Stroke and Outcomes in Patients With Acute Type A Aortic Dissection

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Background—Stroke is a highly dreaded complication of type A acute aortic dissection (TAAAD). However, little data exist on its incidence and association with prognosis.

Methods and Results—We evaluated 2202 patients with TAAAD (mean age 62±14 years, 1487 [67.5%] men) from the International Registry of Acute Aortic Dissection to determine the incidence and prognostic impact of stroke in TAAAD. Stroke was present at arrival in 132 (6.0%) patients with TAAAD. These patients were older (65±12 versus 62±15 years; \(P=0.002\)) and more likely to have hypertension (86% versus 71%; \(P=0.001\)) or atherosclerosis (29% versus 22%; \(P=0.04\)) than patients without stroke. Chest pain at arrival was less common in patients with stroke (70% versus 82%; \(P<0.001\)), and patients with stroke presented more often with syncope (44% versus 15%; \(P<0.001\)), shock (14% versus 7%; \(P=0.005\)), or pulse deficit (51% versus 29%; \(P=0.001\)). Arch vessel involvement was more frequent among patients with stroke (68% versus 37%; \(P<0.001\)). They had less surgical management (74% versus 85%; \(P<0.001\)). Hospital stay was significantly longer in patients with stroke (median 17.9 versus 13.3 days; \(P<0.001\)). In-hospital complications, such as hypotension, coma, and malperfusion syndromes, and in-hospital mortality (adjusted odds ratio, 1.62; 95% confidence interval, 1.62; 95% confidence interval, 0.46–2.89). Among hospital survivors, follow-up mortality was similar between groups (adjusted hazard ratio, 1.15; 95% confidence interval, 0.46–2.65) were higher among patients with stroke. Among hospital survivors, follow-up mortality was similar between groups (adjusted hazard ratio, 1.15; 95% confidence interval, 0.46–2.89).

Conclusions—Stroke occurred in >1 of 20 patients with TAAAD and was associated with increased in-hospital morbidity but not long-term mortality. Whether aggressive early invasive interventions will reduce negative outcomes remains to be evaluated in future studies. (Circulation. 2013;128[suppl 1]:S175-S179.)

Key Words: aortic dissection ■ mortality ■ stroke management

Stroke is a highly dreaded complication of type A acute aortic dissection (TAAAD). Brain tissue ischemia from hypotension and direct compromise of cerebral circulation are believed to be the underlying mechanisms of stroke in patients with TAAAD. Single-center studies of few patients have reported a stroke incidence between 3% and 32% and demonstrated increased morbidity and mortality in these patients. Accordingly, we evaluated a large cohort of >2000 patients with TAAAD enrolled in the International Registry of Acute Aortic Dissection (IRAD) to determine the incidence, presentation, management, prognosis, and outcomes of stroke in this cohort.

Methods

Study Population
We analyzed data on 2202 TAAAD IRAD patients enrolled from January 1, 1996, to August 18, 2012, at 25 aortic centers. The structure and methods of IRAD have been previously published. Patients were identified prospectively at presentation and retrospectively via discharge diagnoses, imaging, and hospital databases. Diagnosis was confirmed by imaging, surgical visualization, or autopsy. Each site’s institutional review committee approved participation.

Data Collection and Definitions
Data on 290 variables were recorded on a standardized form detailing demographics, history, clinical presentations, imaging results,
treatment, and outcomes. TAAAD was defined as any nontraumatic dissection of the aorta proximal to the left subclavian artery presenting within 14 days of symptom onset. Stroke was defined in the database lexicon as a cerebrovascular accident representing a loss of neurological function (loss or slurring of speech, altered state of consciousness) caused by an ischemic event, confirmed by computed tomography or MRI. This definition of stroke was formulated to be conservative, considering that not all patients had routine neurological consults postdissection. Therefore, we have probably somewhat underestimated the incidence of less obvious neurological injuries. Other definitions were similar to those in previous publications.6–8

Statistical Analysis
Data are shown as frequencies and percentages, means±SD, or medians with first and third quartiles. Univariate comparisons between patients with and without stroke were performed using the χ² test for categorical data and Student t test for continuous variables with normal data distributions. Nonparametric test of medians was used for data with skewed distributions. In all cases, missing data were not defaulted to negative, and denominators reflect cases for which information was reported. Binary logistic regression analysis was performed to determine the independent correlates of presenting stroke and to assess the independent association of presenting stroke with in-hospital mortality. Cox proportional hazard models were used to identify the independent association of presenting stroke with in-hospital mortality. Odds ratios and hazard ratios with their corresponding 95% confidence intervals were generated to provide an estimate of these associations. All P values were 2-sided, with values <0.05 considered statistically significant. Analyses were performed using SPSS 20.0 statistical analysis software (IBM Corporation).

Results
Incidence, Demographics, History, and Clinical Symptoms and Signs
Among 2202 patients with TAAAD enrolled in IRAD, 132 (6.0%) had stroke at presentation (Table 1). These patients were older, with only 1 stroke patient <40 years of age. A history of hypertension was 1.2× more common in patients with stroke, and atherosclerosis was 1.4×-fold higher in the stroke cohort compared with nonstroke patients. Presentation with chest or back pain was less frequent, whereas presentation with syncope was 3-fold higher among TAAAD patients with stroke. Shock and pulse deficit were 2-fold higher, and the combination of shock, hypotension, and cardiac tamponade was 1.4× higher among patients with stroke. Other demographics, clinical features, and presenting symptoms were similar between groups (Table 2).

Diagnostic Imaging and Use of Medications
The use of diagnostic imaging techniques was similar in patients with and without stroke. Chest radiograph, ECG, and imaging study findings were also similar between cohorts, with the exception of more arch involvement in patients with stroke (Table 3).

Complications and In-Hospital Mortality
In-hospital complications, such as hypotension and coma, were significantly higher in patients with stroke, who also demonstrated a trend toward greater incidence of malperfusion syndrome (Table 5). Although almost all other complications were higher in patients with stroke, these differences did not reach statistical significance. Median length of stay was 4.8 days longer in patients with stroke (17.8 days with stroke, Q1–Q3: 12.1–31.1 days; 13.0 days without, Q1–Q3: 8.6–21.0 days; P<0.001). Finally, overall mortality was 1.8-fold higher in patients with stroke (adjusted odds ratios, 1.62; 95% confidence interval, 0.99–2.65; P=0.055). Mortality was higher in patients with stroke compared with nonstroke patients with

Table 2. Presenting Sign and Symptoms in TAAAD Patients With and Without Stroke

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall n (%)</th>
<th>Stroke n (%)</th>
<th>No Stroke n (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presenting symptoms and signs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest pain</td>
<td>1744 (81.6)</td>
<td>85 (69.7)</td>
<td>1659 (82.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Back pain</td>
<td>889 (42.8)</td>
<td>36 (32.4)</td>
<td>853 (43.4)</td>
<td>0.023</td>
</tr>
<tr>
<td>Abrupt onset of pain</td>
<td>1729 (83.4)</td>
<td>95 (84.1)</td>
<td>1634 (83.4)</td>
<td>0.85</td>
</tr>
<tr>
<td>Migrating pain</td>
<td>284 (14.1)</td>
<td>17 (16.0)</td>
<td>267 (14.0)</td>
<td>0.56</td>
</tr>
<tr>
<td>Syncope</td>
<td>358 (17.0)</td>
<td>54 (43.5)</td>
<td>304 (15.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>151 (6.9)</td>
<td>10 (8.1)</td>
<td>141 (6.9)</td>
<td>0.61</td>
</tr>
<tr>
<td>Mean systolic blood pressure=SD mm Hg</td>
<td>122.3±18.2</td>
<td>127.7±41.6</td>
<td>122.1±16.3</td>
<td>0.31</td>
</tr>
<tr>
<td>Mean diastolic blood pressure=SD mm Hg</td>
<td>69.7±11.4</td>
<td>69.3±10.3</td>
<td>69.7±11.4</td>
<td>0.80</td>
</tr>
<tr>
<td>Shock</td>
<td>154 (7.4)</td>
<td>17 (13.8)</td>
<td>137 (7.0)</td>
<td>0.005</td>
</tr>
<tr>
<td>Hypotension/tamponade/shock</td>
<td>565 (27.2)</td>
<td>46 (37.4)</td>
<td>519 (26.5)</td>
<td>0.009</td>
</tr>
<tr>
<td>Any pulse deficit</td>
<td>504 (29.9)</td>
<td>54 (50.5)</td>
<td>450 (28.5)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

IRAD indicates International Registry of Acute Aortic Dissection.
similar management. Among hospital survivors, follow-up mortality (median follow-up 2 years, Q1–Q3: 1–4 years) was not different between groups (adjusted hazard ratio, 1.15; 95% confidence interval, 0.46–2.89; \( P=0.76 \)). Estimates using Cox proportional hazard model suggested excellent 5-year survival (median follow-up 2 years, Q1–Q3: 1–4 years) was similar between groups, with the lower use of in-hospital medical therapies in hospital and at discharge were similar in the 2 groups, with the lower use of in-hospital medical therapies in hospital and at discharge were similar in the 2 groups, with the lower use of in-hospital medical therapies in hospital and at discharge were similar in the 2 groups, with the lower use of in-hospital medical therapies in hospital and at discharge were similar in the 2 groups, with the lower use of in-hospital medical therapies in hospital and at discharge were similar in the 2 groups, with the lower use of in-hospital medical therapies in hospital and at discharge were similar in the 2 groups, with the lower use of in-hospital medical therapies in hospital and at discharge were similar in the 2 groups, with the lower use of in-hospital medical therapies in hospital and 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Variable Odds Ratio Lower Upper Wald χ² P Value
Any arch vessel involvement 3.393 1.932 5.961 18.063 <0.001
Syncope on presentation 3.117 1.781 5.457 15.845 <0.001
History of hypertension 3.275 1.450 7.397 8.149 0.004
Abdominal pain on presentation 0.347 0.165 0.729 7.800 0.005
Any pulse deficit 2.019 1.172 3.479 6.410 0.011
Abnormal chest radiograph without associated pain 1.932 1.077 3.466 4.874 0.027

Hosmer–Lemeshow test P=0.525. C=0.780. CI indicates confidence interval; and TAAAD, type A acute aortic dissection.

**Table 7. Independent Clinical Correlate of In-hospital Death Among TAAAD Patients Presenting With Stroke**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>Lower</th>
<th>Upper</th>
<th>Wald χ²</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥70 y</td>
<td>1.622</td>
<td>0.379</td>
<td>6.937</td>
<td>0.426</td>
<td>0.514</td>
</tr>
<tr>
<td>Surgical management</td>
<td>0.015</td>
<td>0.002</td>
<td>0.129</td>
<td>14.555</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coma</td>
<td>10.081</td>
<td>1.317</td>
<td>77.161</td>
<td>4.952</td>
<td>0.026</td>
</tr>
<tr>
<td>Pleural effusion on any test</td>
<td>4.303</td>
<td>1.031</td>
<td>17.959</td>
<td>4.007</td>
<td>0.045</td>
</tr>
<tr>
<td>Any pulse deficit</td>
<td>6.629</td>
<td>1.483</td>
<td>29.624</td>
<td>6.130</td>
<td>0.013</td>
</tr>
<tr>
<td>Mesenteric ischemia</td>
<td>47.605</td>
<td>3.458</td>
<td>655.452</td>
<td>8.336</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Hosmer–Lemeshow test P=0.387. C=0.908. CI indicates confidence interval; and TAAAD, type A acute aortic dissection.

Our findings may have several implications for patients with TAAAD and presenting stroke. In addition to chest or back pain preceding the stroke, this and other studies suggest that a high index of suspicion should also be made for TAAAD in stroke patients who present with syncope, hypotension, pulse deficit, and a murmur of aortic regurgitation. In patients with these symptoms, early imaging would enable diagnosis of TAAAD if present and help prevent inadvertent use of fibrinolytic therapy that could lead to fatal outcomes in this cohort.10,12,17–19

Urgent surgical repair is required for TAAAD because conservative management is associated with a high incidence of early mortality.4 However, some studies have suggested that immediate surgical repair of TAAAD in the presence of stroke has a prohibitive risk associated with hemorrhagic worsening of an ischemic infarction after reperfusion subsequent to cardiopulmonary bypass and full anticoagulation.20,21 Others have suggested that delaying repair until cerebral injury stabilizes may minimize these concerns, albeit exposing patients to an early hazard of death from rupture.22 However, Fann et al1 reported no worsening of cerebral symptoms in 7 surgically treated patients with TAAAD. Several small studies have since corroborated the feasibility and safety of early surgical repair in TAAAD patients with stroke.9,11,16,23,24 In fact, 1 study suggested no benefit of surgery beyond 12 hours when cerebral damage is almost complete.16 Deeb et al25 have suggested good results with a hybrid approach involving fenestrations for immediate percutaneous reperfusion followed by surgery after the brain tissue has healed. Although our data suggest that surgically treated TAAAD patients with stroke had higher mortality than those without stroke, surgical patients had much lower mortality than patients treated medically, regardless of whether they presented with stroke. Furthermore, adjusted survival estimates for patients with TAAAD suggested that among surgically treated patients with TAAAD discharged alive at index hospitalization, ≈4 of 5 patients survived at 5-year follow-up, whereas long-term outcomes were dismal among stroke patients treated medically (100% mortality). Our results and those of previous studies suggest, compared with medical therapy, that definitive early repair in TAAAD patients presenting with stroke is safe and likely associated with lower short- and long-term mortality. Further studies are warranted in TAAAD patients presenting with stroke to determine which stroke patients will benefit more from surgery and whether or not stroke severity impacts outcomes. In addition, analyses should be performed to determine the optimal timing of surgery (early versus late) and to compare outcomes between surgical strategies used in this cohort.

**Limitations**

Patients in this study had TAAAD and were admitted to centers specializing in aortic disease. Thus, our results may not be applicable to those with chronic TAAAD, type B AAD,
or those treated at smaller centers. IRAD data are collected retrospectively and prospectively through voluntary site participation and are subject to incomplete information, particularly with regard to long-term outcomes. As such, some strokes may have not been adequately captured in the registry. Furthermore, because IRAD is composed of tertiary care centers, patients with TAAAD and stroke who died at primary care centers or who were unable to be transferred secondary to their acute illness were not included. Treatment strategies were not protocol driven and were determined by the treating physicians. Thus, inference regarding the effectiveness of various strategies on outcomes in these patient cohorts should be made with caution. Imaging results were based on interpretation at the IRAD center and were not independently adjudicated. We are also unable to provide any details on stroke size, extent of debilitation after stroke, or improvement or resolution of neurological symptoms.

Conclusions
Stroke occurred in >1 of 20 patients with TAAAD and was associated with increased morbidity and in-hospital mortality, but not higher long-term mortality among survivors. Our data suggest that aggressive early intervention with rapid establishment of cerebral flow and surgical repair of dissection have significant potential for reducing morbidity and improving mortality.

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Disclosures
None.

References
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