Cerebral Aneurysms and Variations in the Circle of Willis

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SUMMARY In order to obtain information about the relationship between variations in the circle of Willis and aneurysms, 44 complete circles of Willis with aneurysm were studied macroscopically.

The incidence of variations was significantly higher in the aneurysm series than in the control circles without aneurysm. There was a definite correlation between asymmetric proximal segments of the anterior cerebral artery and aneurysms of the anterior communicating artery, and a tendency to correlation was found in the case of asymmetric posterior communicating arteries and aneurysms on the internal carotid artery-posterior communicating artery junction.

In the light of these findings it seems likely that through hemodynamic changes variation in the circle of Willis plays some role in the development of cerebral aneurysms.

THE CIRCLE OF WILLIS has been shown to exhibit many kinds of anatomical variations.1-3 A possible relationship between these variations and aneurysms has been the subject of some reports in the literature, particularly in regard to congenital association and hemodynamic factors. However, most of such studies were unsatisfactory because of their methodology, that is poor handling of statistical data, lack of control series.4,8

The purpose of the present macroscopical study of 44 cases of complete circles of Willis with aneurysms was to obtain wider, more precise and more detailed information about the relationship between variations of the circle of Willis and aneurysms. We focussed on a) the incidence of variations in the aneurysm series and b) the relation between variations and aneurysm sites. We compared the results on incidence with our previous data from 148 circles of Willis without aneurysm.5

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TABLE 1 Distribution of Aneurysms

<table>
<thead>
<tr>
<th>Site of aneurysm</th>
<th>Right</th>
<th>Midline</th>
<th>Left</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACA</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>AComA</td>
<td>10</td>
<td>10</td>
<td>7</td>
<td>27</td>
</tr>
<tr>
<td>ICA-PComA</td>
<td>2</td>
<td>6</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>ICA-AChA</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>AChA</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>ICA Bif</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>MCA</td>
<td>8</td>
<td>7</td>
<td>15</td>
<td>22.4%</td>
</tr>
<tr>
<td>BA</td>
<td>4</td>
<td>4</td>
<td>8</td>
<td>6.0%</td>
</tr>
<tr>
<td>VA</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>8.9%</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>14</td>
<td>26</td>
<td>67</td>
</tr>
</tbody>
</table>

aneurysms of the basilar artery (BA an), and 9) aneurysms of VA (VA an).

In order to study the relationship between variations and aneurysm sites, the following two ratios (Ratio 1 and Ratio 2) were statistically compared (see table 3).

Ratio 1:
Circles with variation (α) and aneurysm in site (β)
All circles with aneurysms in site (β)

Ratio 2:
Circles with variation (α) and without aneurysm in site (β)
All circles with aneurysms in sites other than site (β)

Results
Distribution of the aneurysms is shown in table 1. The most numerous aneurysms were those in AComA (40.3%) followed by aneurysms in MCA (22.4%) and ICA-PComA (11.9%). There were slightly more aneurysms on the right side of the circle of Willis than the left.

Table 2 shows the incidence of variations of circles of Willis in the aneurysm series compared to the control. The incidence of “typical” circles of Willis was significantly lower in the aneurysm series (p < 0.01). Variations showing a significantly higher incidence in the aneurysm group were Asym ACA (p < 0.05), Asym PComA (p < 0.01). Med ACA was shown to have a higher incidence in the aneurysm series than the control but the difference was not significant. On the other hand, X ACA and Fen ACA showed though
### TABLE 2  Incidence of Variations in Aneurysm and Control Series

<table>
<thead>
<tr>
<th>Variations</th>
<th>Aneurysm series</th>
<th>Control series</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fen AComA</td>
<td>20.5% (9/44)</td>
<td>29.9% (43/144)</td>
</tr>
<tr>
<td>X ACA</td>
<td>11.3% (5/44)</td>
<td>21.1% (31/147)</td>
</tr>
<tr>
<td>Med ACA</td>
<td>22.7% (10/44)</td>
<td>14.6% (21/144)</td>
</tr>
<tr>
<td>Asym ACA</td>
<td>22.7% (10/44)†</td>
<td>11.0% (16/146)</td>
</tr>
<tr>
<td>Acces MCA</td>
<td>9.1% (4/44)</td>
<td>6.8% (10/146)</td>
</tr>
<tr>
<td>Earl Dupl MCA</td>
<td>11.3% (5/44)</td>
<td>4.0% (5/125)</td>
</tr>
<tr>
<td>bil Str PComA</td>
<td>4.5% (2/44)</td>
<td>6.0% (8/134)</td>
</tr>
<tr>
<td>Asym PComA</td>
<td>36.3% (16/44)*</td>
<td>16.4% (22/134)</td>
</tr>
<tr>
<td>unil Prim PComA</td>
<td>6.8% (3/44)</td>
<td>8.3% (11/133)</td>
</tr>
<tr>
<td>bil Prim PComA</td>
<td>9.1% (4/44)</td>
<td>6.0% (8/133)</td>
</tr>
<tr>
<td>Asym VA</td>
<td>20.5% (9/44)</td>
<td>20.8% (25/120)</td>
</tr>
<tr>
<td>No variation</td>
<td>11.3% (5/44)*</td>
<td>46.3% (62/134)</td>
</tr>
</tbody>
</table>

*Statistically significant difference between the two series (p < 0.01) by chi-square test.
†Statistically significant difference between the two series (p < 0.05) by chi-square test.

lower less than significant incidences in the aneurysm series.

In order to understand better the relationship between variations and sites of aneurysms, 5 variations, namely 1) Fen AComA, 2) Med ACA, 3) Asym ACA, 4) Asym PComA and 5) Asym VA are illustrated in figures 2–6. These variations have been chosen because their numbers are sufficient for statistical analysis. As shown in figure 2, five out of 10 circles of Willis with Fen AComA showed aneurysms in AComA. One of them (No. 38) also had Asym ACA. The aneurysms in the 4 remaining circles of Willis with Fen AComA were localized in different places such as BA, VA, ICA Bif and AChA. Out of 10 circles with Med ACA, 6 showed aneurysms in AComA (fig. 3). Two of them (No. 30 and 31) also had Asym ACA and one case at the same time X ACA (No. 30). The remaining aneurysms were located in other sites. In 9 circles among 10 circles of Willis with Asym ACA (fig.

![FIGURE 2. Fenestration in anterior communicating artery. Five out of 10 circles with this variation showed aneurysms in anterior communicating artery. Note additional variations in the anterior part of the circle in the case of No 38 (asymmetry of proximal parts of anterior cerebral arteries), No 4 and 8 (median anterior cerebral artery). No 21 was associated with Moya-Moya disease.](image-url)

![FIGURE 3. Median anterior cerebral artery. Six circles showed aneurysms in anterior communicating artery. Note additional variations in the case of No 30 and 31 (X-shaped anterior cerebral arteries and asymmetry of anterior cerebral arteries).](image-url)

4), aneurysms were located in AComA. Additional variations were seen in 4 circles (No. 29, 30, 31 and 40), 2 cases being combined with Med ACA and 2 with Acces MCA. Seven aneurysms in AComA occurred on the thicker side or midline and 2 on the thinner side. In the case of Asym PComA, 9 aneurysms were located in AComA and 5 in ICA-PComA (fig. 5). All aneurysms in ICA-PComA occurred on the thicker side. In 9 circles with Asym VA, 4 aneurysms were observed in AComA and 2 in VA, the latter occurring on the thinner side (fig. 6).

The ratio, with respect to one specific site, of variations in circles with aneurysms to the total number of circles with aneurysms and the ratio of variations in circles without aneurysms to the total number of circles with aneurysms at other sites are shown in table 3. Statistical comparison between the two ratios showed a significant correlation between Asym ACA and
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1) SO M  2) S3  F  ))>4U 7)1IF  '»>  "  M  13)  73  M  
15) 34 M  10)6»F 1T)O4U ,g) |1 F 21) 64 F

FIGURE 5. Asymmetry of posterior communicating arteries. The five aneurysms in the internal carotid artery-posterior communicating artery junction were all located on the thicker side.

AComA aneurysms ($p < 0.05$). A tendency to correlation was found in the case of Asym PComA and ICA-PComA aneurysms ($p < 0.10$).

Discussion

In the present study, the incidence of variations in the circle of Willis was shown to be significantly higher in the aneurysm series than in the control. It has long been suspected that variations in the circle of Willis may play some role in the development of cerebral aneurysms. However, the findings and views as to the relationship between variations and aneurysms have been controversial. Padget was one of the first to state that variations in the circle were statistically more frequent in the aneurysm series than in a series without aneurysm, her contention being based on a combined analysis of the reports of several authors. Her work was, however, criticised because of inadequate data and poor statistical methodology. Some authors reported that atypical configurations of the circle of Willis were present in 95% of their aneurysm series, and others reported the incidence to be 79%. Their figures are close to our results, but don’t have a control series. In the studies of Alpers et al, the incidence of atypical circles in the aneurysm and control series were 63 and 48% respectively, showing no significant difference. The figure for the control is very close to our data, while that of the aneurysm series seems to be somewhat low compared to ours and others. As far as our data is concerned, there is a clear correlation between variations of the circle and cerebral aneurysms, which leads one to the assumption that the variations are a factor in the occurrence of aneurysms.

Although the association of variations and aneurysms had been used as an argument in favor of a congenital theory of aneurysmal development, it should be interpreted in terms of the hemodynamic stress caused by variations. In order to obtain information about the hemodynamic factors working in the pathogenesis of aneurysms, it is important and necessary to analyse the relationship between variations and the site of aneurysms. There are very few reports dealing with this aspect of the problem. If it is shown that for some specific site of aneurysm a certain variation is observed more than it is seen associated with aneurysms in other sites, then a definite correlation between this variation and the aneurysm can be safely presumed. Stehbens was the only one who studied the relationship with this adequate methodology. However he applied it to only one variation. We applied this to all variations with a statistically sufficient number of

![TABLE 3 Relationship between Variations and Sites of Aneurysms](http://stroke.ahajournals.org/)

<table>
  <tr>
    <th>Variation (α)</th>
    <th>Site (β)</th>
    <th>Ratio 1</th>
    <th>Ratio 2</th>
  </tr>
  <tr>
    <td>Fen AComA</td>
    <td>AComA</td>
    <td>18.5% (5/27)</td>
    <td>23.5% (4/17)</td>
  </tr>
  <tr>
    <td>Med ACA</td>
    <td>AComA</td>
    <td>22.2% (6/27)</td>
    <td>23.5% (4/17)</td>
  </tr>
  <tr>
    <td>Asym ACA</td>
    <td>AComA</td>
    <td>33.3% (9/27)*</td>
    <td>5.8% (1/17)</td>
  </tr>
  <tr>
    <td>Asym PComA</td>
    <td>AComA + ACA</td>
    <td>33.3% (9/27)*</td>
    <td>47.1% (8/17)</td>
  </tr>
  <tr>
    <td>Asym VA</td>
    <td>AComA</td>
    <td>33% (4/12)</td>
    <td>29.4% (5/17)</td>
  </tr>
  <tr>
    <td>VA</td>
    <td>33% (2/6)</td>
    <td>18.4% (7/38)</td>
  </tr>
</table>

*Statistically significant difference between the two ratios ($p < 0.05$) by chi-square test.

Ratio 1: Circle with variation (α) and aneurysm in site (β)

Ratio 2: Circles with variation (α) and without aneurysm in site (β)

All circles with aneurysms in site (β)

All circles with aneurysms in sites other than site (β)

![FIGURE 6. Asymmetry of vertebral arteries. Note the two aneurysms in the thinner vertebral artery at the junction between the posterior inferior cerebellar artery and the vertebral artery (No 4 and 14).](http://stroke.ahajournals.org/)
cases, and found a definite correlation between Asym ACA and aneurysms in A ComA \( (p < 0.05) \). Stehbens\(^7\) and Wilson et al\(^6\) obtained the same results. Asym PComA and ICA-PComA aneurysms showed a tendency to correlation \( (p < 0.10) \).

In case of Asym ACA, the AComA aneurysm seems to be caused by an increased hemodynamic stress due to the compensatory shunting of blood through AComA.\(^7\)\(^-\)\(^10\) This hypothesis was confirmed by our experimentally induced aneurysm.\(^11\) That is, when an unilateral common carotid artery was ligated in rats with hypertension and fed on \( \beta \)-aminopropionitrile, aneurysms occurred in the AComA complex and the proximal segments of PCA on the side of the carotid ligation, while bilateral ligation of the common carotid arteries resulted in developing aneurysms in the proximal segments of posterior cerebral artery and basal artery. Such localization corresponds to where hemodynamic stresses were apparently increased.

As mentioned by Moritake et al,\(^8\) aneurysms occurred always on the thicker side of the ICA-PComA junction in the case of Asym PComA, while in the case of Asym ACA, such a difference was not clear. Development of aneurysms cannot be explained only by an increased impingement of axial flow to an apex,\(^12\)\(^-\)\(^13\) and some other hemodynamic factors such as secondary flow as well as local structural factors\(^14\)\(^-\)\(^15\) must be taken into consideration.

Correlation between variation and the sites of aneurysms could not be confirmed in other cases than Asym ACA and Asym PComA because of an insufficient number of cases. Further research with larger series is required for more information about the problem.

In many cases of aneurysm, a combination of several variations was observed. Such combination may increase or decrease the incidence of aneurysms in some sites. Besides doing statistical investigation, it is necessary to analyse each case in detail in order not to overlook any incidental factors that could elucidate the pathogenetic role of variation in the development of particular aneurysms.

In conclusion, there is a definite correlation between variation and aneurysm, and between variations and some sites of aneurysm. It can also be said that variations in the circle of Willis play some role in the development of cerebral aneurysms.

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