

## Position Statement on the International Subarachnoid Aneurysm Trial -ISAT

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The International Subarachnoid Aneurysm Trial (ISAT), a prospective, randomized trial comparing surgery (craniotomy for clipping) to endovascular therapy (coiling) in the treatment of ruptured intracranial aneurysms, was recently published in *The Lancet* (1). The study results demonstrate that, for a particular subset of aneurysm patients cared for in designated study centers mostly outside of the United States, patients with ruptured aneurysms treated with coiling fared better at one year than patients with ruptured aneurysms treated by clipping. We congratulate the organizers and participants of the ISAT for their critical thinking and dedicated clinical work. We believe, however, that the ISAT study results have been inaccurately reported in the media and that specific data from the trial have been and will be inappropriately applied and generalized to all patients with intracranial aneurysms. The purpose of this position paper is to identify points that we believe warrant emphasis and clarification. These points are meant to educate fellow neurosurgeons about the ISAT study, its results and the concern many have about the potential misrepresentation of the ISAT results to the public and our patients.

The reported ISAT data demonstrate that patients with ruptured intracranial aneurysms treated with craniotomy for clipping had a 30.6% chance of a poor outcome at one-year follow-up. Patients with ruptured aneurysms treated by endovascular coiling had a 23.7% chance of a poor outcome at one-year follow-up. Therefore, the absolute risk reduction, at one-year follow-up, when comparing aneurysm coiling to aneurysm clipping was 6.9%. Media reports have attributed a 22.6% risk reduction to endovascular coiling compared to craniotomy for aneurysm clipping. The figure of 22.6%, the overall study relative risk reduction, suggests there was a dramatic reduction in the number of poor outcomes among patients whose aneurysms were treated with coiling as compared to those patients whose aneurysms were surgically clipped. This is not the case. It is the absolute risk reduction that is of greatest importance to patients. Importantly, the absolute risk reduction of 6.9% reported by the ISAT authors should not be inappropriately generalized.

Most centers involved in ISAT were located in Europe (particularly England) Australia and Canada. Only two patients were entered into the study from a single center in the United States. The results from ISAT may not be applicable to patients in the United States where practice patterns, particularly in reference to the degree of sub-specialization of neurovascular surgeons in major centers, are different.

It is essential to know how many practitioners in ISAT performed craniotomies for aneurysm clipping and how many practitioners performed endovascular procedures for aneurysm coiling. If the number of coiling cases per endovascular practitioner is significantly greater than the number of clipping cases per neurosurgical practitioner, the better outcome at one-year follow-up for patients who were treated with aneurysm coiling (6.9% absolute risk reduction) could be completely explained by a difference in practitioner experience and expertise. The numbers of craniotomies per neurosurgeon and the number of coiling procedures per endovascular specialist involved in the ISAT study have not been (but should be) published.

Most importantly, physicians and surgeons involved in ISAT felt that one form of treatment was preferred in almost 80% of patients considered for study. Of 9,278 patients with ruptured intracranial aneurysms assessed for ISAT eligibility, only 2,143 were randomized. In those 7135 patients not randomized, more patients underwent craniotomy for aneurysm clipping than endovascular aneurysm coiling. Over the course of the ISAT study, neurovascular teams in the participating centers felt that surgery was the best option for the majority of patients with ruptured aneurysms who were not randomized. Therefore, if an experienced vascular neurosurgeon thinks that craniotomy for aneurysm clipping is the best option for a patient with a ruptured intracranial aneurysm, the patient should continue to be offered surgery as the treatment of choice. The results of ISAT do not apply to this larger group of patients, as they were excluded from the randomized trial. Disappointingly, outcomes and follow-up were not provided for the non-randomized patients.

Neurosurgeons await with interest the long-term follow-up data on the 2143 ISAT patients. It is crucial to determine whether or not aneurysm coiling will be as effective as craniotomy for aneurysm clipping after subarachnoid hemorrhage in preventing re-bleeding over the lifetime of the patient. During the short follow-up period of the interim report, 2.6% of patients whose aneurysms were treated with coiling suffered a hemorrhage after treatment as opposed to 0.9% of patients treated with craniotomy for aneurysm clipping. Although re-bleeding more than one year after treatment was low in both ISAT treatment groups, if the early differential rate of hemorrhage were to persist, the 6.9% absolute risk reduction attributed to endovascular aneurysm coiling at one year follow-up in the ISAT study would soon disappear. In addition, more than four times more patients treated with aneurysm coiling required additional treatment for their ruptured aneurysm than did patients treated with craniotomy for aneurysm clipping. The 2143 randomized patients in the ISAT study will need to be followed for many years before legitimate conclusions can be drawn about whether aneurysm clipping or aneurysm coiling is the preferred form of treatment for ruptured intracranial aneurysms in patients suitable for either form of therapy.

We believe that an accurate interpretation of the ISAT study would be: "In a patient whose ruptured aneurysm is considered suitable for clipping or coiling, and for whom the neurovascular surgeon and the endovascular surgeon do not know, after considering all factors, which treatment option is better for a specific patient with a ruptured aneurysm, aneurysm coiling, at the centers involved in the ISAT study, yielded a 6.9% chance of a better functional outcome at one year follow-up compared to similar patients with ruptured aneurysms treated with craniotomy for clipping. Long term follow-up of these patients will be essential to determine which of these two forms of treatment is safer and more effective for this subgroup of patients over their lifetimes".

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The ISAT report is an important step in defining the roles of endovascular and microsurgical treatment of patients with ruptured intracranial aneurysms. The points noted above are raised to remind all of us that much more study is needed to develop definitive medical evidence on this issue. To extrapolate the early results of this study to all patients with intracranial aneurysms (ruptured or not) would be a misinterpretation of the ISAT data and a serious disservice to our patients and our profession.

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1. International subarachnoid aneurysm collaborative group. International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomized trial. *The Lancet* 360: 1267-1274, 2002.