

## Intracranial aneurysms: individualising the risk of rupture



The decision of what to do with asymptomatic unruptured intracranial aneurysms is a fairly new problem. Although these aneurysms have been known to exist for centuries through autopsies and for several decades through catheter angiography, their true prevalence did not begin to emerge until the use of non-invasive angiograms became widespread in the recent past. Now we know that nearly 3% of the general population has an unruptured intracranial aneurysm.<sup>1</sup> Comparatively, subarachnoid haemorrhages from aneurysmal rupture are relatively uncommon. This discrepancy indicates that many intracranial aneurysms are not destined to rupture. Yet, the consequences of rupture can be devastating.<sup>2</sup> Treatment of the aneurysm by craniotomy and clipping or by endovascular coiling can effectively eliminate the risk of subarachnoid haemorrhages, but treatment of all unruptured intracranial aneurysms is neither prudent, because of the risk of iatrogenic complications, nor parsimonious, because of the high financial cost.<sup>3</sup> Thus, when advising a patient with an asymptomatic unruptured intracranial aneurysm we face a difficult problem. An adequate solution can only be based on individualisation of the rupture risk.

In *The Lancet Neurology*, Jacoba Greving and colleagues<sup>4</sup> present their analysis of individual patient data pooled from six prospective cohort studies on the natural history of unruptured intracranial aneurysms (three from Japan, one from the Netherlands, one from Finland, and one from the USA, Canada, and various European countries). The large sample size of the combined population allowed the researchers to refine the estimation of rupture risk at 1 and 5 years, define the strongest predictors of rupture among those evaluated in the original studies, and develop a score (named PHASES) to gauge the individual risk of rupture using readily available information. The information provided is solid and has practical value. I plan to use it when advising my patients, although keeping in mind certain caveats.

The PHASES score is calculated from the region of origin of the patient (attributing a higher risk to Finnish and Japanese patients than to all others, although specific information is not available for most world regions), presence of hypertension, patient's age

(dichotomised at 70 years), maximum diameter of the aneurysm (by far the strongest predictor of rupture), previous history of subarachnoid haemorrhage from another aneurysm, and the site of the aneurysm (with a higher risk assigned to aneurysms arising from the anterior cerebral arteries, posterior communicating arteries, or the posterior circulation vessels). Notable absences include smoking (at entry and on follow-up),<sup>5</sup> hypertension control, family history of subarachnoid haemorrhage, multiplicity of unruptured intracranial aneurysms, other anatomical and haemodynamic factors of the aneurysm (inflow angle, concentrated inflow jets, complex flow patterns, non-spherical shape, dome-to-neck ratio),<sup>6</sup> and, most importantly, evidence of aneurysm growth over time.<sup>7</sup> Yet, these additional factors also deserve careful consideration. Smoking cessation and control of hypertension might reduce rupture risk.<sup>8</sup> Follow-up imaging to exclude aneurysm growth is necessary because growth is strongly associated with increased risk of subarachnoid haemorrhage,<sup>7</sup> although the optimum frequency and duration of radiological follow up is not well defined.

The Article also incorporates charts offering specific 5-year risk prediction for different populations. Readers should note that the chart that would apply to North America and European countries other than Finland is based on information from the large ISUIA cohort (1691 patients with a median follow-up of 9 years)<sup>9</sup>

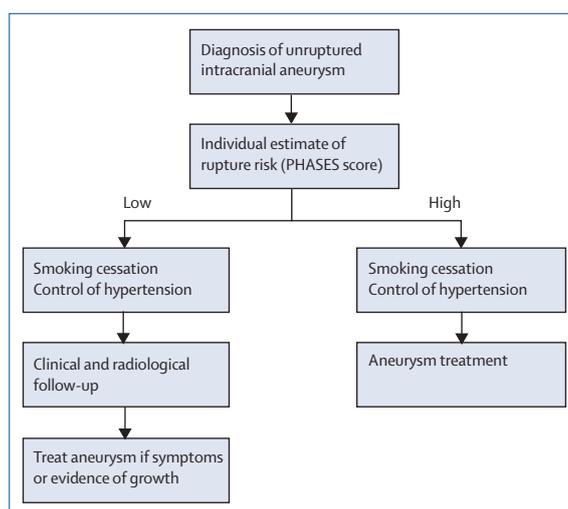


Figure: Proposed algorithm for the management of unruptured intracranial aneurysms

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and the much smaller Dutch cohort of the study by Wermer and colleagues (93 patients with a median follow-up of 2.2 years).<sup>10</sup> The risk predictions on this chart are therefore mainly derived from the ISUIA cohort, which highlights the limitations of pooling data from heterogeneous cohorts of very different sizes. Nonetheless, the information on this chart is presented in a visually appealing and user-friendly format and represents a refinement of individual risk stratification.

The greatest caveat in the interpretation of these risk estimates is that they are based on cohorts of patients for whom treatment of the aneurysm was left at the discretion of the patient's physician. Patients thought to be at high risk of rupture might have been treated at first recognition of the aneurysm (thus not being entered into the observational cohort) or after developing symptomatic or asymptomatic aneurysm growth without rupture (thus being censored from the cohort in which they had been enrolled). This selection bias affects the reliability of the risk predictions presented in this analysis. If aneurysms deemed at greatest risk of rupture had not been treated, the observed rates of rupture would probably have been higher. Consequently, the rupture rates presented in this pooled analysis might be an underestimation of the actual risks. Yet, this bias should not affect the value of the predictive factors for rupture identified in the proposed model.

As correctly pointed out by the investigators, a pure natural history study on the risk of rupture of intracranial aneurysms is impossible because treatment is favoured over observation in a substantial proportion of cases. Whether treatment is truly a better option for all patients with unruptured intracranial aneurysm is

a question that could only be answered by a rigorous randomised clinical trial. As the matter stands, we have to rely on our clinical judgment and the best available information about risk of rupture to offer individualised advice to our patients (figure). Such information is provided by Greving and colleagues' study<sup>4</sup> and pragmatically summarised in the PHASES score.

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I declare that I have no conflicts of interest.

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