Intra-aneurysmal Pressure Measurements in Experimental Saccular Aneurysms in Dogs

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Intra-aneurysmal pressure was studied in an experimental model of saccular aneurysm in dogs, using a vein pouch grafted onto a common carotid arterial bifurcation. The mean and the pulse pressures were recorded simultaneously from within the aneurysm and within the common carotid artery, before and after 50% proximal carotid artery stenosis. These experiments were performed under systemic normotension, hypotension, and hypertension. Normal data suggest that mean intra-aneurysmal and intra-arterial pressures are similar and relate in a nearly linear fashion to mean arterial pressure. However, after 50% stenosis, the data had a cubic relationship, the reduction of pressure occurring only in the middle range of mean arterial pressure. Both intra-aneurysmal and intracarotid pulse pressures displayed less dependence on mean arterial pressure. However, sigmoid curves also were observed with the pulse pressures after 50% proximal common carotid artery stenosis. In all cases, after 50% stenosis, the rate of increase of the pulse pressures with mean arterial pressure was greater for higher mean arterial pressures. Our preliminary data indicate that a detailed study of intra-aneurysmal pressure and blood flow in relation to systemic variables such as mean arterial pressure, cardiac output, and peripheral resistance may not only suggest improved means of managing patients with intracranial aneurysms, but also may raise the possibility that, under certain conditions, higher intra-aneurysmal pressures may be induced by downstream stenosis. (Stroke 1988; 19:352-356)

Few experimental studies have examined the physical factors responsible for the growth and rupture of intracranial aneurysms. A more complete understanding of such factors may help to prevent the development and consequent rupture of such aneurysms and may indicate revised strategies for the medical management of patients with ruptured aneurysms who are awaiting surgery.1-6

Among the factors thought to be responsible for growth and rupture of aneurysms, intra-aneurysmal pressure and blood flow have been considered important.7 Three human studies of intra-aneurysmal pressure have been conducted that have yielded somewhat conflicting results. Wright8 measured the pressure inside three middle cerebral artery (MCA) aneurysms and the common carotid artery (CCA) and found the intra-aneurysmal pressure to be lower. This was thought to be due to a narrow aneurysmal neck in one patient and to intense MCA spasm in another. Ferguson,9 in a study of four human cerebral aneurysms, found mean intra-aneurysmal pressure to be equal to mean systemic arterial pressure, given allowance for head elevation, whereas intra-aneurysmal pulse pressure was lower in two cases. However, he considered this latter effect to be a result of damping caused by the length of the needle used to record the pressure. Coll et al10 recorded mean pressure inside an anterior communicating artery aneurysm and an MCA aneurysm and found them to be an average of 5 torr lower than pressure in the CCA. The relation of mean intra-aneurysmal pressure to occlusion of the CCA also was examined in two of these studies. During temporary CCA occlusion, the intra-aneurysmal pressure was greatly reduced.7,9 Coll et al10 also found that during induced systemic hypotension there was a corresponding reduction in intracarotid and intra-aneurysmal pressures. During carotid angiography, the intra-aneurysmal and intra-arterial pressures increased by an average of 11 torr.

All of the above investigators assumed that pressure inside the CCA approximated that inside the vessel feeding the aneurysm, namely the MCA or the anterior cerebral artery. Although this assumption may be valid under physiologic conditions, it is often invalid when the CCA is occluded, depending on collateral blood flow through the external carotid artery and the circle of Willis.11-12

To define the relations between mean arterial pressure (MAP) and the pressures inside a feeding artery and an attached aneurysm, we studied the mean and pulse pressures inside the CCA and an attached vein pouch aneurysm in dogs before and after 50% proximal CCA stenosis. These experiments were performed under systemic normotension, induced hypotension, and induced hypertension. Fifty percent stenosis was chosen because it is a degree of stenosis that reduces intravascular blood pressure without reducing intravascular blood flow.
Materials and Methods

Aneurysm Model

Ten experiments (two aneurysms created per dog on opposite carotid arteries) were carried out on five adult mongrel dogs weighing 17–23 kg. The dogs were anesthetized with intravenous pentobarbital, intubated, paralyzed with pancuronium bromide, and artificially ventilated to maintain physiologic conditions. Anesthesia was maintained by intermittent administration of pentobarbital and pancuronium bromide. An intravenous line was used for the administration of fluids and drugs. A femoral intra-arterial line was placed and connected to a Statham transducer (Gould-Statham Instruments, Oxnard, California) at the level of the heart and connected to a Grass polygraph (Grass Instrument Co., Quincy, Massachusetts) for continuous recording of the systemic arterial pressure.

Dissection was performed on either side of the neck to isolate a 10-cm segment of the CCA and a short length of its superior thyroid branch. A segment of the external jugular vein was removed and ligated at one end. After the application of temporary clips to the CCA and its branch, an oval arteriotomy was made on the CCA at the branching of the superior thyroid artery. The open end of the segment of the external jugular vein then was sutured to the arteriotomy site using 7-0 or 8-0 Prolene sutures (Davis and Geck, Danbury, Connecticut) and magnification afforded by an operating microscope. After the aneurysm was created, the temporary clips were removed. The diameter of the aneurysmal neck and sac and the length of the aneurysm were measured with calipers.

Aneurysms of different sizes and shapes were created by the experimental technique (Figure 1). The dimensions of the aneurysmal sac could be varied by altering the length of the vein segment and the diameter of the vein harvested. The aneurysmal neck diameter could be varied by altering the dimensions of the arteriotomy in the CCA. A bilobed aneurysm could be created by including a tributary of the vein in the segment.

A 22-gauge 2.5-cm Quickcath (Travenol Labs, Deerfield, Illinois) was inserted into the aneurysm such that its tip lay within the aneurysmal sac. This catheter was connected through heparinized saline-filled extension tubing to a Statham transducer and Grass polygraph for continuous recording of intra-aneurysmal pressures. A similar catheter was introduced into the CCA so that its tip lay just distal or proximal to the mouth of the aneurysm. Both transducers were leveled to the CCA, and the polygraph was calibrated before each set of experiments by using a mercury barometer. Pressures were measured on a scale of 10 mV/cm on Grass eight-channel strip chart recorder.

Experimental Protocol

The systemic arterial pressure, the intra-aneurysmal pressure, and the intracarotid pressure first were recorded under normal conditions. Similar recordings then were made during systemic hypotension induced with intravenous sodium nitroprusside and during systemic hypertension induced with intravenous phenylephrine hydrochloride (Neo-Synephrine, Winthrop-Breon Laboratories, New York, New York). Next, a ligature was placed around the CCA proximal to the aneurysm and the intracarotid catheter to constrict the diameter of the CCA by 50%. The experimental measurements then were repeated.

Analysis of Data

MAP was computed as the sum of two-thirds of the diastolic pressure and one-third of the systolic pressure over the average of 25 consecutive values. The pulse pressure was computed as the difference between the peak systolic and end-diastolic pressures over the average of 25 consecutive values.

Statistical Methods

A polynomial regression analysis of the intracarotid and intra-aneurysmal pressures in relation to MAP was performed using the MINITAB computer program (Minitab Inc. and Pennsylvania State University, 1985). Five high outliers (pulse pressures >2×mean) were eliminated from the data pool before analysis. The data were fit with up to a third-order polynomial of the form \( Y = a_0 + a_1X + a_2X^2 + a_3X^3 \) (Table 1). Coefficients for values higher than the third degree had a nonsignificant effect on the regression equation. \( R^2 \), the ratio of the sum of squares due to regression to the total sum of squares, also was computed (Table 1). The fitted regression curves and 95% confidence intervals were plotted (Figures 2, 3, and 4). The number of data points was not sufficiently large to test the differences between the pressures statistically; however, consistent trends can be seen in the curves with 95% confidence limits.

Results

Aneurysmal Dimensions

Aneurysms of different sizes and shapes were created. The mean ± SD aneurysmal neck diameter was 0.8 ± 0.2
TABLE 1. Regression Coefficients of lntracarotid and Intra-arterial Mean and Pulse Pressures vs. Mean Arterial Pressure in Dogs With Experimental Saccular Aneurysms

<table>
<thead>
<tr>
<th>Regression</th>
<th>Normal conditions</th>
<th>50% proximal stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid mean pressure</td>
<td>-0.611 0.713 -0.58 0.502</td>
<td>-0.821 0.874 -0.799 0.723</td>
</tr>
<tr>
<td>Aneurysm mean pressure</td>
<td>-0.363 0.548 -0.475 0.481</td>
<td>-1.000 1.000 -0.880 0.736</td>
</tr>
<tr>
<td>Carotid pulse pressure</td>
<td>0.303 -0.200 0.370 0.359</td>
<td>-0.332 0.344 -0.38 0.356</td>
</tr>
<tr>
<td>Aneurysm pulse pressure</td>
<td>-0.114 0.144 -0.150 0.149</td>
<td>-0.114 0.144 -0.150 0.149</td>
</tr>
</tbody>
</table>

Values ($a_i$, where $i=0, 1, 2, 3$) to which numbers are scaled: 212.8 5.818 0.04279 0.94

Regression equation $Y = a_0 + a_1X + a_2X^2 + a_3X^3$; values normalized in each column to maximum value.

Figure 2. Third-order polynomial regression curves with 95% confidence bands relating (top) intracarotid mean pressure and (bottom) intra-aneurysmal mean pressure to mean arterial pressure (MAP) with (dashed lines) and without (solid lines) 50% proximal carotid artery stenosis. 95% confidence intervals lie between dashed or solid lines. Notice that data are more scattered after 50% stenosis, and that curves are sigmoid, with reduction of pressures occurring only in middle range of systemic MAP.

Mean Pressures

When the mean intracarotid and intra-aneurysmal pressures under normal conditions were plotted against MAP, the data exhibited a good linear fit ($R^2 = 0.94$ intracarotid pressure, $R^2 = 0.95$ intra-aneurysmal pressure) (Figure 2, solid lines). The 95% confidence intervals of the mean intracarotid and intra-aneurysmal pressures nearly overlap, suggesting that there is no significant difference between the relationships of the two pressures (Figure 4, top).

With 50% proximal stenosis (Figure 2, dashed lines), there was more scattering of the data, and $R^2$ decreased ($R^2 = 0.67$ intracarotid pressure, $R^2 = 0.63$ intra-aneurysmal pressure). However, the fitted curves with 95% confidence intervals again suggest no differences between intracarotid and intra-aneurysmal mean pressures for 50% proximal stenosis (Figure 4, bottom).

Under conditions of 50% stenosis, mean intracarotid pressure showed a definite reduction from normal values in the range 102–165 torr MAP, where the 95% confidence intervals of the two curves did not overlap (Figure 2, top). The curve for the 50% stenosis group exhibited a flatter slope in this range, below which the slope was essentially unchanged from normal and above which the slope was greater; that is, after stenosis, higher MAP produced greater than expected mean intracarotid and intra-aneurysmal pressures.

A reduction of intra-aneurysmal mean pressures was observed with 50% stenosis between a MAP range of 108–170 torr (Figure 2, bottom). Once again, the relationship between aneurysm mean pressure and MAP for 50% stenosis was cubic.

Pulse Pressures

The intracarotid and intra-aneurysmal pulse pressures before and after 50% proximal stenosis are illustrated in Figure 3. Before stenosis, the intracarotid
pulse pressure was poorly correlated with MAP ($R^2=0.10$), exhibiting a scattered pattern over the range studied; the intra-aneurysmal pulse pressure was also poorly correlated with MAP ($R^2=0.12$). After 50% stenosis, the intracarotid pulse pressure was more dependent on MAP ($R^2=0.44$), whereas the intra-aneurysmal pressure reflected the same lack of correlation with MAP. Moreover, both pulse pressure curves became sigmoid with stenosis (Figure 3, Table 1). It should be noted that the intracarotid and intra-aneurysmal pulse pressures were similar to each other over the middle range of systemic MAP (100–140 torr) without and with 50% stenosis (Figure 3).

Both pulse pressures decreased with 50% stenosis, over the range 125–145 torr MAP for intracarotid pressure and 125–160 torr MAP for intra-aneurysmal pressure. The pulse pressure curves obtained after 50% stenosis also were sigmoid, with a flattened slope in the middle range.

**Discussion**

Our experiments suggest that the mean pressures inside an aneurysm and a large feeding artery are similar and have a nearly linear relationship with systemic MAP under normal conditions. However, with 50% stenosis of the feeding artery, the relationship of mean intra-aneurysmal and mean intracarotid artery pressures with MAP became sigmoid. Fifty percent proximal stenosis lowered mean intra-aneurysmal and mean intracarotid pressures only over the middle range of MAP (100–160 torr). Because proximal stenosis of a feeding artery has been used clinically to reduce rebleeding in patients awaiting surgery, this finding has important implications in the blood pressure management of patients with intracranial aneurysms. Further research is required to study the effect of varying degrees of stenosis on intra-aneurysmal pressure.

In our experiments, pulse pressures inside the aneurysm and the carotid artery were poorly related...
with systemic MAP. Presumably, pulse pressures depend more on cardiac stroke volume and peripheral resistance. However, after 50% stenosis, these pulse pressures also exhibited a cubic relationship with MAP. These data suggest that at higher systemic MAPs, pulse pressures could increase significantly. In a computer model of an intracranial aneurysm with the accompanying vessels developed by Austin, increased systemic MAP raised intra-aneurysmal pressure but not blood flow. Our experimental results agree with the theoretical results of Austin, who postulated a "jump phenomenon" of large increases in intra-aneurysmal pulse pressure with small increases in systemic pulse pressure at higher systemic MAPs. This finding may have significant implications for the care of patients.

The neck diameter and the sac dimensions of the 10 experimental aneurysms were varied to obtain a more representative sample of naturally occurring aneurysms. Determination of the direct influence of these factors on pressure requires further study.

Additional research is also necessary to examine the effect of heart rate, cardiac stroke volume, and the effects of extreme elevation of blood pressure on aneurysmal mechanics. Intra-aneurysmal blood flow velocities can be measured experimentally with the use of a 20-mHz micro-Doppler probe placed on the aneurysm (L.N. Sekhar, M. Sun, R.J. Sclabassi, H.B. Blue, and J.F. Wasserman, unpublished data). These and other such experiments may suggest possible mechanisms for aneurysmal rupture and may lead to improved ways of managing patients with ruptured or unruptured aneurysms.

Acknowledgments

Wendy Fellows and Janet Forgione assisted with the laboratory experiments. Kim Luyckx assisted in data analysis. Judy Campbell prepared the manuscript. Helene Hoekman edited the manuscript.

References


KEY WORDS • cerebral aneurysms • dogs
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doi: 10.1161/01.STR.19.3.352

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1988 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
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