Critical Pressure for Arterial Wall Rupture in Major Human Cerebral Arteries

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Background and Purpose—Intracranial bleeding is linked to hemodynamic stress factors, such as hypertension. However, there are no studies that tested the breaking pressure of normal large cerebral arteries in humans.

Methods—The brains of 10 cadavers (age, 47±14 years; 9 men) were harvested within 48 hours postmortem for 31 segments of the main intracranial arteries. After careful microsurgical preparation, the vessels were pressurized with saline and observed until they ruptured.

Results—Vessel diameters averaged 2.6±0.3 mm (range, 1.2–4.3 mm). The average rupture pressure was 2.21±0.59 atm (range, 1.13–4.3 atm) and decreased with age at −0.025 atm/y ($R^2$=40%; $P<0.0002$). The maximum diameter distention at rupture was 30±9% (13%–52%), which also decreased with age (−0.5%/y; $R^2$=78%; $P<0.00001$). Neither the rupture pressure nor the maximum distention showed significant dependence on the resting vessel diameter. No significant dependencies were found on the vessel origin, vascular configuration, direction of the rupture, or the presence of minor coexisting pathology.

Conclusions—Human cerebral arterial wall breaks only at extremely high intravascular pressures, exceeding several times the highest observed systolic blood pressure, even accounting for age trends. Systolic hypertension alone may not be sufficient to cause intracranial hemorrhage, and there may be additional contributing factors. (Stroke. 2013;44:00-00.)

Key Words: arterial pressure ■ cardiovascular diseases ■ cerebrovascular circulation ■ hemorrhage

Spontaneous intracranial hemorrhage is one of the most devastating neurological events commonly linked to vascular pathology, such as aneurysm or arteriovenous malformation. Systemic hypertension has consistently been cited as a risk factor for intracranial aneurysm development and subsequent bleeding. Among patients with unruptured aneurysms, hypertension is found in 43% cases compared with 34% of controls. The coincidence of bleeding with strenuous activities in 43% of patients is commonly used to support the hypothesis of mechanical rupture because of increased transmural pressure. Although any vessel will eventually break at sufficiently high pressures, the quoted rupture pressures of the aortic wall are extremely high at $≈3000$ mm Hg. Such gross discrepancy with the range of observed systolic pressures prompts an investigation on the rupture pressure of smaller arteries in the neck and head.

Materials and Methods

We studied 10 human cadaver brains presented for autopsy in the Department of Forensic Medicine of Warsaw Medical University. The donor age was 47±14 years (range, 24–80 years; 9 men) within 48 hours postmortem. In total, 31 segments of the main cerebral arteries at the level of the circle of Willis were harvested using microsurgical techniques under an operating microscope. The specimens included typically 1 to 2 cm long intracranial vessel segments. Two vessel segments had silent aneurysms, each from men, one aged 50 years (middle cerebral artery bifurcation) and the other aged 80 years (anterior communicating artery). Each sample was rinsed in normal saline and its inlet end inserted onto a stainless steel needle with a flared tip and secured with silk sutures (Mersilk 6.0). Remaining large openings at the ends were closed with aneurysm clips, and small perforators were ligated with sutures as close as possible to the main trunk (Figure 1). Preparations were mounted above the operating table and connected via a T-joint to a custom-made motorized syringe pump, with the pressure recorded digitally on a standard PC with A/D converter (DI-194, http://www.dataq.com). A fast digital camera filmed the rupture (CASIO EXILIM EX-FC150, 420–1000 frames/s), and 21 films were adequate to measure the relative change in the diameter from baseline to the maximum prerupture size, which were averaged between 2 independent observers. The vessels were pressurized at $≈0.1$ atm/s until the rupture of the main trunk was recorded. If a leak or rupture was observed at any of the sutures or perforators, the experiment was stopped and repeated again after improving the preparation. The damaged vessels were cut along the unruptured wall to examine the inside and outside appearance of the rupture microscopically (Nikon 1500, magnification, ×7.5–110; Figure 1).

All variables are expressed as mean±SD with optional ranges. Regressions are described by the coefficient of explained variance ($R^2$ Pearson regression coefficient squared) and probability. ANOVA was performed in STATISTICA (version 7, www.statsoft.com) after compensating for the observed linear age trends.

Results

The vessels in this material averaged 2.6±0.3 mm (range, 1.6–3.8 mm) in diameter and presented a variety of rupture patterns.

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Only 1 of the 2 aneurysms identified turned into a rupture site. Although this occurred at a low pressure outside the confidence bounds of the age regression line (Figure 2, arrows), this was not remarkably different from other outliers. All other (30 of 31) ruptures occurred either at the main vessel trunk or at the bifurcation point. Nine (69%) of the 13 bifurcations ruptured at the junction (Figure 1D). When the main trunk was affected, only 8 of 21 ruptures (38%) occurred along the length of the vessel (Figure 1A). These longitudinal ruptures occurred predominantly but not exclusively in the internal carotid artery and middle cerebral artery vessels (63%). Conversely, of the 11 vessels that ruptured across the transverse line (Figure 1B), 64% belonged to the posterior circulation bed. Both observed spiral ruptures occurred in vertebral arteries (Figure 1C).

The average rupture pressure was 2.35±0.55 atm, ranging from 1.19 atm (middle cerebral artery; the oldest 80-year donor) to 4.3 atm (middle cerebral artery; the youngest 24-year donor). Between these extremes, the rupture pressure showed a consistent dependence on age (Figure 2A) with a linear trend slope of −0.25 atm per decade of age (CoEV=40%; P<0.0002). The prerupture diameter increased on average 30±9% (13%–52%) from baseline, with an even stronger dependence on age (−5%/decade; CoEV=78%; P<0.00001). Neither the rupture pressure nor the maximal distention showed dependence on the baseline vessel diameter (CoEV<10%; P>0.3; CoEV<1% after compensating for age).

Compensating for age trends, ANOVA did not reveal any significant differences between the rupture pressures and vessel location (P>0.6), presence of bifurcation (P>0.29), and type of rupture (P>0.11). Similarly, the observed presence of plaque depositions near the rupture point (n=3; Figure 1D) or the presence of aneurysm (n=2) did not result in any

Figure 1. Examples of the observed ruptures (red arrows). A, Longitudinal, as expected for a uniform vessel wall (vertebral artery, 24-year male); B, transverse (middle cerebral artery, 29-year male); C, spiral (vertebral artery, 50-year male); and D, typical rupture at a vessel bifurcation (middle cerebral artery, 80-year male). Blue arrows indicate visible atherosclerotic plaque deposits near the rupture site.

Figure 2. The age dependence of (A) the rupture pressures and (B) the maximal prerupture increase in diameter. Arrows indicate the identified aneurysms. ACoA indicates anterior communicating artery; ICA, internal carotid artery; MCA, middle cerebral artery; and VA-BA, vertebral and basilar arteries.
statistically significant effect on the rupture pressure or maximum vessel distensibility \((P>0.39)\).

**Discussion**

This is the first observation of the heterogeneity in rupture patterns of medium-sized intracranial arteries. Independent of the identified age trend, the measured rupture pressures for these medium-sized cerebral arteries decreased on average to only about half of those for aorta\(^3\) and remained in striking disproportion to the physiological pressures in those arteries.\(^4\) There was no direct dependence of the rupture on the vessel sizes studied. This may indicate that the rupture pressures are related to other factors, such as the functional type of the vessel.

The most interesting observation is the presence of transverse and spiral ruptures. Although there was no significant difference in the rupture pressure for these types of ruptures, they confirm that the vascular wall cannot be treated as a uniform substance. From Laplace laws we expect that, in a tied-up short vessel segment, the circumferential stress is twice as large as its longitudinal counterpart, and the vessel should split along its length. Our findings only support this scenario in <50% of apparently straight vessels, which prompt future clarification on which particular aspect(s) of vessel wall heterogeneity is responsible for the rupture pattern.

Our finding of lower rupture pressures in intracranial arteries is consistent with the precautions of using lower pressures during cerebral balloon angioplasty to decrease the risk of iatrogenic vessel rupture.\(^5\) However, the relationship between the balloon pressure and wall distention is complicated. Balloon pressures routinely reach 16 atm \((\approx 12000 \text{ mm Hg})\) within a comparable-sized coronary arteries,\(^6\) but the arterial wall strain originates from the physical distention of the relatively noncompliant balloon to force the vessel beyond its resting diameter. The relationship between age and the prerupture diameter may, therefore, provide a better target for numeric safety guidelines in angioplasty.\(^7,8\)

This work is limited by a small number of individuals and sampling bias from selecting suitable vessels to undergo the cumbersome experimental procedures. The typical yield of 2 to 3 vessel segments from a single individual reflects the difficulty of the microsurgical preparation. Potential increase in the number of studied vessels and individuals with and without disease may improve the understanding of the expected links among rupture pressures, types, and pathology. However, this small sample suggests that these dependencies may be secondary to the larger age effect confirmed in this study. We concentrated on the large vessels and ligated all small perforators. These small vessels are a known source of intracranial bleeding subject to further study.

**Conclusions**

We identified a significant dependence of the human intracranial arterial wall resilience on age. Despite identifying divergent patterns of wall rupture, there seemed to be little effect of vessel morphology or minor pathology on rupture pressures, which consistently exceeded the highest possible systolic blood pressures at the level of the circle of Will's.

**Disclosures**

None.

**References**

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