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).

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.1 Single-center studies of few patients have reported a stroke incidence between 3% and 32% and demonstrated increased morbidity and mortality in these patients.2–5 Accordingly, we evaluated a large cohort of >2000 patients with TAAAD enrolled in the International Registry of Acute Aortic Dissection (IRAD)6–8 to determine the incidence, presentation, management, prognosis, and outcomes of stroke in this cohort.

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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.1–8 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, imaging results, and in-hospital complications and outcomes. The Primary End Point was in-hospital mortality. The incidence of stroke was the critical secondary end point.

Data analysis

Mortality and stroke were selected as the key outcomes because of their high clinical and public health relevance. Risk factors for mortality and stroke were selected a priori.

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treatment, and outcomes. TAAAD was defined as any nontraumatic
dissection of the aorta proximal to the left subclavian artery pre-
senting 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 neurologi-
cal 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
under estimated the incidence of less obvious neurological injuries.
distributions. Nonparametric test of medians was used for data with
skewed distributions. In all cases, missing data were not defaulted to
negative, and deno minators reflect cases for which information was
reported. Binary logistic regression analysis was performed to deter-
mine the independent correlates of presenting stroke and to assess the
independent association of presenting stroke with in-hospital mortal-
ity. Cox proportional hazard models were used to identify the inde-
pendent association of stroke with long-term mortality among patients
discharged alive at hospitalization. Odds ratios and hazard ratios with
their corresponding 95% confidence intervals were generated to pro-
vide an estimate of these associations. All P values were 2-sided, with
values <0.05 considered statistically significant. Analyses were per-
formed 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

Table 1. Patient Characteristics in TAAAD Patients With and
Without Presenting 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>Demographics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean±SD, y</td>
<td>61.3±14.4</td>
<td>65.0±11.5</td>
<td>61.7±14.6</td>
<td>0.002</td>
</tr>
<tr>
<td>Age &lt;40 y</td>
<td>167 (7.6)</td>
<td>1 (0.8)</td>
<td>166 (8.0)</td>
<td>0.002</td>
</tr>
<tr>
<td>Male</td>
<td>1487 (67.5)</td>
<td>82 (62.1)</td>
<td>1405 (67.9)</td>
<td>0.17</td>
</tr>
<tr>
<td>White</td>
<td>1837 (80.9)</td>
<td>109 (88.6)</td>
<td>1728 (89.1)</td>
<td>0.88</td>
</tr>
<tr>
<td>Transferred to IRAD sites</td>
<td>1654 (75.1)</td>
<td>95 (72.0)</td>
<td>1559 (75.3)</td>
<td>0.39</td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marfan syndrome</td>
<td>88 (4.1)</td>
<td>2 (1.6)</td>
<td>86 (4.3)</td>
<td>0.14</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1554 (72.3)</td>
<td>110 (85.9)</td>
<td>1444 (71.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cocaine abuse</td>
<td>27 (1.3)</td>
<td>2 (1.6)</td>
<td>25 (1.3)</td>
<td>0.68</td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td>470 (22.1)</td>
<td>37 (29.4)</td>
<td>433 (21.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>Bicuspid aortic valve</td>
<td>86 (4.6)</td>
<td>7 (6.4)</td>
<td>79 (4.5)</td>
<td>0.38</td>
</tr>
<tr>
<td>Iatrogenic dissection</td>
<td>56 (2.6)</td>
<td>1 (0.8)</td>
<td>55 (2.8)</td>
<td>0.26</td>
</tr>
<tr>
<td>Prior aortic dissection</td>
<td>89 (4.2)</td>
<td>4 (3.1)</td>
<td>85 (4.2)</td>
<td>0.56</td>
</tr>
<tr>
<td>Prior aortic aneurysm</td>
<td>269 (12.6)</td>
<td>13 (10.3)</td>
<td>256 (12.7)</td>
<td>0.43</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>125 (5.9)</td>
<td>10 (7.8)</td>
<td>115 (5.7)</td>
<td>0.33</td>
</tr>
<tr>
<td>Prior cardiovascular surgery</td>
<td>291 (13.5)</td>
<td>12 (9.5)</td>
<td>279 (14.0)</td>
<td>0.15</td>
</tr>
</tbody>
</table>

IRAD indicates International Registry of Acute Aortic Dissection.

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 excep-
tion of more arch involvement in patients with stroke (Table 3).

Patients with stroke had lower in-hospital â-blocker use;
otherwise, use of e evidence-based medical therapies at presen-
tation and discharge was similar between groups (Table 4). Patients with stroke were twice as likely to undergo nonopera-
tive management compared with those without stroke.

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 malperfu-
sion 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% confi-
dence 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>PValue</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>Ablupt 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 mmHg</td>
<td>122.3±18.2</td>
<td>122.7±16.1</td>
<td>122.1±16.3</td>
<td>0.31</td>
</tr>
<tr>
<td>Mean diastolic blood pressure±SD mmHg</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>

TAAAD indicates type A 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 in 4 of 5 TAAAD surgically treated stroke patients who survived past index hospitalization; conversely, 5-year survival among medically managed stroke patients was dismal (estimated mortality of 100%).

**Independent Clinical Correlates of Presenting Stroke and In-Hospital Mortality**

Arch vessel involvement on imaging was the greatest predictor of stroke (Table 6). In addition, syncope, abdominal pain, presenting pulse deficit, abnormal chest radiograph without accompanying pain, and history of hypertension had significant independent adjusted correlations with stroke in our cohort.

In TAAAD patients presenting with stroke, surgical management had strong independent adjusted associations with improved survival (Table 7). Variables with independent adjusted associations with decreased survival included coma, pleural effusion, pulse deficit on presentation, and mesenteric ischemia.

**Discussion**

Our study, the largest to date, suggests that stroke at hospital admission is observed in 6% of patients with TAAAD. These patients were older, more often had hypertension and atherosclerosis, and presented more frequently with symptoms such as syncope rather than the more classic presentation of chest or back pain. Patients with stroke were also likely to have signs of hypotension, shock, and pulse deficit. Except for the association of arch involvement, imaging study findings were similar between groups. Medical therapies in hospital and at discharge were similar in the 2 groups, with the lower use of in-hospital β-blocker among stroke patients likely a reflection of the more frequent hypotension and shock in these patients. Patients with stroke were more likely to be managed medically and had greater length of stay. In-hospital mortality was higher in patients with stroke compared with nonstroke patients, regardless of the management strategy; however, postdischarge mortality did not differ between groups.

Few studies have focused on stroke in patients with TAAAD, most of which are single-center case reports, evaluating a small number of patients with few stroke events. These studies described a stroke incidence between 3% and 32% in 24 to 174 patients with TAAAD. Similar to our findings, some studies reported more frequent painless presentation, syncope, and hypotension in patients with stroke. Furthermore, most studies suggested a higher mortality for patients with stroke compared with those without it. Most of these reports focused primarily on patients undergoing surgery, and many did not characterize the factors associated with risk of presenting stroke and mortality in those with stroke.
In-hospital complications

In-hospital mortality

Overall 555 (25.2) 56 (42.4) 599 (24.1) <0.001
Surgically treated patients 371 (19.9) 30 (30.9) 341 (19.3) 0.005
Medically treated patients 184 (36.3) 24 (77.4) 160 (31.7) 0.012
5-year mortality estimate (Kaplan–Meier)
Overall 17.6% 24.1% 17.2% 0.30
Surgery 14.1% 22.1% 14.1% 0.51
Medical therapy only 62.0% 100.0% 58.7% 0.56

TAAAD indicates 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.6 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 al3 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.5,9,11,16,23,24 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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