# Unruptured intracranial aneurysm rupture risk

see also Unruptured intracranial aneurysm treatment decision.

Findings suggest that unruptured intracranial aneurysms seem to represent no increased risks of poor outcome after local thrombolysis for intracerebral hematomas <sup>1)</sup>.

(1) IA location is the strongest factor associated with IA rupture status at diagnosis

(2) Risk factor awareness (hypertension, smoking) increases the likelihood of being diagnosed with unruptured IA

(3) Patients with ruptured IAs in high-risk locations tend to be older, and their IAs are smaller

(4) Smokers with ruptured IAs tend to be younger, and their IAs are larger

(5) Female patients with ruptured IAs tend to be older, and their IAs are smaller

(6) IA size and age at rupture correlate. The assessment of associations regarding patient and IA characteristics with IA rupture allows us to refine IA disease models and provide data to develop risk instruments for clinicians to support personalized decision-making <sup>2)</sup>.

There are substantial differences in patient and intracranial aneurysm characteristics between ruptured intracranial aneurysm and unruptured intracranial aneurysms. These findings support the hypothesis that different pathological mechanisms are involved in the formation of ruptured aneurysms and incidentally detected unruptured aneurysms. The potential protective effect of aspirin might justify randomized prevention trials in patients with unruptured aneurysms<sup>3)</sup>.

The exact prevalence of unruptured intracranial aneurysms (UIAs) is unknown, but at least one in 20 to 30 adults is likely to carry an asymptomatic UIA. Approximately one quarter of these UIAs rupture in a lifetime. Complex methodological challenges in conducting studies of epidemiology and risk factors for UIAs and SAH might have led to conclusions being drawn on the basis of epidemiological data of variable quality. Korja et al. believe that, as a result, misconceptions about UIAs and SAH may have arisen. They discuss three possible misconceptions about the epidemiology of UIAs and SAH, and suggest how the quality of future research could be improved <sup>4)</sup>.

Aneurysm location and other morphologic variables could play a role in predicting overall risk of rupture. Morphological parameters can be divided into 3 main groups, those that are intrinsic to the aneurysm, those that are extrinsic to the aneurysm, and those that involve both the aneurysm and surrounding vasculature (transitional).

By studying the morphology of aneurysms and their surrounding vasculature, Ho et al. identified

several parameters associated with ruptured aneurysms that include intrinsic, transitional, and extrinsic factors of cerebral aneurysms and their surrounding vasculature <sup>5)</sup>.

Despite the fact that ruptured intracranial aneurysm (RIAs) can be prevented by microsurgical clipping or endovascular coiling, there are no reliable means of effectively predicting IA patients at risk for rupture.

In patients of working age alcohol consumption and cigarette smoking are modifiable risk factors for untimely death through several causes and should be taken into account when treatment is considered <sup>6)</sup>.

## Score

## see PHASES score

## Size

Unruptured saccular aneurysms less than 10 mm in diameter have a very low probability of subsequent rupture. The mean diameter of the aneurysms that subsequently ruptured was 21.3 mm, compared with a diameter of 7.5 mm for aneurysms defined after rupture at the same institution. Part of the explanation for this discrepancy may be that the size of the filling compartment of the aneurysm decreases after rupture. There is also evidence from a study that intracranial saccular aneurysms develop with increasing age of the patient and stabilize over a relatively short period, if they do not initially rupture, and that the likelihood of subsequent rupture decreases considerably if the initial stabilized size is less than 10 mm in diameter. Consequently, the critical size for aneurysm rupture is likely to be smaller if rupture occurs at the time of or soon after aneurysm formation. There seems to be a substantial difference in potential for growth and rupture between previously ruptured and unruptured aneurysms<sup>7)</sup>.

The annual rupture rate associated with small unruptured aneurysms is quite low. Careful attention should be paid to the treatment indications for single-type unruptured aneurysms <5 mm. If the patient is <50 years of age, has hypertension, and multiple aneurysms with diameters of >or=4 mm, treatment should be considered to prevent future aneurysmal rupture<sup>8</sup>.

Cigarette smoking, patient age inversely, and the size and location of the unruptured intracranial aneurysm seem to be risk factors for aneurysm rupture. The risk of bleeding decreases with a very long-term follow-up <sup>9)</sup>.

The association of morphological characteristics with ruptured aneurysms has not been established in a systematic and location specific manner for the most common aneurysm locations.

# Geometric or hemodynamic considerations

see Intracranial aneurysm hemodynamics.

## Fragility of the aneurysmal wall

The fragility of the aneurysmal wall is an important predictive factor of rupture. Presently, however, it is difficult to determine when an operation for an unruptured tiny aneurysm is indicated; new neuroimaging techniques that detect the fragility of the aneurysmal wall are needed <sup>10</sup>.

Fifty unruptured middle cerebral artery aneurysms were analyzed. Spatial and temporal maximum pressure (Pmax) areas were determined with a fluid-flow formula under pulsatile blood flow conditions. Intraoperatively, thin walled regions (TWRs) of aneurysm domes were identified as reddish areas relative to the healthy normal middle cerebral arteries; 5 neurosurgeons evaluated and divided these regions according to Pmax area and TWR correspondence. Pressure difference (PD) was defined as the degree of pressure elevation on the aneurysmal wall at Pmax and was calculated by subtracting the average pressure from the Pmax and dividing by the dynamic pressure at the aneurysm inlet side for normalization.

In 41 of the 50 cases (82.0%), the Pmax areas and TWRs corresponded. PD values were significantly higher in the correspondence group than in the noncorrespondence group (P = .008). A receiver-operating characteristic curve demonstrated that PD accurately predicted TWRs at Pmax areas (area under the curve, 0.764; 95% confidence interval, 0.574-0.955; cutoff value, 0.607; sensitivity, 66.7%; specificity, 82.9%).

A high PD may be a key parameter for predicting TWRs in unruptured cerebral aneurysms <sup>11</sup>.

Suzuki et al., present in this issue the findings of their research on intracranial aneurysms and report the work on pressure elevations at the thin walled regions of an aneurysm dome using computational fluid dynamics (CFD) modeling in 51 unruptured middle cerebral artery aneurysms. The authors attempt to show that areas of maximum pressure may be important markers of thin-wall regions in unruptured cerebral aneurysms and theorize that by calculating the pressure difference value for each aneurysm type using computational fluid dynamics, it is possible to estimate the accuracies of predictions regarding thin-wall regions. It would seem that this is a good study and a worthwhile contribution to the literature. At the same time, it appears that not much has changed since Kallmes <sup>12)</sup> wrote his poignant and perhaps provoking but timely editorial 4 years ago, and there continue to be publications that fail basic tests or internal consistency and validity.CFD modeling for intracranial aneurysms has emerged from an arcane interest of a few to a field producing a significant number of articles. A simple search in PubMed yields <2 results for the years 1990 to 1999 and >19 for the years 2015 to 2016 alone. This of course reflects the greater affordability and easier access to highperformance computing platforms, overall advances in computing power, and easier-to-use software packages complete with graphical user interfaces. A number of articles by very experienced researchers have questioned in the past the validity and value of CFD modeling <sup>13) 14) 15) 16) 17) 18).</sup>

CFD analysis in particular is a field that is prone to data dredging and exploratory analysis. It should be considered paramount to raise the quality of the research done by requiring authors to clearly state the hypothesis tested in their work. It remains a basic, albeit often overlooked and perhaps at times consciously evaded, requirement for publication of research findings that the methods described allow a knowledgeable expert in the field to reproduce the findings. In line with the publishing of research in such a manner that it, in theory, could be reproducible and verifiable and with the almost limitless space offered by online supplementary data appendixes, we should call for, perhaps in an online appendix, a framework for defining physical quantities and boundary conditions and a demonstration that the modeling setup is able to reproduce parameters of basic known CFD experiments such as flow development in a curved tube or a stenotic tube. Demonstration of grid and mesh density independently of results should require authors to provide clearly stated definitions for these parameters and the details of their approximations in computational and experimental studies. This is especially important for research groups publishing their first results in this field, although perhaps less so for groups that can reference a body of previous works in which such testing of their setup was done in the past.CFD is exquisitely sensitive to assumptions made and boundary conditions entering the simulation, and results must be presented and analyzed with these assumptions in mind. Internal controls are difficult to come by, but it has been a best practice to explicitly describe the flow and wall parameter conditions in a assumed normal vessel segment. In other words, unless the simulation predicts a rather normal flow environment and wall shear conditions in the parent vessel of a side wall aneurysm proximal and distal to the aneurysmal segment, why abnormal values in the aneurysmal segment predicted by the simulation should be taken at face value deserves some explanation.

It is worth repeating the questions raised by Robertson and Watton<sup>19)</sup> when conducting CFD research on intracranial aneurysms, asking to make judicious assumptions about boundary conditions, and an effort should be made to conduct an error or sensitivity analysis for assumptions that may influence the hemodynamics in the parent vessel tree and the aneurysm sac, especially when we have limited information about such assumptions. Idealizations are important and necessary tools for developing models and assumptions, but conclusions based on one specific anatomy may not hold up for other geometries. Using patient-based geometries but assuming the same inflow boundary condition for all cases would lead to unrealistic results, even when the model would be a simple straight vessel, disregarding the complication of an aneurysm attached to such a vessel. We know that shear conditions in a normal vessel are somewhat tightly regulated to ensure a healthy hemodynamic milieu for the endothelial cells.

The present publication not only adds another metric to the extensive table compiled by Xiang et al <sup>20)</sup> but is more significant for the seemingly arbitrary construction of a dimensionless parameter called the pressure difference, which has the physical properties of a friction coefficient.

Perhaps on a more optimistic note, this continues to be a field with great potential, and more often than not, we see studies with innovative design and interesting approaches <sup>21)</sup>.

The value in simulation lies in linking physiological measurements to processes that cannot readily be measured but need to be quantified to explain the underlying mechanisms and processes and, in enhancing our understanding of these processes, to ultimately help our patients <sup>22)</sup>.

## Posterior communicating artery aneurysm

Morphological parameters associated with aneurysm rupture in that location were evaluated to generate 3-D models of the aneurysms and surrounding vasculature. Univariate and multivariate analyses were performed to evaluate morphological parameters including aneurysm volume, aspect ratio, size ratio, distance to ICA bifurcation, aneurysm angle, vessel angles, flow angles, and vessel-to-vessel angles. From 2005-2012, 148 PCoA aneurysms were treated in a single institution. Preoperative CTAs from 63 patients (40 ruptured, 23 unruptured) were available and analyzed. Multivariate logistic regression revealed that smaller volume (p=0.011), larger aneurysm neck diameter (0.048), and shorter ICA bifurcation to aneurysm distance (p=0.005) were the most strongly

associated with aneurysm rupture after adjusting for all other clinical and morphological variables. Multivariate subgroup analysis for patients with visualized PCoA demonstrated that larger neck diameter (p = 0.018) and shorter ICA bifurcation to aneurysm distance (p = 0.011) were significantly associated with rupture. Intracerebral hemorrhage was associated with smaller volume, larger maximum height, and smaller aneurysm angle, in addition to lateral projection, male sex, and lack of hypertension. Ho et al., found that shorter ICA bifurcation to aneurysm distance is significantly associated with PCoA aneurysm rupture. This is a new physically intuitive parameter that can be measured easily and therefore be readily applied in clinical practice to aid in the evaluation of patients with PCoA aneurysms<sup>23</sup>.

#### 1)

Xu F, Lian L, Liang Q, Pan C, Pan C, Hu Q, Chen R, Wang F, Zhang M, Tang Z, Zhu S. Is it dangerous to treat spontaneous intracerebral hemorrhage by minimally invasive surgery plus local thrombolysis in patients with coexisting unruptured intracranial aneurysms? Clin Neurol Neurosurg. 2019 Mar 15;180:62-67. doi: 10.1016/j.clineuro.2019.03.013. [Epub ahead of print] PubMed PMID: 30947028.

Morel S, Hostettler IC, Spinner GR, Bourcier R, Pera J, Meling TR, Alg VS, Houlden H, Bakker MK, Van't Hof F, Rinkel GJE, Foroud T, Lai D, Moomaw CJ, Worrall BB, Caroff J, Constant-Dits-Beaufils P, Karakachoff M, Rimbert A, Rouchaud A, Gaal-Paavola El, Kaukovalta H, Kivisaari R, Laakso A, Jahromi BR, Tulamo R, Friedrich CM, Dauvillier J, Hirsch S, Isidor N, Kulcsàr Z, Lövblad KO, Martin O, Machi P, Mendes Pereira V, Rüfenacht D, Schaller K, Schilling S, Slowik A, Jaaskelainen JE, von Und Zu Fraunberg M, Jiménez-Conde J, Cuadrado-Godia E, Soriano-Tárraga C, Millwood IY, Walters RG, The neurIST Project, The Ican Study Group, Genetics And Observational Subarachnoid Haemorrhage Gosh Study Investigators, International Stroke Genetics Consortium Isgc, Kim H, Redon R, Ko NU, Rouleau GA, Lindgren A, Niemelä M, Desal H, Woo D, Broderick JP, Werring DJ, Ruigrok YM, Bijlenga P. Intracranial Aneurysm Classifier Using Phenotypic Factors: An International Pooled Analysis. J Pers Med. 2022 Aug 30;12(9):1410. doi: 10.3390/jpm12091410. PMID: 36143196; PMCID: PMC9501769.

Hostettler IC, Alg VS, Shahi N, Jichi F, Bonner S, Walsh D, Bulters D, Kitchen N, Brown MM, Houlden H, Grieve J, Werring DJ; Genetics and Observational Subarachnoid Haemorrhage (GOSH) Study investigators. Characteristics of Unruptured Compared to Ruptured Intracranial Aneurysms: A Multicenter Case-Control Study. Neurosurgery. 2018 Jul 1;83(1):43-52. doi: 10.1093/neuros/nyx365. PubMed PMID: 28973585.

Korja M, Kaprio J. Controversies in epidemiology of intracranial aneurysms and SAH. Nat Rev Neurol. 2016 Jan;12(1):50-5. doi: 10.1038/nrneurol.2015.228. Epub 2015 Dec 16. Review. PubMed PMID: 26670298.

Ho AL, Lin N, Frerichs KU, Du R. Intrinsic, Transitional, and Extrinsic Morphological Factors Associated With Rupture of Intracranial Aneurysms. Neurosurgery. 2015 Sep;77(3):433-42. doi: 10.1227/NEU.00000000000835. PubMed PMID: 26075307.

#### long:25568291

7)

long:3783255

Sonobe M, Yamazaki T, Yonekura M, Kikuchi H. Small unruptured intracranial aneurysm verification study: SUAVe study, Japan. Stroke. 2010 Sep;41(9):1969-77. doi: 10.1161/STROKEAHA.110.585059. Epub 2010 Jul 29. PubMed PMID: 20671254.

Juvela S, Poussa K, Lehto H, Porras M. Natural history of unruptured intracranial aneurysms: a longterm follow-up study. Stroke. 2013 Sep;44(9):2414-21. doi: 10.1161/STROKEAHA.113.001838. Epub 2013 Jul 18. PubMed PMID: 23868274.

update: 2024/06/07 unruptured	_intracranial_aneurysm_rupture	_risk https://neurosurgerywiki.cor	n/wiki/doku.php?id=unruptured	_intracranial_aneur	ysm_rupture_ri	sk
02:48						

10)

Kawahara I, Tsutsumi K, Fujimoto T, Hirose M, Shirakawa Y, Toba T. [Ruptured tiny middle cerebral artery aneurysm]. No Shinkei Geka. 2015 Mar;43(3):207-13. doi: 10.11477/mf.1436202988. Japanese. PubMed PMID: 25748805.

11)

Suzuki T, Takao H, Suzuki T, Kambayashi Y, Watanabe M, Sakamoto H, Kan I, Nishimura K, Kaku S, Ishibashi T, Ikeuchi S, Yamamoto M, Fujii Y, Murayama Y. Determining the Presence of Thin-Walled Regions at High-Pressure Areas in Unruptured Cerebral Aneurysms by Using Computational Fluid Dynamics. Neurosurgery. 2016 Oct;79(4):589-95. doi: 10.1227/NEU.000000000001232. PubMed PMID: 27028475.

12) 13)

Kallmes DF. Point: CFD: computational fluid dynamics or confounding factor dissemination. AJNR Am J Neuroradiol. 2012;33(3):395–396.

14)

Steinman DA. Computational modeling and flow diverters: a teaching moment. AJNR Am J Neuroradiol. 2011;32(6):981–983.

15)

Cebral JR, Meng H. Counterpoint: realizing the clinical utility of computational fluid dynamics-closing the gap. AJNR Am J Neuroradiol. 2012;33(3):396–398.

Robertson AM, Watton PN. Computational fluid dynamics in aneurysm research: critical reflections, future directions. AJNR Am J Neuroradiol. 2012;33(6):992–995.

Strother CM, Jiang J. Intracranial aneurysms, cancer, x-rays, and computational fluid dynamics. AJNR Am J Neuroradiol. 2012;33(6):991–992.

Xiang J, Tutino VM, Snyder KV, Meng H: CFD: computational fluid dynamics or confounding factor dissemination? The role of hemodynamics in intracranial aneurysm rupture risk assessment. AJNR Am J Neuroradiol. 2014;35(10):1849–1857.

21)

Goubergrits L, Schaller J, Kertzscher U, et al. Statistical wall shear stress maps of ruptured and unruptured middle cerebral artery aneurysms. J R Soc Interface. 2012;9(69):677–688.

Schirmer CM. Commentary: Determining the Presence of Thin-Walled Regions at High-Pressure Areas in Unruptured Cerebral Aneurysms by Using Computational Fluid Dynamics. Neurosurgery. 2016 Oct;79(4):596-7. doi: 10.1227/NEU.0000000001350. PubMed PMID: 27438407.

Ho A, Lin N, Charoenvimolphan N, Stanley M, Frerichs KU, Day AL, Du R. Morphological parameters associated with ruptured posterior communicating aneurysms. PLoS One. 2014 Apr 14;9(4):e94837. doi: 10.1371/journal.pone.0094837. eCollection 2014. PubMed PMID: 24733151.

