Basic Summary of Recent Significant Cerebrovascular Studies

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ISUIA (International Study of Unruptured Intracranial Aneurysms)

Prior to 1998, most studies reported an annual rate of about1-2% for rupture of an intracranial aneurysm. Also, as reported in the Cooperative Study of Intracranial Aneurysms and SAH involving over 6,000 patients, the critical size for rupture was found to be 7-10mm.

The ISUIA was published in NEJM in 1998. This study (retrospective data on 1500 patients over 21 years) found an extremely low rate of rupture for aneurysms < 10mm in size (0.05% annual risk for rupture) in patients who had never experienced a SAH (Group I). In patients who had previously suffered a SAH from another aneurysm (Group II), the study found that the risk for rupture of a remaining aneurysm was 0.5%, irregardless of size.

Also, in ISUIA I, the morbidity of surgical treatment was higher than anticipated and it was directly related to age (prospective data on 1,100 patients collected over 4 years). This mainly involved cognitive alteration on mini-mental status examination. Surgical M&M for incidental aneurysms was found to be 6.5% in patients < 45 years old, 14.4% in patients 45-65 years old, and 32% in patients >65 years old. Therefore, in the ISUIA I, the risk for rupture appeared much lower than previously reported and the risk of treatment much higher.

There were significant issues raised about the validity of ISUIA I. Given the risk for rupture based on ISUIA I, there would need to be a 20% incidence of aneurysms in the general population, which greatly exceeds the generally reported incidence of 2-5%.. Also, aneurysms less than 10mm in size in Group I (no prior SAH) were not further stratified. Only about 25% of aneurysms in Group I were 6-9 mm in size (which is the critical size reported in the Cooperative Study on Intracranial Aneurysms and SAH) and intracavernous aneurysms and aneurysms 2-5 mm in size constituted 50% of the aneurysms studied. These factors were felt to give a false impression of a low risk for rupture in patients without prior SAH. Furthermore, the natural history component of the ISUIA I is retrospective. This introduces unrecognized bias because patients may have been excluded from follow-up by death, non-compliance, relocation, and subsequent surgical treatment.

With regard to treatment, there was a higher proportion of aneurysms in the posterior circulation and substantially fewer PCoA aneurysms compared to the natural history group. Nearly 50% of the surgically treated aneurysms were larger than 1 centimeter.

only addressed safety issues at one year. There is an expected 10 year follow-up for the UK patients and some from other centers.

There are several significant criticisms of ISAT. First, there was no adjudification of the operators. Endovascular treatment was conducted by physicians with an experience of a minimum of 30 aneurysms coiled, whereas neurosurgeons were not required to provide any outcome figures before being permitted to participate in the study. It is felt that this factor may have contributed to the seemingly high rate of poor surgical results. The study population was biased to small, anterior circulation aneurysms. The 31% of surgically-treated patients with a modified Rankin score of 3-6 at one year is higher than that reported in other series for similar lesions. There was a statistically significant difference between clip and coil for those with modified Rankin scores of 3-6, but not for scores of 1-2. Also, it cannot be determined if the aneurysms selected for possible coiling were "cherry picked." The endovascular therapists may only have picked those aneurysms which were felt to be most optimal for coiling. The results of ISAT probably cannot be generalized to different populations of patients with SAH. However, it is unlikely that a similar study of this size will be repeated or that the anticipated 10 year follow-up for late aneurysm recurrence and rebleeding will occur at a rate that would affect the significance difference in outcome noted at one year.

Campi *et al* analyzed the need for retreatment in ISAT in the endovascularly and surgically treated patients. Follow-up angiography was obtained in 88.2% and 45.8% respectively. Retreatment was defined as 'late' if it was performed more than 3 months after coiling or 1 month after surgery. They considered late retreatments as a surrogate for aneurysm recurrence. Early retreatments were attributed to incomplete or failed primary treatment. Nine percent of endovascular and 0.9% of clipped patients underwent late retreatment (30 days – 1 year). Early retreatment was performed in 8.8% of coiled patients and 2.9% of surgical patients. Retreated aneurysms tended to be larger and only PCoA aneurysms underwent significantly more retreatments than other locations. The 'treatment received' rebleed rates more than one year after treatment are 0.24% per patient-year for coiling and 0.032% per patient-year for clip ligation.

In a follow-up analysis of the ISAT data, Mitchell *et al* noted that the 1-year poor outcome rates were age dependent for coil embolization, being much more favorable in the younger population but with a significant rise in older patients whereas the surgical group showed a steady rise in the poor outcome rates with advancing age. Based on the findings that there is a higher rebleeding rate after coil embolization than surgery, and partly because the difference between poor outcome rates (between clip and coil occlusion) is much smaller for younger patients, the authors concluded that the advantage of coil embolization over clip ligation for ruptured intracranial aneurysms cannot be assumed for patients < 40 years old.

The Barrow Ruptured Aneurysm Trial (BRAT) published results of one year outcome in 2012. This was designed as a pilot study to further elucidate the outcome of clip vs. coil in a setting more reflective of cerebrovascular practices. The trial pre-supposed equivalence between the two treatments (null hypothesis). The results of BRAT are

at the base) is not well understood at the present time (Murayama *et al*, J Neurosurg 2003; Raymond *et al*, Stroke 2003, Bracard *et al*, J Neurosurg 2010). If other techniques such as balloon remodeling or stenting are required to treat an aneurysm, the risk of a significant complication related to the endovascular procedure rises dramatically (Sluzewski *et al*, J Neurosurg 2006; Lylyk *et al*, J Neurosurg 2005).

Lanzino *et al* reviewed their experience with an approach where clipping and coiling were felt to be complementary treatment techniques. Currently, they feel that the majority of ruptured MCA, small PCoA, and small ACoA aneurysms should be considered for primary surgical treatment, unless the patient is elderly. Treatment of very small ruptured aneurysms (< 3mm) is associated with a significantly higher risk for intra-procedural rupture.

In my opinion, the following issues need to be considered when counseling a patient with an incidental aneurysm:

1. Most aneurysms less than 7mm in size appear to have a very low risk for rupture according to the ISUIA studies and UCAS Japan. The presence of irregularities or blebs and/or location at the PCoA may be more dangerous. There was a difference between the two studies in the risk associated ACoA and posterior circulation locations.
2. Younger age and psychological issues (the patient's psychological tolerance to harbor an intracranial aneurysm) may influence one toward more aggressive strategies (van der Schaaf *et al*, Stroke 2002).
3. Older patients have an increased morbidity with treatment, especially surgical.
4. Endovascular treatment is generally a safer procedure. However, the issues of incomplete treatment and durability are still concerns which need to be settled. Most facilities or institutions will have a preferential strength for either an endovascular or surgical approach. This will influence the treatment paradigm at any given facility and should rightly be part of the decision making process. There will be escalating pressure to pursue treatment of aneurysms only at facilities that are equally capable of offering surgical or endovascular treatments.
5. Based on the results of ISAT and BRAT, a policy of intent-to-treat ruptured intracranial aneurysms (when appropriate for GDC coiling) by endovascular therapy in patients older than 40 years of age will result in significantly less death and disability at one year. As endovascular technology advances and the potential risk for rebleed from coiling diminishes, the age cut-off may dissipate. However, not all aneurysms are currently well-suited for endovascular approaches.

Key References

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