Natural history of unruptured intracranial aneurysms

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The natural history of unruptured intracranial aneurysms (UIAs) continues to be a matter of debate, and there remains considerable controversy regarding optimal management. In this issue of the Journal of Neurosurgery, Lee and coworkers6 nicely summarize the risk of rupture of UIAs in South Korea. These authors utilized a retrospective cohort design and tried to identify patients with newly diagnosed unruptured aneurysms in 2006. To do so, they used data from the national health-claim database, which, given the organization and delivery of health care in South Korea, is likely to capture the majority of diagnosed and treated UIAs. To minimize potential “contamination” with patients with a known diagnosis of unruptured aneurysms, they excluded patients in whom subarachnoid hemorrhage (SAH) had been diagnosed, coiling or clipping of an intracranial aneurysm had been performed, or UIA had been diagnosed during the preceding year. Eventually, they were able to narrow their focus onto more than 7000 patients with UIAs diagnosed in 2006. Of these patients, approximately 20% underwent either endovascular (50%) or surgical (49%) treatment. As expected, based on baseline information available from the database, younger patients were more likely to be offered treatment. Five thousand nine hundred sixty-three patients (mean age 57.6 years) who did not undergo treatment were followed up for 3 years. Overall, 2.7% suffered an SAH supposedly from the originally unruptured aneurysm for a rupture rate of 0.9 cases/100 patient-years. It was noteworthy that the majority (128 of 163) of the ruptures occurred within the 1st year of diagnosis. An older age seemed to predispose to a higher risk of rupture, and women had 20% more ruptures than men.

How can we interpret these data? Administrative databases are being used with increasing frequency to detect trends, outcomes, and potential effectiveness of various therapeutic interventions. The main advantage of these databases is the ability to analyze a large volume of data based on prospective, objective data submission, often based on discharge codes and less likely to be influenced by the bias of a treating physician. Numerous limitations exist, and the conclusions of these analyses must be interpreted with caution. The database utilized in the Korean study provides information regarding hospitalization. However, important information concerning aneurysm size and location, the presence or absence of an aneurysm “daughter sac” or multiple lobes, other morphological characteristics, a family history of intracranial aneurysms and/or aneurysmal SAH, and symptomatic status is not provided, and these factors have all been shown to be potential risk factors for aneurysm rupture. The authors acknowledge the limitation that the definitions of risk factors for aneurysm rupture were not a key goal in their study. Potential aneurysm characteristic differences between patients treated with surgical or endovascular treatment, and those treated conservatively could not be defined. The limitation of the potential inaccuracy of a key end point coded in an administrative database, without the potential for objective confirmation, is also noteworthy.

Despite some of the limitations intrinsic to this type of analysis and unclear generalizability of data to other populations, some of the results are of particular note. The observation that the risk of rupture is higher during the 1st year after diagnosis is an important one and in line with growing evidence.8,9 The same pattern was noted in the International Study of Unruptured Intracranial Aneurysms (ISUIA) for large and giant aneurysms, although not for smaller ones.10 The higher incidence of rupture during the 1st year after diagnosis may suggest that many aneurysms that go on to rupture do so relatively soon after their formation, at a time when the wall is weaker and before possible healing mechanisms take place. The aneurysms that do not rupture at this early stage may reach a “steady state,” their growth is arrested, the potential for rupture is decreased, and they remain quiescent. This observation is consistent with the apparently opposing observations that while the risk of rupture of small incidental aneurysms at selected locations is low, the majority of ruptured aneurysms encountered in practice are of this small size. A higher rate of rupture shortly after the formation of small aneurysms also explains why a marked increase in the number of unruptured aneurysms treated with surgical or endovascular therapy in the past 20 years in the US has done little to affect the incidence of aneurysmal SAH, which has remained relatively unaffected during this time interval.1,5 One also wonders whether these aneurysms that rupture soon after detection might be detected with repeat imaging performed intermittently during follow-up. Available data suggest that there is 7% risk of aneurysm growth over the first 4 years following diagnosis among smaller aneurysms, that is, those < 8 mm in diameter.7 Whether these enlarging aneurysms have a heightened risk of rupture is unclear, and
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there are limited data available regarding factors predicting such enlargement.

The concept that a small aneurysm may have a higher risk of rupture shortly after formation could have important management implications. It is possible that a small aneurysm known about for some period of time should be regarded differently (in terms of potential for rupture) than a similar, recently discovered UIA. Moreover, we pay careful attention to symptoms and signs, which has led to the imaging study that detected the aneurysm. Such symptomatic patients are often treated urgently because of a perceived possible higher risk of rupture. It is noteworthy that during the period of enrollment in the prospective ISUIA cohort at the Mayo Clinic in Rochester, Minnesota, no patient with a possible symptomatic aneurysm smaller than 10 mm was entered in the conservative arm of the study, as they were all treated.4

Are unruptured aneurysms more dangerous in elderly people? In the study by Lee and coworkers, an older age was a factor associated with a higher rupture rate. However, from the data provided it is difficult to discern whether this was a real effect or could have been an artifact related to the higher rate of early invasive treatment in younger patients.

A higher risk of rupture of unruptured aneurysms in the elderly has been suggested by single-center studies from Japan but was not observed in the ISUIA cohort. In a recent study of 212 patients with incidental small aneurysms, no rupture occurred after a mean follow-up of 16.7 months in 125 patients (mean age 64.4 years) who had been treated conservatively (mean age 64.4 years).7 The treatment of UIAs in patients of advanced ages carries additional challenges, as the risks of both endovascular and surgical treatment increases with advancing age.8

Overall, despite the limitations intrinsic to large administrative databases, this study provides some interesting data in a population that has not been studied in detail before. These data, specifically as they relate to an increased risk of rupture shortly after diagnosis (and possibly formation), raise provocative questions. Despite a wealth of data provided by numerous studies with different methodologies, several important questions remain unanswered regarding the natural history and management of small UIAs.2 These questions can only be answered by a well-designed prospective study with large numbers of untreated and treated patients, detailed aneurysm assessment, repeat imaging during follow-up for those treated conservatively, objective outcome assessment (including cognitive outcome), and many years of follow-up. Such randomized clinical trials or comparative efficacy analysis should concentrate on small unruptured aneurysms and provide detailed data for all aneurysm locations, leading to individualized optimal treatment recommendations for our patients with these commonly detected lesions.

Disclosure

The authors report no conflict of interest.

References


Response

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We greatly appreciate the valuable and generous comments of Drs. Lanzino and Brown, who mentioned the higher risk of rupture shortly after the formation of small aneurysms while referring to our data. Based on their comments, our salient points became apparent. Sonobe et al.4 classified cerebral aneurysms into 4 types: 1) those that rupture shortly after formation, 2) those that grow slowly and then rupture after a few years, 3) those that grow slowly without rupturing, and 4) those that grow slowly and then remain stable without changing size. In clinical practice, the first type is seen relatively frequently in the ruptured small aneurysms, whereas observational and clinical studies may deal mostly with the second type. In our study we might have mostly detected the first type of cerebral aneurysm because our study reflected the real world situation through our use of the national claims database, which contains approximately 99% of the South Korean