

# Unruptured intracranial aneurysm case series

## 2021

A total of 38,207 patients were treated for UIAs. Among these, 22,093 (57.8%) patients underwent coiling and 16,114 (42.2%) patients underwent clipping. The incidence of ICRH, requiring a secondary operation, within 3 months in patients  $\geq 65$  years that underwent coiling and clipping was 1.13% and 4.81%, respectively, and that of both groups assessed were significantly higher in patients  $\geq 75$  years (coiling,  $P = 0.013$ , relative risk (RR) 1.81; clipping,  $P = 0.015$ ) than younger patients. The incidence of CI within 3 months in patients aged  $\geq 65$  was 13.90% and 9.19% in the coiling and clipping groups, respectively. The incidence of CI after coiling in patients aged  $\geq 75$  years ( $P < 0.001$ , RR 1.96) and after clipping in patients aged  $\geq 70$  years ( $P < 0.001$ , RR 1.76) was significantly higher than that in younger patients. The mortality rates within 1 year in patients with perioperative ICRH or CI were 2.41% and 3.39% for coiling and clipping groups, respectively, in patients  $\geq 65$ . These rates increased significantly at age 70 in the coiling group and at age 75 for the clipping group ( $P = 0.012$  and  $P < 0.001$ , respectively).

The risk of treatment increases with age, and this risk increases dramatically in patients aged  $\geq 70$  years. Therefore, the treatment decisions in patients aged  $\geq 70$  years should be made with utmost care <sup>1)</sup>.

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In a retrospective analysis, red (R), green (G), blue (B), and **RGB color model** signal intensities of aneurysm were quantitatively measured using an intraoperative digital picture in 150 cases. Color intensities were measured by two independent investigators. Aneurysm redness was defined as an R/RGB ratio since the brightness of the operative field differed by each surgery or angle of the microscope.

The median aneurysm size was 4.9 mm (IQR 3.9-5.9 mm). Median color intensity of R, G, B, RGB, and R/RGB ratio were 206 (185-215), 129 (107-150), 136 (115-157), 157 (140-174), and 1.26 (1.20-1.38), respectively. The intraclass correlation coefficient for R/RGB ratio was 0.73 ( $P < 0.0001$ ). The proportion of female sex was significantly higher for EUCA ( $p = 0.019$ ). Median R/RGB ratio in GUCA was significantly larger than that of non-EUCA (OR 1.25, 95% CI 1.19-1.35) ( $p = 0.035$ ). Even after adjustment of female sex, a R/RGB ratio  $\geq 1.36$  was related to EUCA (OR 3.02, 95% CI 1.30-7.02).

The present study showed that an R/RGB ratio could be calculated easily and a larger R/RGB ratio was related to EUCA. When EUCA is managed by surgical treatment, more careful manipulation should be needed compared to non-EUCA due to a "red" wall of EUCA <sup>2)</sup>.

## 2020

In total, 74 patients harboring 96 **unruptured intracranial aneurysm** (UIAs) were included in a study. The mean patient age was  $64.7 \pm 12.4$  years, and 60 patients (81%) were women. Multivariate

analysis showed that age (OR 1.12, 95% CI 1.05-1.19), aneurysm size  $\geq 7$  mm (OR 21.3, 95% CI 4.88-92.8), and location in the anterior communicating, posterior communicating, and basilar arteries (OR 10.7, 95% CI 2.45-46.5) were significantly associated with increased wall enhancement on [High-resolution vessel wall imaging](#) (HR-VWI). On the other hand, the use of [aspirin](#) (ASA) was significantly associated with decreased aneurysmal wall enhancement on HR-VWI (OR 0.22, 95% CI 0.06-0.83,  $p = 0.026$ ).

The study results establish a correlation between use of ASA daily for  $\geq 6$  months and significant decreases in wall enhancement of UIAs on HR-VWI. The findings also demonstrate that detection of wall enhancement using HR-MRI may be a valuable noninvasive method for assessing aneurysmal wall inflammation and UIA instability <sup>3</sup>.

## 2019

A study aimed to clarify the risk factors of treatment for unruptured cerebral aneurysms (UCAs) in elderly patients by comparing the morbidity at discharge between surgical clipping and endovascular coiling in nonelderly ( $<65$  years) and elderly ( $\geq 65$  years) patients based on a national database in Japan.

A total of 36,017, including 15,671 patients with UCA after exclusion of unknown location, were registered in the Diagnosis Procedure Combination, the nationwide database, from 2010 to 2015 in Japan. Outcome of Barthel Index at discharge was investigated and multivariate logistic regression analysis identified risk factors for the morbidity of Barthel Index  $<90$  at discharge in nonelderly and elderly patient groups.

Risk factors for morbidity at discharge were basilar artery aneurysm compared with internal carotid artery (ICA), diabetes mellitus (odds ratio [OR], 2.0-2.5; 95% confidence interval [CI], 1.6-3.7), antiplatelet drug, and anticoagulation drug; however, highest hospital volume compared with lowest was an inverse risk factor in both age groups. Endovascular coiling (OR, 0.4; 95% CI, 0.3-0.5) was a significantly inverse risk in the elderly group. Anterior communicating artery aneurysm compared with ICA was a significant risk (OR, 1.6; 95% CI, 1.0-2.6) in the nonelderly group; on the other hand, anterior communicating artery aneurysm (OR, 0.7; 95% CI, 0.5-0.95) and middle cerebral artery aneurysm (OR, 0.6; 95% CI, 0.5-0.8) compared with ICA were significantly inverse risks in the elderly group.

Endovascular coiling after control of diabetes mellitus was recommended for the treatment of UCA in elderly patients. The ICA location of aneurysm in the elderly should be paid attention as the treatment risk <sup>4</sup>.

## 2017

A series of 296 UIA patients (including 162 treated and 134 untreated) were analyzed. Postal questionnaires were sent to these patients, included Self-Rating Anxiety Scale (SAS), Self-Rating Depression Scale (SDS) and Short Form-36 (SF-36). In total, 198 (66.9%) patients responded to our questionnaires. Patients with surgical clipping or endovascular coiling had a significant improvement in the physical function, body pain and mental health domains. No significant difference in the SAS,

SDS and SF-36 was observed between the clipping and coiling group, while SF-36 in body pain domain was significant higher in the coiling group. Moreover, patients diagnosed 5years ago with or without treatment got lower score of SAS and SDS, higher SF-36 score than those diagnosed one year ago. Neurological complications may be an important factor causing lower quality of life. The QoL of patients with endovascular coiling appear to be better than those of surgical clipping, with no difference in anxiety or depression <sup>5)</sup>.

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8705 patients underwent treatment for unruptured intracranial aneurysms.

Of these patients, 2585 (29.7%) had surgical clipping and 6120 (70.3%) had endovascular coiling. Instrumental variable analysis demonstrated no difference between coiling and clipping in 1-year postoperative mortality (OR 1.25, 95% CI 0.68-2.31) or 90-day readmission rate (OR 1.04, 95% CI 0.66-1.62). However, clipping was associated with a greater likelihood of discharge to rehabilitation (OR 6.39, 95% CI 3.85-10.59) and 3.6 days longer length of stay (LOS; 95% CI 2.90-4.71). The same associations were present in propensity score-adjusted and inverse probability-weighted models.

In a cohort of Medicare patients, there was no difference in mortality and the readmission rate between clipping and coiling of unruptured cerebral aneurysms. Clipping was associated with a higher rate of discharge to a rehabilitation facility and a longer length of stay <sup>6)</sup>.

## 2016

Murayama et al., <sup>7)</sup> conservatively followed up a cohort of 1960 aneurysms for up to 10 years and performed a risk analysis of rupture. From January 2003 to December 2012, the authors enrolled 1556 patients with 1960 aneurysms of 2665 patients with 3434 aneurysms screened. Patients were eligible for the study if they had an aneurysm at least 2 mm in its largest dimension. Exclusion criteria included fusiform, traumatic, or mycotic aneurysms; treatment before enrollment in the study; carotid cavernous aneurysms; and infundibular dilations. The authors recommended observation for aneurysms <5 mm and treatment for aneurysms >10 mm. For aneurysms between 5 and 10 mm, risks of treatment vs observation were discussed with the patients. Patients were followed up until time of subarachnoid hemorrhage (SAH), death resulting from any cause, or last possible follow-up contact. Patients were divided into 2 groups. Group 1 was composed of patients with no history of SAH, and group 2 was composed of patients with a history of SAH. Patients who presented with signs and symptoms of mass effect were treated urgently. Mean follow-up was 7388 aneurysm-years. The most common was middle cerebral artery (MCA) aneurysms (535 aneurysms, 27.3%), followed by internal carotid artery (ICA) aneurysms not connected to the origin of the posterior communicating artery (PCoM; 525 aneurysms, 26.8%). Aneurysms at the origin of the PCoM were the third most common (401 aneurysms, 20.5%), followed by vertebral artery-basilar artery aneurysms (169 aneurysms, 8.6%). Fifty-six aneurysms ruptured during the follow-up period, with an overall annual incidence SAH of 0.76%. Mean duration to rupture from initial presentation was 547 days. Regarding the rupture risk factors, aneurysm size, specific location, history of SAH, and the presence of a daughter sac were found to be independent risk factors in both single and multivariate Cox proportional-hazard models. On the other hand, and surprisingly, smoking, family history of SAH, age, female sex, hypertension, and diabetes mellitus were not associated with risk of rupture. Average rupture size was  $7.5 \pm 5.74$  mm. Of note, 39 ruptures (69.6%) occurred in aneurysms <7 mm in size. The probability of rupture increased with size. The authors then performed multiple analyses with the cutoff size set at 5, 6, 7, 8, 9, and 10 mm. They noted a statistical significance in all selected cutoff

sizes with and without adjustment for other risk factors. In terms of locations, vertebrobasilar aneurysms were associated with the highest rupture risk, followed by PCom, MCA, anterior cerebral artery (ACA), and then finally ICA aneurysms. Vertebrobasilar and PCom aneurysms had a significantly higher hazard ratio of rupture, whereas MCA and ACA aneurysms had only a moderate increase in risk. Fifteen of the 56 aneurysm ruptures (26.8%) resulted in death, and 16 of the 56 (28.65) ended in moderate to severe disability (modified Rankin Scale score of 3-5). Fewer than half of the patients with ruptures returned to normal life. None of the patients who had large or giant aneurysms recovered without deficits. The mortality rate of these patients was 69% (9 of 13), whereas the mortality rate of aneurysms <5 mm was 18% (4 of 22).

This study confirms many concepts about intracranial aneurysms. More than half of the ruptured aneurysms ended in at least moderate disability, further revealing the devastating effect of aneurysmal SAH. Size and location have again been shown to be independent risk factors for rupture. Unlike ISUIA, however, this study showed what was suspected all along: that even small aneurysms rupture. Although the authors are to be commended for their efforts, this study has obvious limitations. First, there is a clear selection bias. Aneurysms suspected to be of high risk of rupture were treated outside of this cohort, which would explain the low incidence of SAH in their population. These include irregular aneurysms and aneurysms that presented with mass effect. In terms of risk factors, some findings replicated what has been previously published in the literature (eg, size, location, daughter sac, and history of SAH). Other conclusions failed to corroborate findings from other studies (eg, smoking, hypertension). Although this could be due to selection bias or small population size, it could also be explained by the variability in aneurysm natural history and further highlights our lack of understanding of the pathology. Although statistics generated by large-scale studies help us to better understand diseases, it should be noted that they apply for the general masses and give a global perspective and therefore have little implication for an individual in the clinic. This is particularly an issue when the number of variables increases such as in the case of aneurysms. As an example, a patient with a connective tissue disease with a 5-mm ACA aneurysm might be at a higher risk than an otherwise healthy patient with a 9-mm MCA aneurysm. When other variables such as age, aneurysm growth, shape, smoking, and SAH history are factored in, the complexity increases exponentially. In addition, aneurysm formation risk factors are not necessarily the same as rupture risk factors. In an ideal world, mathematically generated individualized risk assessment models would assist in decision-making and treatment algorithms. At this point in time, however, such a model remains out of immediate and practical reach. Further studies are required to improve our understanding of aneurysms on multiple levels, including clinical, biological, and mechanical <sup>8)</sup>.

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Over an 11.5-year period, Serrone et al, recommended surveillance imaging to 192 patients with 234 UIAs. The incidence of UIA growth and de novo aneurysm formation was assessed. With logistic regression, risk factors for UIA growth or de novo aneurysm formation and patient compliance with the surveillance protocol was assessed.

During 621 patient-years of follow-up, the incidence of aneurysm growth or de novo aneurysm formation was 5.0%/patient-year. At the 6-month examination, 5.2% of patients had aneurysm growth and 4.3% of aneurysms had grown. Four de novo aneurysms formed (0.64%/patient-year). Over 793 aneurysm-years of follow-up, the annual risk of aneurysm growth was 3.7%. Only initial aneurysm size predicted aneurysm growth (UIA < 5 mm = 1.6% vs UIA ≥ 5 mm = 8.7%, p = 0.002). Patients with growing UIAs were more likely to also have de novo aneurysms (p = 0.01). Patient compliance with this protocol was 65%, with younger age predictive of better compliance (p = 0.01).

Observation of low-risk UIAs with surveillance imaging can be implemented safely with good adherence. Aneurysm size is the only predictor of future growth. More frequent (semiannual) surveillance imaging for newly diagnosed UIAs and UIAs  $\geq 5$  mm is warranted <sup>9)</sup>.

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A prospective consecutive cohort of 292 patients (2006-2014) and 368 SUIAs (anterior circulation aneurysms (ACs) smaller than 7 mm and posterior circulation aneurysms smaller than 4 mm without previous subarachnoid haemorrhage) was observed (mean follow-up time of 3.2 years and 1177.6 aneurysm years). Factors associated with aneurysm growth were systematically reviewed from the literature.

The aneurysm growth probability was  $2.6 \pm 0.1\%$  per year. The rate of unexpected aneurysm rupture before treatment was 0.24% per year (95% CI 0.17% to 2.40%). The calculated rate of aneurysm rupture after growth was 6.3% per aneurysm-year (95% CI 1% to 22%). Aneurysms located in the posterior circulation and aneurysms with lobulation were more likely to grow. Females or patients suffering hypertension were more likely to have an aneurysm growing. The probability of aneurysms growth increased with the size of the dome and was proportional to the number of aneurysms diagnosed in a patient.

It is safe to observe patients diagnosed with SUIAs using periodic imaging. Intervention to secure the aneurysm should be performed after growth is observed <sup>10)</sup>.

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Bekelis et al performed a cohort study of 100% Medicare fee-for-service claims data for elderly patients who underwent treatment for unruptured cerebral aneurysms from 2007 to 2012. In order to control for measured confounding we used multivariable regression analysis with mixed effects to account for clustering at the Hospital Referral Region (HRR) level. An instrumental variable (regional rates of endovascular treatment) analysis was used to control for unmeasured confounding by creating pseudo-randomization on the treatment method.

During the study period 8705 patients underwent treatment for unruptured cerebral aneurysms and met the inclusion criteria. Of these, 2585 (29.7%) had surgical clipping and 6120 (70.3%) had endovascular treatment. The median total Medicare expenditures in the first year after the admission for the procedure were \$46 800 (IQR \$31 000-\$74 400) for surgical clipping and \$48 100 (IQR \$34 500-\$73 900) for endovascular therapy. When we adjusted for unmeasured confounders, using an instrumental variable analysis, clipping was associated with increased 7-day Medicare expenditures by \$3527 (95% CI \$972 to \$5736) and increased 1-year Medicare expenditures by \$15 984 (95% CI \$9017 to \$22 951).

In a cohort of Medicare patients, after controlling for unmeasured confounding, we demonstrated that surgical clipping of unruptured cerebral aneurysms was associated with increased 1-year expenditures compared with endovascular treatment <sup>11)</sup>.

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198 unruptured cerebral aneurysms for whom clinical observation and follow-up with imaging surveillance was recommended at 4 clinical centers were prospectively recruited into this study. Imaging data (predominantly CT angiography) at initial presentation was recorded. Computational geometry was used to estimate numerous metrics of aneurysm morphology that described the size and shape of the aneurysm. The nonlinear, finite element method was used to estimate uniform

pressure-induced peak wall tension. [Computational fluid dynamics](#) was used to estimate blood flow metrics. The median follow-up period was 645 days. Longitudinal outcome data on these aneurysm patients-whether their aneurysms grew or ruptured (the unstable group) or remained unchanged (the stable group)-was documented based on follow-up at 4 years after the beginning of recruitment.

Twenty aneurysms (10.1%) grew, but none ruptured. One hundred forty-nine aneurysms (75.3%) remained stable and 29 (14.6%) were lost to follow-up. None of the metrics-including aneurysm size, nonsphericity index, peak wall tension, and low shear stress area-differentiated the stable from unstable groups with statistical significance.

The findings in this highly selected group do not support the hypothesis that image-derived metrics can predict aneurysm growth in patients who have been selected for observation and imaging surveillance. If [aneurysm shape](#) is a significant determinant of invasive versus expectant management, selection bias is a key limitation of this study <sup>12)</sup>.

## 2015

One thousand twelve patients with 1440 UIA underwent 1080 craniotomies. 10.1% (95% [confidence interval](#) [CI], 8.4-12.0) of craniotomies resulted in a complication leading to a [modified Rankin Scale](#) score >1 at 12 months. [Logistic regression](#) found age ([odds ratio](#), 1.04; 95% CI, 1.02-1.06), size ([odds ratio](#), 1.12; 95% CI, 1.09-1.15), and posterior circulation location ([odds ratio](#), 2.95; 95% CI, 1.82-4.78) to be significant. Cumulative 10-year risk of retreatment or rupture was 3.0% (95% CI, 1.3-7.0). The complication-effectiveness model was derived by dividing the complication risk by the 10-year cumulative freedom from retreatment or rupture proportion. Risk per effective treatment ranged from 1% for a 5-mm anterior circulation UIA in a 20-year-old patient to 70% for a giant posterior circulation UIA in a 70-year-old patient.

Complication-effectiveness analyses increase the information available with regard to outcome for the management of UIAs <sup>13)</sup>.

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Of 1231 UIAs in 1124 patients, 625 (50.7 %) aneurysms were treated with surgery, and 606 (49.3 %) aneurysms were treated with EVT. The overall complication rate of UIA treatment was 3.2 %. The rate of adverse events was 2.4 %, and the rates of morbidity and mortality were 0.6 and 0.2 %, respectively. The rates of adverse events, morbidity, and mortality were not significantly different between surgery and EVT. The rate of hospital use for EVT was stationary over the years of the study. Posterior circulation in surgery, large aneurysms (>15 mm) in EVT, and stent- or balloon-assisted procedures in EVT were associated with the occurrence of complications. Poor clinical outcome (mRS of 3-6) was 0.8 % at hospital discharge <sup>14)</sup>.

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