Clipping Versus Coil: the debate remains.

RESUMO
Introdução: Atualmente dois métodos estão disponíveis para o tratamento dos aneurismas intracranianos, endovascular e microcirurgia. A publicação do ISAT tem gerado uma tendência em favor da embolização apesar de erros metodológicos e de interpretação. O objetivo deste estudo é discutir o tratamento atual dos aneurismas cerebrais com foco nas conclusões do ISAT. Materiais e Métodos: Os autores executaram uma revisão da literatura estudando artigos e discutindo os resultados do ISAT com o objetivo de fazer uma análise crítica acerca da metodologia, interpretações e aplicações destes resultados. Resultados: Devido a falhas metodológicas, critérios de seleção incongruentes, a não quantificação de parâmetros secundários de prognóstico e a seguimento clínico curto, o ISAT está longe de fornecer uma resposta definitiva sobre o tratamento ideal para os aneurismas intracranianos. Conclusões: Nenhuma conclusão pode ser formulada confirmando a superioridade da embolização sobre a clipagem. A generalização e aceitação dos resultados do ISAT é precoce e é uma medida que não beneficia a maioria dos pacientes com aneurismas cerebrais.

ABSTRACT
Introduction: Currently, there are two available methods for aneurysms treatment, endovascular and microsurgery. The publication of ISAT has been producing a tendency towards coiling in spite of methodological mistakes and misinterpretation. The objective of this study is to discuss the current treatment of the cerebral aneurysms, considering the conclusions of ISAT review and perhaps enhancing its influence in the contemporary treatment of intracranial aneurysms. Material and Methods: The authors carried out a review of the literature, studying articles and discussing the results of ISAT aiming to perform a critical analysis of its methodology and practical interpretations of these results. Results: Due to the controversial methodology, incongruous criteria of selection, statistical faults, no quantification of the secondary outcome, ISAT review was not able to provide definitive answers about the ideal treatment to the intracranial aneurysms. Conclusions: No conclusions can be formulated confirming the superiority of coiling over clipping. Generalization and acceptance of ISAT conclusions are precocious and it is not in the best interest of patients harboring intracranial aneurysms.

Key-words: cerebral aneurysm, microsurgery, endovascular, coiling, clipping, International subarachnoid aneurysm trial.

Camila Flores 1
Eberval Gadelha Figueiredo 2
Manoel Jacobsen Teixeira 3

1 Acadêmica de Medicina da Universidade Nove de Julho – Brasil
2 Supervisor Divisão de Clínica Neurocirúrgica – ICHC - Coordenador do Grupo de Neurocirurgia Vascular HCFMUSP
3 Professor Titular. Disciplina de Neurocirurgia FMUSP - Diretor de Divisão ICHC

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Clipping has been successfully used in the cerebrovascular surgery for decades. In 1911, Harvey Cushing produced what was to become the first vascular clip, known as “the silver clip” or Cushing’s clip. However, this device was actually used to clip an aneurysm for the first time only in 1937 by Walter Dandy. In this way, the modern aneurysm surgery began when this brand new technique allowed surgeons to exclude an aneurysm selectively from the collateral circulation. 7

The contemporary microsurgery was created and shaped by three major aspects: the development of microneurosurgical techniques, the surgical microscope, and the appraisal and visualization of the detailed microneuroanatomy from a surgical viewpoint. 2,9 The microscope was not reported as an adjunct to aneurysm surgery until 1966, when Dr Gazi Yasargil started his pioneering work developing this approach. 7 Microneurosurgery pushed an extra importance on clip development, demanding more slender clips that would allow the neurosurgeons to approach even more narrow spaces of the intracranial anatomy. 7

Endovascular technique has increasingly gained defenders all over the world, since 1991. Its advantages are intuitive and include a relatively easier access to the arterial tree, mainly the vertebrobasilar system, a possible faster learning curve and a reduction on the invasiveness compared to craniotomy. 5

The efficiency of both treatments basically depends on two major factors: safety and its role in preventing rehemorrhage and morbi-mortality. 5 Objectively, questions remain regarding the long-term efficacy of coiling mainly due to the higher rates of rebleeding and recurrence, as well as the lower rates of complete occlusion when compared with microsurgery clipping. 5

In October 2002, the first International subarachnoid aneurysm trial (ISAT) paper was released comparing outcomes in coiling versus clipping. 9 ISAT was designed as a randomized trial comparing endovascular clipping versus neurosurgical clipping in patients with ruptured brain aneurysms. 6 After its publication, a shift towards coiling has been seen, mainly in Europe, but increasingly worldwide. However, ISAT’s findings have been criticized for its faulty statistical methods, that include tendentious selection criteria of participating centers. 9

The authors carried out a focused and critical review of the literature specifically concerning the methodology and interpretations of the results of ISAT. The authors performed a PubMed research of the literature from October 2002 through March 2008 with the use of the follow key words in all relevant combinations: cerebral aneurysm, microsurgical, endovascular, coiling, clipping and International subarachnoid aneurysm trial.

The International subarachnoid aneurysm trial (ISAT) was funded by the UK’s Medical Research Council, a randomized study, designed to compare neurosurgical clipping with endovascular coiling in patients with ruptured intracranial aneurysms. 6 ISAT included patients from specific centers and enrolled firstly a cohort of patients with small anterior circulation aneurysms representing a high percentage of the aneurysms treated. 9 As a consequence, ISAT impacted the treatment of patients with subarachnoid hemorrhage particularly in Great Britain, the main contributor of the study. 11 After ISAT released its first paper, the number of patients submitted to endovascular treatment increased from 34% to 54% in the Great Britain. 11

The gaps found in this long and very well sponsored project basically are the fundamental to question its validity. The selection of patients, the rebleeding rates, shunt dependency rates, the absence of secondary outcome measures, the need for second procedures, angiographical follow-up, the occlusion rates, the centers selected and the modified Rankin score pooling outcomes are the main critical concerns.

Related to the patients enrolled, several arguments raise doubts about the actually low percentage of individuals who were randomized. Of 9559 patients with subarachnoid hemorrhage applied for eligibility, only 2143 were selected. The decision to ignore such a large number of patients likely reflected the preexisting biases of enrolling medical centers participating. 9

Also, on ISAT, the rebleed rate was twice for endovascular cohort in relation to the neurosurgery cohort. More episodes of recurrent bleeding were found in the first year after coil embolization (3%) than after clipping (1,3%). The primary outcome measure for bleeding aneurism treated after one year occurred in one patient treated with coiling and none with clipping. 9

Another important consideration to be made is about the rate of shunt dependency and occurrence of vasospasm after endovascular procedures. Even though controversial, the capacity to open the cistern and remove clot and blood products during surgery consequently may diminish the risk of vasospasm and hydrocephalus and shunt dependency. 8

Significantly more patients treated with coiling required repeat treatment during the first year, and continued to require additional treatment, although infrequently, as long as 5 years after the initial procedure. 10 It is important to remember that repeat procedure rate in this study was 12.7% in the endovascular group as compared to 3.2% in the surgical group. 11

In the ISAT study, one third of the endovascular procedures did not achieve complete obliteration. The rates of total aneurysm...
occlusion were not considered as criteria of outcome, making quite nebulous what ISAT study meant by cure.\textsuperscript{11} Post-operative angiogram was not obligatory in the microsurgical group. This also overestimates the real number of suboptimal clipping, which is another reason for the unfavorable outcome results in the surgical group, since postoperative angiograms were only preformed in complex surgical cases. Therefore, this creates some ambiguity concerning the efficacy of the coiling modality.\textsuperscript{11}

ISAT showed concerns about the long-term durability of coil occlusion, as well as the need for follow-up imaging and further treatment if aneurysm recurrence is detected.\textsuperscript{11} However, it did not consider in its final conclusion that recurrence after complete aneurysm clipping is extremely unlikely and late imaging follow up is probably not required. Also, it was not considered in its final conclusion the results about occlusion, rebleeding and mortality after one year of the procedure. The criteria used to select the participating centers on this complex study are also good argument against it. No objective minimum case experience was set out for neurosurgeons as it was for neuroradiologists.\textsuperscript{7} Therefore, the lack of surgical experience may have contribute for the bad performance of clipping and, as a consequence, impacting surgical outcomes. This fact raised the question of whether there was an inclination to one of the treatment modalities in those centers with higher rates of patient recruitment. It was stated that the major contributing centers had more expertise in endovascular treatment.\textsuperscript{9}

Another particular question could be observed, this time, regarding the modified rankin score (mRS). ISAT presented an absolute risk reduction of dependency/death (mRS 3 to 6) in coiling versus clipping ruptured aneurysms.\textsuperscript{2} Nevertheless, these results are consistent only when groups are pooled together.\textsuperscript{9} If the outcome were evaluated individually the statistical significance remains only for the group with mRS=3. This was the only possible combination that maintains the statistical differences. In other studies, outcome scores using mRS are listed individually or pooled as 0 - 1 and 2-6, or 1-3 and 4-6.\textsuperscript{11} Other weak point is that ISAT allocated to neurosurgery, patients that had a 50% or higher rebleed rate before treatment and also considered those patients as in the safety evaluation favoring coiling.\textsuperscript{9}

ISAT sought, therefore, to provide doctors with the first clear evidence on which to base treatment decisions. But it’s clearly necessary to watch out what kind of evidence it has provided. How huge is the financial influences up on this study are also not clear. To some eyes this ISAT project could be seen as a very convenient study. To other eyes would be considered quite naive. In one way or another, to remain in silence facing so concrete evidences about the suitability of this project place the world academic society as conniving with a dangerous tendency of influencing patients to a treatment which scientific value is far from the consagration.

It is increasingly clear that excellent results can be achieved with clipping and that outcomes are better in centers with experience and expertise in this technique.\textsuperscript{10} It’s important to understand that especially in aneurysm surgery, the results are reflected by the quality of the team, by the skills and experience of the surgeon, and surely by some mentioned referral biases.\textsuperscript{1}

Hence, in the present environment, it is unreasonable to doubt clipping as a successful tool, especially at a large-volume centers, with vast experience in both modalities and when long-term follow-up of coiled aneurysms is showing recurrence and retreatment rates significantly higher that with clipped aneurysms.\textsuperscript{6}

Surgeons and their ingenious tools have transformed the natural history of aneurysm progression from a once discouraging and lethal vascular pathological entity into a mostly curable neurosurgical lesion.\textsuperscript{7} On the other hand, coiling, so far, have transformed these same vascular pathology, in some extent, into a chronic vascular disease; for all the papers confirming the high rates of rebleeding and recurrence after endovascular treatment. However, to reach a dreamt necessary skill and be able to carry out an aneurysm surgery, dedication and training are necessary. Time commitment is an embarrassing question for neurosurgeons nowadays.\textsuperscript{3}

Can we do better? This is the main question for those really concerned about their patients. Maybe in five years the defenders of clipping will be smashing their faces and clipping will no longer be considered the gold standard treatment for aneurysms. Right now that’s not what it shows. Clipping is safe if practiced by surgeons with expertise, prevents rebleeding and reduces the need for further procedures when compared to coiling. Additionally, it is more accessible treatment for its lowers costs. A coiled aneurysm is a thrombosed one and follow-up requires repeat angiograms which may impact the final outcome rates. Generalization and blind acceptance of ISAT conclusions are precocious and are not in the best interest of patients harboring intracranial aneurysms.
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CORRESPONDING AUTHOR

Dr. Eberval G. Figueiredo
Divisão de Clínica Neurocirúrgica ICHC
Rua Eneas de Carvalho Aguiar, 255, 5º Andar
São Paulo-SP
E-mail: ebgadelha@yahoo.com