Larger A1/M1 Diameter Ratio Predicts Embolic Anterior Cerebral Artery Territorial Stroke

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**Background and Purpose**—In contrast to middle cerebral artery territory strokes, anterior cerebral artery strokes (ACAS) occur rarely. The low frequency of ACAS, in relation to middle cerebral artery territory strokes, may be explained by differences in ACA and middle cerebral artery anatomy influencing their respective flow-directed embolism rates. We aimed to determine whether variability in ACA anatomy, and in particular A1 segment diameter, is associated with embolic ACAS.

**Methods**—Consecutive patients admitted to Boston Medical Center with embolic ACAS were reviewed. Ipsilateral and contralateral A1 diameters, M1 diameters, and terminal internal carotid artery bifurcation angles were measured from computed tomographic angiography and MRI angiography images. We compared these measurements between cases of ACAS and consecutive cases of embolic middle cerebral artery territory strokes.

**Results**—The study comprised 55 individuals (27 ACAS, 28 middle cerebral artery territory strokes) with mean age of 69 years. In multivariate regression analysis, larger ipsilateral A1 diameters (odds ratio per 1 mm increment: 8.5; 95% confidence interval, 1.4–53.3) and ipsilateral A1/M1 diameter ratio (odds ratio per 10% increment: 1.8; 95% confidence interval, 1.2–2.9) were associated with ACAS, whereas larger ipsilateral M1 diameters was protective for ACAS (odds ratio per 1 mm increment: 0.8; 95% confidence interval, 0.0–0.9).

**Conclusions**—Larger ipsilateral A1 diameters and A1/M1 diameter ratio are associated with embolic ACAS. These findings suggest that A1 diameters and M1 diameters are important in determining the path of emboli that reach the terminal internal carotid artery. *(Stroke. 2014;45:00-00.)*

**Key Words:** cerebral infarction ▪ cerebrovascular circulation ▪ embolism ▪ hemodynamics

In contrast to middle cerebral artery territory strokes (MCAS), anterior cerebral artery strokes (ACAS) occur rarely.1,2 As a large proportion of infarcts in both vascular territories result from embolic pathogeneses, it has been postulated that anatomic differences between the ACA and MCA influence their respective flow-directed embolism rates.3,4 However, the specific vascular anatomic parameters that govern the path of flow-directed emboli that reach the terminal internal carotid artery (ICA) have yet to be fully determined.

Poiseuille equation states that flow through a cylindrical tube is proportional to its radius to the fourth power. Consequently, a small change in vessel diameter will have a significant impact on blood flow. Accordingly, we aimed to determine whether individual variability in ACA and MCA diameters are associated with embolic ACAS. We hypothesized that cases of ACAS have larger ipsilateral A1 segment diameters (A1D) and A1/M1 diameter ratios than cases of MCAS.

**Methods**

**Study Design**

This is a retrospective cross-sectional analysis of consecutive cases of ischemic stroke captured in the Boston Medical Center Stroke Database. Approval for the study was obtained from the Boston Medical Center Institutional Review Board.

**Study Population and Data Collection**

Consecutive patients admitted to Boston Medical Center with nonlacunar ischemic strokes involving the ACA territory between January 2008 and October 2012 were reviewed (84/624 ischemic strokes). Consecutive patients admitted between January 2012 and October 2012 with nonlacunar strokes involving the MCA territory served as controls (56/257 ischemic strokes). All territorial strokes were confirmed on neuroimaging. Excluded were patients with nonembolic stroke pathogeneses (n=13), cases where arterial measurements were unobtainable (n=23), the causative artery was questionable (n=20), and cases with concomitant ipsilateral ACAS and MCAS (n=29).

Hospital admission records were reviewed for demographic information and vascular risk factors. Ipsilateral carotid stenosis was

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Table 1. Demographics and Arterial Measurements in ACA Compared With MCA Strokes

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>ACA Strokes (n=27)</th>
<th>MCA Strokes (n=28)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, mean (SD)</td>
<td>70.6 (±11.5)</td>
<td>67.9 (±14.7)</td>
<td>&gt;0.20</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>15 (56%)</td>
<td>16 (57%)</td>
<td>&gt;0.20</td>
</tr>
<tr>
<td>Vascular risk factors n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>18 (67%)</td>
<td>12 (43%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Hypertension</td>
<td>23 (79%)</td>
<td>22 (85%)</td>
<td>&gt;0.20</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>20 (74%)</td>
<td>18 (64%)</td>
<td>&gt;0.20</td>
</tr>
<tr>
<td>Smoking</td>
<td>13 (48%)</td>
<td>13 (46%)</td>
<td>&gt;0.20</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>9 (33%)</td>
<td>6 (21%)</td>
<td>&gt;0.20</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>4 (15%)</td>
<td>12 (43%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Ipsilateral carotid stenosis (&gt;50%)</td>
<td>4 (15%)</td>
<td>5 (18%)</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>Ipsilateral arterial measurements mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A1 diameter, mm</td>
<td>2.5 (±0.5)</td>
<td>2.1 (±0.5)</td>
<td>0.003</td>
</tr>
<tr>
<td>M1 diameter, mm</td>
<td>2.6 (±0.5)</td>
<td>2.9 (±0.5)</td>
<td>0.11</td>
</tr>
<tr>
<td>A1/M1 diameter ratio</td>
<td>1.0 (±0.2)</td>
<td>0.7 (±0.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICA-ACA angle, °</td>
<td>109 (±13)</td>
<td>108 (±18)</td>
<td>&gt;0.20</td>
</tr>
<tr>
<td>ICA-MCA angle, °</td>
<td>142 (±16)</td>
<td>136 (±14)</td>
<td>0.15</td>
</tr>
<tr>
<td>ICA-ACA/ICA-MCA angle ratio, mean (SD)</td>
<td>0.8 (±0.2)</td>
<td>0.8 (±0.2)</td>
<td>&gt;0.20</td>
</tr>
<tr>
<td>Contralateral aplastic or hypoplastic A1 segment, n (%)</td>
<td>11 (41%)</td>
<td>1 (4%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

ACA indicates anterior cerebral artery; CVD, cardiovascular disease; ICA, internal carotid artery; and MCA, middle cerebral artery.

defined as >50% stenosis by North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria.

Vascular Imaging and Measurements

Measurements were rated on computed tomographic angiography (n=22) or time-of-flight MRI angiography (n=33) images when computed tomographic angiography was not available. A1D and M1 diameters (M1D) were measured on axial source images at their most proximal segment captured in longitudinal section by one rater. The intrarater agreement for vessel diameter in a subset of 40 measurements was excellent (intraclass correlation coefficient: 0.90). All measurements were performed without knowledge of patient characteristics or stroke topography.

Statistical Analysis

Categorical variables were analyzed by Pearson \( \chi^2 \) or Fisher exact test and continuous variables by the 2-sample \( t \) test (all normally distributed). Variables associated with ACAS (P≤0.1) were included in backward regression analysis models. Model A was additionally adjusted for A1D, M1D and ICA-ACA/ICA-MCA angle ratio and model B for A1/M1 diameter ratio and ICA-ACA/ICA-MCA angle ratio. Receiver operating characteristic curves were constructed, and C-statistics were determined for A1D and A1/M1 diameter ratios. A \( P<0.05 \) was considered statistically significant.

Results

We studied 55 cases of ischemic stroke involving the anterior circulation (27 ACAS, 28 MCAS). The mean age of the sample was 69.2 years (SD±13.2). The proportion of measurements performed on computed tomographic angiography, rather than MRI angiography, did not differ between cases of ACAS and MCAS (37% versus 43%; \( P=0.66 \)), and in a subset of individuals with both computed tomographic angiography and MRI angiography, the intermodality agreement for vessel diameter (intraclass correlation coefficient: 0.77) and angle (intraclass correlation coefficient: 0.86) were good. In the entire sample, ICA-ACA branching angles were more acute than ICA-MCA angles (mean: 108° [±15°] versus 141° [±15°]; \( P<0.0001 \)) and A1D were smaller than M1D (mean: 2.1 [±0.5] versus 2.8 mm [±0.5], \( P<0.0001 \)).

In comparison with cases of MCAS, those with ACAS (Table 1) were less likely to have atrial fibrillation (15% versus 43%; \( P=0.04 \)) and tended to have more diabetes mellitus (67% versus 43%; \( P=0.08 \)). In addition, cases of ACAS had larger ipsilateral A1D (mean: 2.5 versus 2.1 mm; \( P=0.003 \)) and A1/M1 diameter ratios (1.0 versus 0.7; \( P<0.001 \)) and were more likely to have a contralateral aplastic or hypoplastic A1 segment (41% versus 4%; \( P<0.001 \)). There were no differences in ICA bifurcation angles between cases of ACAS and MCAS.

Univariate analysis results are shown in Table 2. After multivariable analysis, larger ipsilateral A1D (odds ratio per 1 mm increment: 8.5; 95% confidence interval [CI], 1.4–53.3) and ipsilateral A1/M1 diameter ratio (odds ratio per 10% increment: 1.8; 95% CI, 1.2–2.9) were associated with ACAS, whereas larger ipsilateral M1D were found to be protective (odds ratio per 1 mm increment: 0.8; 95% CI, 0.0–0.9). A1/M1 diameter ratio (C-statistic: 0.81; 95% CI, 0.70–0.93; \( P<0.001 \)) was a stronger predictor of embolic ACAS than A1 diameter alone (C-statistic: 0.71; 95% CI, 0.57–0.84; \( P=0.009 \)).

Data driven exploratory analysis demonstrated that A1D contralateral to an aplastic/hypoplastic A1 were larger than A1D in normal variants (mean: 2.7 versus 2.1 mm; \( P=0.002 \)), resulting in larger A1/M1 diameter ratios contralateral to the aplastic/hypoplastic A1 segment (mean: 1.0 versus 0.8; \( P<0.001 \)).

Discussion

The primary findings in our study are that embolic ACAS is associated with wider ipsilateral A1 segment, narrower ipsilateral M1 segment, larger ipsilateral A1/M1 diameter ratio, and overrepresentation of contralateral A1 segment aplasia/hypoplasia. These findings suggest that A1D, M1D, and particularly A1/M1 diameter ratio are important in determining the path of emboli that reach the terminal ICA.

Our observations concur with previous studies reporting a high prevalence of contralateral A1 segment aplasia/hypoplasia in embolic ACAS.3,5,6 Our data imply that these observations are partly explained by compensatory enlargement or dilatation of the A1 segment contralateral to the aplastic/hypoplastic side resulting in increased entry of flow-directed emboli into the ACA. Alternate plausible mechanisms include facilitation of emboli entry into the ACA by way of increased...
branching angulation, with reduced embolism rates into vessels emboli in the cerebral circulation is attributable to differences in multivariate analysis despite its large effect size may be attrib-
uted to the relative lack of power of dichotomous variables, as
lateral aplastic/hypoplastic A1, a dichotomous variable, in our
hypoplastic side. The loss of statistical significance of contra-
in the event of ACA embolism contralateral to the aplastic/
flowing angulation of the ACA may contribute to the lower overall
rates of ACAS, terminal ICA branching angulation does not
seem to be a significant determinant of individual variability in
ACAS risk because of the relative lack of variability in these
measures among stroke patients. In vitro experimental models
have highlighted the additional importance of the particle-to-
branch diameter ratio in preferentially guiding the trajectory of
larger emboli into wider bifurcation branches. This notion could
possibly explain the higher prevalence of atrial fibrilla-
tion, which is known to cause large emboli, observed in cases of
territorial infarction of the MCA, which typically has the larger
terminal ICA bifurcation branch diameter.

Our results are limited by small sample size and do not exclude the potential value of other predictors. Our cross-sectional analysis does not allow for causal inferences or can we exclude the possibility of residual confounding. Variability in the rating of arterial measurements, which were vulnerable to how the vascular anatomy had been captured in 3-dimensional space on neuroimaging (depending on head positioning, etc), could have limited our findings, despite our high rater agreement. Although a systematic method was used to rule out nonembolic strokes, it is possible that some of the included ischemic strokes had nonembolic pathogeneses, which would have biased our results toward the null. We are unable to determine for certain that A1 segments deemed as aplastic or hypoplastic were not occluded or stenotic vessels acquired during life. However, even if this were to be true, the resulting hemodynamic changes in the anterior circulation would likely be similar to those of congenital cases. A final limitation is that the cases of MCAS were selected consecutively rather than randomly, introducing the possibility of selection bias.

Conclusions

Our results suggest that A1D and M1D are important in determin-
ing the path of emboli that reach the terminal ICA and that larger ipsilateral A1/M1 diameter ratios and contralateral A1 segment aplasia/hypoplasia are risk factors for embolic ACAS. Although these findings contribute to the understand-
ing of the difference in incidence between ACAS and MCAS, as well as the hemodynamics of cerebral circulation that could possibly apply to arterial bifurcations elsewhere in the systemic vasculature, their practical clinical significance remains undetermined at this time.

Disclosures

None.

References


Table 2. Univariable Logistic Regression and Multivariable Backward Regression Analysis Determining Predictors of ACA Stroke

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unadjusted</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipsilateral A1D (per 1 mm increment)</td>
<td>5.7</td>
<td>1.7–19.9</td>
<td>0.006</td>
</tr>
<tr>
<td>Ipsilateral M1D (per 1 mm increment)</td>
<td>0.4</td>
<td>0.1–1.2</td>
<td>&gt;0.20</td>
</tr>
<tr>
<td>Ipsilateral A1/M1 diameter ratio (per 10% increment)</td>
<td>2.1</td>
<td>1.4–3.3</td>
<td>0.01</td>
</tr>
<tr>
<td>Contralateral aplastic/hypoplastic A1 segment</td>
<td>18.6</td>
<td>2.2–157.5</td>
<td>0.007</td>
</tr>
<tr>
<td><strong>Adjusted final models</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model A*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipsilateral A1D (per 1 mm increment)</td>
<td>8.5</td>
<td>1.4–53.3</td>
<td>0.02</td>
</tr>
<tr>
<td>Ipsilateral M1D (per 1 mm increment)</td>
<td>0.2</td>
<td>0.0–0.9</td>
<td>0.04</td>
</tr>
<tr>
<td>Contralateral aplastic/hypoplastic A1 segment</td>
<td>8.1</td>
<td>0.84–78.3</td>
<td>0.07</td>
</tr>
<tr>
<td>Model B†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipsilateral A1/M1 diameter ratio (per 10% increment)</td>
<td>1.8</td>
<td>1.1–2.9</td>
<td>0.01</td>
</tr>
<tr>
<td>Contralateral aplastic/hypoplastic A1 segment</td>
<td>8.3</td>
<td>0.9–77.6</td>
<td>0.06</td>
</tr>
</tbody>
</table>

A1D indicates A1 diameter; ACA, anterior cerebral artery; CI, confidence interval; M1D, M1 diameter; and OR, odds ratio.


† Covariates entered into stepwise regression: diabetes mellitus, atrial fibrillation, contralateral hypoplastic/aplastic A1, ipsilateral A1/M1 diameter ratio, and ICA-ACA/ICA-MCA angle ratio.
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