>19.7 (12.7)</td>
<td>14.9 (6.7)</td>
<td>9.8 (3.7)</td>
<td>0.003</td>
</tr>
<tr>
<td>Mortality index (SD)</td>
<td>1.5 (0.9)</td>
<td>1.1 (0.5)</td>
<td>0.8 (0.3)</td>
<td>0.004</td>
</tr>
<tr>
<td>Discharge to home, % (SD)</td>
<td>16.1 (11.5)</td>
<td>16.9 (6.5)</td>
<td>21.5 (6.7)</td>
<td>0.155</td>
</tr>
<tr>
<td>Discharge to SNF, % (SD)</td>
<td>21.6 (12.5)</td>
<td>19.5 (8.4)</td>
<td>21.4 (8.0)</td>
<td>0.566</td>
</tr>
</tbody>
</table>

SNF indicates skilled nursing facility; and tPA, tissue-type plasminogen activator.

### Table 3. Comparison of Mortality Between Low-, Medium-, and High-Volume Centers*

<table>
<thead>
<tr>
<th>Group</th>
<th>Mortality rate, % (SD)</th>
<th>Comparison</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low: cases &lt;27 (n=28)</td>
<td>19.7 (12.7)</td>
<td>L to M</td>
<td>0.010</td>
</tr>
<tr>
<td>Medium: cases ≥27–&lt;132 (n=79)</td>
<td>14.9 (6.7)</td>
<td>L to H</td>
<td>0.001</td>
</tr>
<tr>
<td>High: cases ≥132 (n=11)</td>
<td>9.8 (9.8)</td>
<td>M to H</td>
<td>0.058</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>Mortality index, (SD)</th>
<th>Comparison</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low: cases &lt;27 (n=28)</td>
<td>1.5 (0.9)</td>
<td>L to M</td>
<td>0.007</td>
</tr>
<tr>
<td>Medium: cases ≥27–&lt;132 (n=79)</td>
<td>1.1 (0.5)</td>
<td>L to H</td>
<td>0.003</td>
</tr>
<tr>
<td>High: cases ≥132 (n=11)</td>
<td>0.8 (0.3)</td>
<td>M to H</td>
<td>0.130</td>
</tr>
</tbody>
</table>

Hi indicates high; L, low; and M, medium.

*Low, medium, and high procedural volume determined by number of cases performed over >45-mo study period.
ties with endovascular capabilities. Strategies to counteract implications for the endovascular treatment of AIS, mainly effect needs to be confirmed, an association of transfer with of endovascular centers. Although the generalizability of this effect needs to be confirmed, an association of transfer with worse outcomes after revascularization would have significant implications for the endovascular treatment of AIS, mainly because of the limited current number of healthcare facilities with endovascular capabilities. Strategies to counteract a detrimental effect of transfer would potentially include an increase in the number of endovascular centers, allowing more frequent direct admission to an endovascular facility. Our finding that patients transferred to high-volume centers had lower mortality than patients directly admitted to a low-volume center suggests, however, that a greater number of facilities each performing a small number of procedures may not necessarily improve patient outcomes, and that transfer to an experienced center may provide the best chance for beneficial endovascular intervention. To mitigate and potentially avoid the inevitable delay associated with transfer, however, strategies to identify patients with large vessel occlusion before admission at a primary center should be devised and implemented to facilitate direct admission to an endovascular center whenever feasible.

Access to high-volume centers is likely limited to a small proportion of the general population of the United States. Among the 135 institutions reporting outcomes after endovascular intervention, only 8.1% (11/135; 17 were excluded from analysis because of reporting outcomes from <5 admission) met our criteria for high volume (>132 cases over the study period; 35.2 cases per year). Whether or not the observed proportion of institutions classified as high volume in our study is representative of the true number of high-volume institutions across the country is difficult to assess. A nationwide longitudinal analysis of trends in stroke care identified 454 hospitals offering endovascular intervention from 2003 to 2013. Among these institutions, only 99 provided continuous access to endovascular intervention. In a study using the Nationwide Inpatient Sample, 296 hospitals offering endovascular intervention were identified. Of these hospitals, only 78 performed >10 procedures in the year 2008, with only 4 meeting our criteria for high volume. Although the availability of endovascular therapy has likely increased in the recent past, these figures suggest that the actual number of high-volume institutions around the country is likely to be small and perhaps not much greater than the number of institutions meeting criteria for high volume in our study.

**Limitations**

A major limitation of our study is the lack of information on preprocedural National Institutes of Health (NIH) stroke scale. NIH stroke scale is a strong predictor of successful revascularization and subsequent good functional outcome, and thus it is possible that baseline differences in NIH stroke scale may have contributed to observed differences in mortality between directly admitted and transferred patients and between low-, medium-, and high-volume centers. In addition, our study is limited by the lack of data on patient functional outcomes after hospital discharge. Although identifying factors predisposing to in-hospital mortality is necessary to improve standards of stroke care, the inability to isolate severely disabled patients who nevertheless survived their admission hampers our ability to gauge the full effect of admission source and treatment at a low- versus high-volume institution.

We also observed marked differences in the rate of intravenous tPA administration between directly admitted and transferred patients. We suspect that a large number of transferred patients received intravenous tPA before transferring to an endovascular center, and thus their admission to the receiving
hospital would not be labeled with the ICD-9 and ICD-10 codes for intravenous tPA administration, likely accounting for at least part of the difference between directly admitted and transferred patients. Nevertheless, it is possible that baseline differences existed between directly admitted and transferred patients. Proper patient identification was dependent on accurate diagnostic and procedural coding, the recording of which is susceptible to clerical errors. Outcomes to the CDB/RM are self-reported by affiliated institutions and not subject to mandatory reporting policies, and thus the number of reported cases may not accurately reflect the total number of cases that occurred during the study period. This may have led to the incorrect categorization of certain institutions as low, medium, or high procedural volume. The lack of mandatory reporting policies also allows for the possibility that our results were influenced by selection bias.

Finally, our study is based on data from admissions occurring between 2012 and 2016. Within that time frame, the standard of care for AIS because of large vessel occlusion has evolved to include endovascular intervention when appropriate. The pooling of data from time periods before and after the validation of endovascular therapy may have led to the grouping of institutions for whom different criteria for endovascular eligibility were used, potentially affecting our results. For example, before the general acceptance of endovascular therapy, certain institutions may have reserved endovascular intervention only for patients with the most severe deficits carrying an already high risk of mortality. Information on institutional criteria for selecting endovascular candidates was not available, and thus we were unable to account for how differences in selection criteria over time, as well as interinstitutional differences, might have influenced observed mortality rates.

Conclusions
We observed a reduced rate of mortality among patients treated with endovascular revascularization for AIS who were transferred to high-volume centers relative to those directly admitted to low-volume centers. These findings suggest that the benefit of greater institutional experience may mitigate the delay in reperfusion associated with hospital transfer and argue for the centralization of AIS care.

Disclosures
None.

References
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Lorenzo Rinaldo, Waleed Brinjikji and Alejandro A. Rabinstein

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