Pros and Cons of Incidental Cerebral Aneurysm Treatment

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Many have debated the pros and cons of incidental cerebral aneurysm treatment, and more will in the years to come. The debate is due in large part to the fact that there is no data from randomized studies comparing treatment (clipping/coiling/flow diversion) outcomes with the natural history of these lesions, and no such data is likely to become available any time soon. In fact, the only large-scale effort to develop such data, The Trial on Endovascular Aneurysm Management (TEAM), had to be terminated prematurely due to low patient enrollment and ethical concerns (6). Given the complexity of patient and aneurysm characteristics, the widely varying outcomes for treatment from center to center, the growing number of treatment options, and the long period of follow-up needed, funding agencies have been less than receptive to additional randomization efforts.

We as clinicians are, therefore, left with balancing the results of several observational studies with an honest assessment our own treatment results. Some key observational studies include those by Seppo Juvela, MD, PhD; The International Study of Unruptured Intracranial Aneurysms (ISUIA) investigators and the Unruptured Cerebral Aneurysms Study (UCAS) investigators. Juvela et al. found an average annual risk of rupture of 1.3 percent, with cigarette smoking, aneurysm size and younger age at diagnosis as important predictors of rupture (3). In this cohort, 92 percent (131/142) of patients had a prior history of aneurysmal subarachnoid hemorrhage (aSAH), leading many to suggest that the rate may have been lower if more of the lesions had been found “incidentally.”
For ISUIA, five-year follow up was reported for a cohort 10 times as large (n=1692), and 60 percent of cases were asymptomatic with no history of aSAH (1, 7). Five-year cumulative rates of hemorrhage in untreated patients with non-cavernous, non-Pcom anterior circulation aneurysms were 0 percent, 2.6 percent, 14.5 percent, and 40 percent for aneurysms less than 7 mm, 7-12 mm, 13-24 mm, and 25 mm or greater. For the same size categories and posterior circulation or Pcom aneurysms, the rates were 2.5 percent, 14.5 percent, 18.4 percent, and 50 percent, respectively. While these rates are considerably lower than those reported by Juvela (especially for aneurysms <12mm), the investigators again showed that prior history of aSAH was important (especially for aneurysms <7mm). Nevertheless, the fact that many ISUIA patients also underwent treatment led to criticism that those treated conservatively were highly select population, which may have resulted in underestimation of risk.

ISUIA, however, also gave us new treatment data that was fairly robust for microsurgical clipping (n=1917). With overall death and disability rates of 3.7 percent and increases in procedural risk for larger aneurysms, those in the posterior circulation and older patients, it appeared that for clipping to be of benefit, a patient under the age of 60 would have to have a life expectancy of about 12 years. ISUIA investigators went on to test the hypothesis that most patients under 60 would benefit from clipping by performing a propensity analysis on 1,680 of the 3,608 patients followed for a minimum of nine years [median 15 years] (AANS plenary presentation Torner et al 2010). Microsurgery resulted in a five- to six-fold benefit in preventing hemorrhage, hemorrhage-associated morbidity and mortality, and aneurysm-related poor outcome (p<0.001). Microsurgery also resulted in 10-year reductions in: non-aneurysmal poor outcome (8 percent ARR p=0.003), all-cause poor outcome (12 percent ARR p<0.0001) and all-cause mortality (9 percent ARR; 29% RRR p<0.0001).

What was most interesting was that these findings were true regardless of patient age, aneurysm site and size. The benefit of microsurgery was maintained in the elderly because while older patients did worse with surgery, they also demonstrated a greater benefit from hemorrhage prevention. Unfortunately, gauging the benefit of endovascular repair was more difficult, given: 1) the smaller number of cases (n=451), 2) the fact that the treatment was still evolving during the study period, and 3) the fact that the five-year risk of hemorrhage was
about five times higher for endovascular than surgery and only 18 percent less than conservative management. Recent work shows that as coiling becomes an increasingly popular choice for repair of incidental aneurysms, it is critical to further define its efficacy and safety, perhaps through the use of registries (2, 4).

So how does this data fit with those recently published from the UCAS in Japan (5)? This study followed a similar overall design as the ISUIA, but was nearly three times the size, with 5,720 patients with saccular aneurysms that were 3 mm or larger. Of the 6,697 aneurysms studied, 91 percent were discovered incidentally. The mean (±SD) size of the aneurysms was 5.7±3.6 mm, and the majority of aneurysms were located in the middle cerebral artery (36 percent) and internal carotid artery (34 percent). During the follow-up period (11,660 years total), rupture occurred at an annual rate of 0.95 percent. With 3- to 4-mm aneurysms as the reference, the hazard ratios for size for rupture were 5-6 mm, 1.13 (95 percent CI, 0.58 to 2.22); 7 to 9 mm, 3.35 (95 percent CI, 1.87 to 6.00); 10 to 24 mm, 9.09 (95 percent CI, 5.25 to 15.74); and 25 mm or larger, 76.26 (95 percent CI, 32.76 to 177.54). The larger sample size in this study allowed assessment of rupture rates amongst specific aneurysm locations and confirmed prior notions that Pcom and Acom aneurysms were twice as likely to rupture as middle cerebral artery aneurysms (pcom 1.90 (1.12–3.21) p=0.02; acom 2.02 (1.13–3.58) p=0.02). Aneurysms with a daughter sac also were 1.6 times more likely to rupture [1.63 (1.08-2.48), p=0.02]. Interestingly, even very small Acom aneurysms (3-4mm) had a nearly one percent annual bleed rate (0.90 [0.45-1.80]), and the overall rate of rupture for small aneurysms was significantly higher than found by the ISUIA. Interestingly, smoking and prior SAH did not increase the risk, but hypertension and increasing age did. Symptomatic aneurysms and those with either thrombosis or calcification also demonstrated a greater risk for bleeding.

During the follow-up period, 2,722 patients with 3,050 aneurysms underwent surgical repair before rupture of the aneurysm. Patient data was censored at time of repair, and those receiving surgery significantly differed in nearly every patient and aneurysm attribute. As in the ISUIA and studies by Juvella et al., rates of rupture were assessed from untreated aneurysms deemed low-risk. Thus, the actual rates of rupture may again be underestimated. Nearly 1,500 patients were lost to follow-up during the initial three years of the study, which also may have led to underestimation of events.

So where does this data leave us? Ultimately, it remains difficult to assess the external validity of the data as it relates to patients evaluated on a daily basis. Information from observational rupture and/or high-risk for treatment. By contrast, most surgeons only have anecdotal morbidity data on cases they’ve treated, which tend to be relatively low-risk for treatment or high-risk for rupture. Moreover, most surgeons operate on comparatively few cases, leading to inexact estimates at best. With these limitations, we continue to advocate: 1) that with rare exceptions, all symptomatic unruptured aneurysms be treated; 2) that many small, incidental aneurysms less than 5 mm in diameter can be managed conservatively, but for Acom, and Pcom lesions this size cutoff may be too high; 3) that all asymptomatic cavernous aneurysms be managed conservatively; 4) that non-cavernous aneurysms larger than 5 mm in patients younger than 70 years of age should be seriously considered for treatment; 5) that
microsurgical clipping rather than endovascular coiling should usually be the first treatment choice in low-surgical risk cases; 6) that treatment decisions should be made in a collaborative environment by a highly experienced team of micro-cerebrovascular and endovascular neurosurgeons working at a tertiary medical center with a high case volume and using a decision-making paradigm designed to offer not only low-risk treatments, but also open to continuous improvement through participation in high-quality prospective registries.

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**References**


