Shape Changes at the Apex of Isolated Human Cerebral Bifurcations with Changes in Transmural Pressure

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SUMMARY The geometry of arterial bifurcations appears to play a significant role in the development of vascular disease. We have investigated the changes in bifurcation geometry with changes in distending pressure over the range 0.0 to 190.0 mm Hg. Five cerebral arterial bifurcations from human subjects were studied. The investigation focussed on the shape and on changes in the shape of the leading edge of the flow divider (internal apical curve). The curve outline at each transmural pressure increment (each 10.0 mm Hg) was photographed and digitized. The curves were plotted serially on an expanded scale. Visual comparison of the curves indicated flattening in the central region and broadening of the shoulders of the curves with increasing transmural pressure. Regression analysis using second order polynomials was used to obtain coefficients for equations defining short, overlapping segments of each curve. Twenty-four coordinates were used for each successive regression. Each curve was characterized by 85 to 100 digitized coordinates. The regression equations for each curve were used to calculate the curvature parameter, K, and the radius of curvature, R. Three of the five bifurcations demonstrated a negative correlation of K with increasing transmural pressure (p < .001). This result supports the visual observation that the internal apical curve flattens with increasing transmural pressure. Flattening of the internal apical curve together with thinning of the arterial wall with increasing transmural pressure would contribute to a stress concentration at the apex of a cerebral bifurcation. This stress concentration would be more pronounced in the presence of a medial gap at the apex of the bifurcation. It is on or near this region of stress concentration that aneurysms develop.

IN RECENT YEARS there has been a growing awareness of the importance of vascular geometry and its role in the development of vascular disease. There is strong evidence that arterial geometry is an important factor affecting the pattern of flow, the orientation of endothelial cell nuclei, the initial deposition sites of atheroma, and the localization of cerebral aneurysms. In this paper we will focus on possible reasons for the localization of saccular aneurysms in relation to the geometry of the apex or branching region of cerebral arterial bifurcations. Hassler and Stehbens and Ludatscher have reported that cerebral aneurysms develop almost exclusively at the apices of bifurcations. In previous work, Macfarlane et al. have demonstrated in vitro variations in the deformability of the apical region and nonlinear changes in the size of the internal apical curvature in bifurcations of isolated human cerebral arteries subjected to a range of static pressures. The internal apical curve is the outline of the leading edge of the flow divider which separates the parent trunk into the daughter branches. This curve lies in a plane perpendicular to the plane of bifurcation (fig. 1). It is on or near this curved leading edge of the flow divider that saccular aneurysms develop. The geometry at the apex, the shape of the internal apical curve and the structure of the arterial wall in the apical region are expected to play an important role in determining the apical wall stress distribution.

The curvature, K, of a thin walled vessel subjected to a transmural pressure, P, is the factor which relates pressure to the average tensile stress, σ, in the wall of the vessel. The relationship commonly used to determine this is the Law of Laplace:

\[
P = \frac{R_1 + R_2}{R_1 R_2} \sigma
\]

where P is the transmural pressure, R_1 and R_2 are the principle radii of curvature of the vessel, and T_1 and T_2 are the orthogonal tangential wall tensions acting at positions on the curves corresponding to R_1 and R_2, respectively.

For straight cylindrical segments of artery in which one of the principle radii of curvature, R_3, is infinitely large the relationship is simply:

\[
P = \frac{T}{r}
\]

where r is the radius of the cylindrical segment. For a straight cylindrical segment the circumferential wall stress, σ, is given by:

\[
\sigma = \frac{Pt}{t}
\]

where t is the wall thickness.

The apical region of a bifurcation poses a particular challenge in understanding the distribution of wall stress. At the apex, the directions of the concavity of the internal and external curvatures are opposite. Moreover, the magnitude of the principle radius of the external curvature is small compared to that of the internal curvature. These contrasting features suggest a potential for structural instability in the apical region. Since the direction of concavity of the internal apical curve is positive, and since only the wall components lying along the internal curvature are acting to balance...
HUMAN CEREBRAL BIFURCATIONS/Macfarlane et al.

Figure 1. Schematic diagram of the apical region of a bifurcation showing the internal and external apical curves. The external apical curve is very small in contrast to the internal curve.

The distending pressure, we suggest that the shape of this curve should be studied in relation to varying pressure. We have established, through related work, a method for identifying the shape of the internal apical curve. Based upon data from that work we have conducted a critical examination of the shape of the internal apical curve in relation to changes in transmural pressure.

Methods

The arterial bifurcations that we have studied were prepared as part of a previous study. Five cerebral bifurcations were obtained at autopsy from subjects ranging in age from 40 to 79 years. The specimens were cleared of adventitial connective tissue and perfused with 0.9% saline to remove blood. The bifurcations were cannulated and ligated with 3-0 or 4-0 silk. Care was taken to avoid deformation of the specimens by the cannulation and ligation procedures. The specimens were mounted in a 0.9% saline bath at 21°C. A schematic diagram of the equipment is shown in figure 2. The daughter branches were not tethered and were allowed to move freely in the saline bath. The bifurcation was positioned by rotating the cannula so that the parent and daughter branches were in the horizontal plane of the bath. The tip of a plexiglass light pipe was aligned with the apex of the bifurcation at right angles to the cylindrical axis of the parent branch. The tip of the light pipe was positioned close to the arterial wall but did not touch it. The high intensity transillumination provided by the light pipe and the semi-transparency of cerebral arteries made it possible to observe and to photograph the lumenal geometry of the bifurcations in the apical region. The bifurcations were pressurized by injecting small volumes of 0.9% saline via the cannula. Photographs were obtained at each 10.0 ± 0.5 mm Hg increment of pressure with cameras mounted in the horizontal and vertical planes of the bifurcation. The bifurcations were tested over a pressure range of 0 to 190 mm Hg in multiple trials. Photographs were obtained and printed enlargements made at a magnification from 4 to 16 x. Two photographs of one bifurcation at two widely different values of internal pressure are shown in figure 3.

Measurement of Apical Contour

The photographs were randomized. They were then digitized by an assistant (K. Chan) who was unfamiliar with the project. The assistant was instructed to trace carefully the outline of the internal apical curve using the cursor of a Hewlett-Packard digitizer (Model 9864A) coupled to a Hewlett-Packard computer (Model 9810). The coordinates were digitized relative to the same origin and axes for each photograph. The accuracy of the digitizer was ± 0.254 mm. The uncertainty associated with the X and Y coordinates of ± 0.508 mm was determined by multiple digitization of one of the curves, selected at random. Correction was made for longitudinal strain in the parent trunk which tended to shift the position of the curve relative to the origin and X-axis. The correction was made by increasing or decreasing the Y-coordinate values by the magnitude of the longitudinal deformation of the parent trunk with each increment of pressure. The measurements were transferred for plotting and analysis to the university PDP 10 computing system. An example of the computer-plotted profiles of the apical curve for one bifurcation over the range of distending pressure is shown in figure 4. The size of the plotting symbol corresponds to the calculated maximum coordinate uncertainty.

Analysis

We have used two methods of analysis to obtain values of curvature (K) from each of the digitized...
curves, (i) polynomial regression of fourth degree, and (ii) segmental quadratic fitting with overlapping segments.

**Polynomial regression** was used to obtain coefficients for polynomial equations of degree 2 through 6 using all of the coordinates for each of the apical curve profiles. The closeness of fit of the polynomials was evaluated by (i) visual comparison with the digitized coordinates, (ii) the magnitude of the standard error of estimate (SEE), and (iii) the absence of artefactual local extrema. Based upon these criteria fourth degree polynomial equations provided the best fit to the digitized coordinates (fig. 5). Curvature (K) and radius of curvature (R) were calculated from the fourth degree polynomials using the relation in calculus:

\[
K = \frac{Y''}{\sqrt{1 + (Y')^2}}
\]

where \(Y''\) and \(Y'\) are the second and first derivatives of the polynomial with respect to X. The radius of curvature (R) at any point P(X, Y) lying on the curve is by definition

\[
R = \frac{1}{|K|}
\]

**Segmental regression analysis** was used to obtain quadratic equations for short, overlapping segments of the curves.

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**Figure 3.** (a) Photograph of the internal apical curve at the second bifurcation of the right middle cerebral artery from a 54-year-old male subject. The specimen is subjected to a transmural pressure of 5.0 ± 0.5 mm Hg. Enlargement is nine times the actual size of the specimen. (b) Photograph of the internal apical curve of the same specimen shown in Figure 3(a). The specimen is subjected to a transmural pressure of 165.0 ± 0.5 mm Hg. Enlargement is the same as in Figure 3(a).

**Figure 4.** Computer plots of the internal apical curve of the right vertebral-anterior spinal artery bifurcation from a 56-year-old male subject. The centre-referenced, square symbols represent the digitized curve coordinates (box centres) and the maximum X and Y coordinate errors associated with digitization (± ½ × box side). Curve (a) represents the internal apical curve at a transmural pressure of 0.0 ± 0.5 mm Hg. Curve (b) represents the internal apical curve at a transmural pressure of 20.0 ± 0.5 mm Hg. Curve (c) represents the internal apical curve at a transmural pressure of 150.0 ± 0.5 mm Hg. The curve plots are 38.5 ± 0.7% times larger than the actual internal apical curves.
the internal apical curves. We used this approach to avoid the subjective evaluation of the closeness of fit of the higher order polynomials and to obtain values of curvature in the central region of the apex without the influence of the coordinates well away from the central region. The segmental regression analysis was carried out by successive analysis of sets of coordinates corresponding to short, overlapping segments of the internal apical curve. For example, coordinate pairs 1 through \( n \) were analyzed, then coordinate pairs 2 through \( n + 1 \), then 3 through \( n + 2 \), and so on. The analysis stopped after the \( N-n \) through \( N \) coordinate repair. \( N \), the total number of digitized coordinates characterizing each curve outline, ranged from 85 to 100. The term, \( n \), was the number of coordinate pairs analyzed in each segment. The value \( n = 24 \) was chosen on the basis of an assessment of the effect of \( n \) on the variance of the calculated curvature.

The standard deviation of the curvature for seven repeatedly measured apical profiles was determined in the central region of the apex subtending an arc of \( 30^\circ \). The measurements were obtained over a range of values of \( n \) and are plotted in figure 6. The value of \( n = 24 \) was well beyond the shoulder (near a value of \( n = 16 \)) and yet not so large as to include the sides of the apical profile which were less clearly identified. Curvature, because of its dependence on the second derivative of position, is extremely sensitive to local fluctuations associated with errors of measurement.

The equations obtained by this segmental fitting technique were used to calculate curvature (K) and radius of curvature (R).

**Results**

The parameter curvature is a useful descriptor of the shape of a curve. Curvature is the reciprocal of radius of curvature. For a curve, such as a semicircle, the curvature and radius of curvature are constant at all positions. For a straight line the curvature is zero and radius of curvature is infinitely large. Our photographic data (fig. 3) and the plotted coordinate sets (figs. 4 and 5) suggested that the shape of the internal apical curve changed with changes in transmural pressure. The data for four of the five specimens suggests that the internal apical curve flattens in the central part of the profile, and the shoulder regions broaden with increasing transmural pressure. The fifth one, which was from a 79-year-old female, did not change as did the younger ones. Moreover, the curves did not simply

![Computer drawn serial array of apical curves indicating the digitized coordinates (crosses) and the coordinates generated by fourth-degree polynomial equations corresponding to each coordinate set (continuous line). The specimen is the second bifurcation of the right middle cerebral artery from a 54-year-old, male subject. The bifurcation was subjected to discrete transmural pressures ranging from 5.0 ± 0.5 mm Hg (bottom curve) to 165.0 ± 0.5 mm Hg (top curve) in pressure increments of 10.0 ± 1.0 mm Hg. Only the odd numbered curves are shown. The pressure increment between curves is 20.0 ± 1.0 mm Hg.](image)
Figure 6. Plot of standard deviation of curvature, K, versus number of coordinates, n. See text for discussion.

become larger; their shape changed. We used the curvature parameter to measure these changes. Three specimens exhibited a tendency for the internal apical curve to flatten in the central region (curvature decreased) with increasing transmural pressure. This observation was based upon (i) visual inspection of the plotted curves, (ii) curvature values obtained from the fourth degree polynomial equations, and (iii) curvature values obtained by the segmental quadratic fitting method. We compared the curvature values obtained from the segmental fitting method in the central region of the internal apical curves and found a negative correlation between curvature (K) and transmural pressure. We feel that the segmental regression analysis on sets of coordinates in the central region of the curves, using a quadratic equation, eliminates these biases.

Photographs of the vertical aspects of the specimens were studied to determine the shape and size of the external apical curve (fig. 1). In contrast to the observed changes in the internal apical curve there was no significant change in the shape or size of the external curve. The radius of the external curve was very small compared to that of the internal curve.

Discussion

In contrast to isolated, unpressurized cylindrical segments of cerebral arteries which collapse under their own weight in vitro, the apical region of isolated bifurcations demonstrates little or no conformational change. The unique geometry and structural organization of the arterial wall at the branch point appears to stabilize the structure at zero or a small positive transmural pressure. Moreover, the apical region of cerebral bifurcations tends to resist geometric deformation at small negative transmural pressures in contrast to cylindrical specimens which collapse.

Our investigation has focussed on the apical geometry of pressurized cerebral bifurcations and the potential for structural instability in the apical region under stress based upon geometric considerations. Our data are inadequate to undertake a rigorous stress analysis of the apical region, since we did not measure wall thickness, and curvature was not measured as the specimen was rotated. However, it is helpful through the use of a simple model to consider the implications of the observed geometric changes in the apical region.

The Laplace relationship may be applied to the apical region of a bifurcation if we recall that the directions of concavity of the internal and external curves are opposite. The arterial wall in the apical region is

Table 1

<table>
<thead>
<tr>
<th>Bifurcation specimen</th>
<th>Sex</th>
<th>Age</th>
<th>Number of curves</th>
<th>Trial</th>
<th>Confidence limits</th>
<th>r</th>
<th>Slope mm⁻¹</th>
<th>Intercept mm Hg</th>
<th>mm Hg</th>
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<tbody>
<tr>
<td>A253-72 R. mid. cerebral 2nd</td>
<td>M</td>
<td>54</td>
<td>17</td>
<td>1</td>
<td>1%</td>
<td>.61</td>
<td>.0017</td>
<td>.81</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>16</td>
<td>2</td>
<td>1%</td>
<td>.63</td>
<td>.0022</td>
<td>.79</td>
<td></td>
</tr>
<tr>
<td>A291-72 L. ant. cerebral 1st</td>
<td>F</td>
<td>79</td>
<td>15</td>
<td>1</td>
<td>5%</td>
<td>.57</td>
<td>.0030</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>A294-72 R. mid. cerebral 1st</td>
<td>M</td>
<td>52</td>
<td>17</td>
<td>1</td>
<td>5%</td>
<td>.65</td>
<td>.0024</td>
<td>1.54</td>
<td></td>
</tr>
<tr>
<td>A22-73 R. vertebral-ant. spinal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUH-73 L. ant. cerebral 1st</td>
<td>M</td>
<td>40</td>
<td>16</td>
<td>Specimen exhibited excessive creep</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
Figure 7. Plot of curvature, $K$ versus transmural pressure. Curvature, $K$ was calculated from quadratic equations based upon overlapping segments of the internal apical curve with 24 coordinates per segment. The specimen is the second bifurcation of the right middle cerebral artery from a 54-year-old male subject. These results are representative of those obtained from four of the five specimens tested.

Figure 8. Schematic diagram demonstrating the locations of the radii of curvature for the internal ($R_1$) and external ($R_2$) apical curves and the directions of the corresponding tangential tension vectors $T_1$ and $T_2$. Note that we have intentionally drawn the external curve small in contrast to the internal curve. This is the case for most cerebral bifurcations and $R_2 \ll R_1$ for all positive transmural pressures.

Similar to a saddle surface. The appropriate form of the Laplace relationship:

$$P = \frac{T_1}{R_1} - \frac{T_2}{R_2}$$

takes into account the opposite directions of the concavities (fig. 8). We will choose the direction of the concavity of the internal curve as the positive direction and $R_1$, the principle radius of that curvature. The application of the Laplace relationship is an approximation only. We neglect the restrictions of homogeneity and isotropy. Since $R_1$ is much smaller than $R_2$, and $R_2$ does not change significantly with transmural pressure, the term $T_2/R_2$ varies only with $T_2$. $T_2$ arises primarily from longitudinal loading of the daughter branches, and only the vector components acting tangentially at the centre of the external apical curve need be considered. Thus $T_2/R_2$ makes a minimal contribution to the net stress acting at the apex. The major stress contribution arises from the term $T_1/R_1$. As pressure increases, $R_1$ increases, and the product $PR_1$ increases. As the internal apical curve flattens, $R_1$ increases rapidly.

It is obvious from figure 7 and figures 4 and 5 that the radius of curvature becomes very large at the apex of the internal curve. This should produce a very high tension there. If the volume of the wall is constant as suggested by Carew et al.\(^\text{10}\) then the wall must thin as the radius increases. Thus both factors tend to increase the apical wall stress.

Hassler\(^\text{6}\) and others have reported that medial gaps are common at the apex of bifurcations. We have also seen these gaps (fig. 9). They decrease the wall thickness locally, and so the region becomes a zone of stress concentration which is even more likely to reach the critical yield point reported by Scott et al.\(^\text{11}\) Our data shows why this failure occurs on the internal apical curve rather than the external one, and also shows why aneurysms tend to arise from the centre of the apical
region (where \( R_i \) is high), rather than from the edges (where \( R_i \) is lower). Campbell and Roach\(^{12} \) have recently demonstrated that there are larger fenestrations in the elastic membrane at the apex of human cerebral arterial bifurcations than there are in the branches. These may have been produced by the greater stresses produced there by the geometrical factors described above. Once these larger fenestrations are present, they tend to lead to even greater regions of stress concentration as described by Campbell and Roach.\(^{12} \)

Thus, the three factors: (i) a large internal radius of curvature, (ii) a thin wall, particularly if a medial gap is present, and (iii) large fenestrations in the internal elastic membrane, all tend to add together to make the apex of cerebral arteries prone to fail, and hence to develop aneurysms.

**References**


**Acknowledgment**

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Shape changes at the apex of isolated human cerebral bifurcations with changes in transmural pressure.

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Stroke. 1983;14:70-76
doi: 10.1161/01.STR.14.1.70

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