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Microsurgical clipping of cerebral aneurysms after the ISAT Study

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"The arduous work of countless researchers has already thrown much darkness on the subject, and if they continue, we shall soon know nothing at all about it"
Mark Twain

The ISAT Study nails low case load microsurgery of cerebral aneurysms

This landmark study [9] – somewhat Twainian at first glance – sets the stage for future microsurgery in cerebral aneurysms and SAH. *The ISAT Study does not nail microsurgery – it will nail microsurgery in low case load neurosurgical centers and in inexperienced hands*. In future neurovascular centers, exovascular and endovascular surgeons are forced to support each other by having the full responsibility over the population in a defined geographical area. Exosurgeons will become far more experienced – less in number but not the last Mohicans.

Population based treatment of cerebral aneurysms and SAH

In the national health ministries, it is wise to remember when deciding on the guidelines and facilities for endosurgery and exosurgery that aneurysmal SAH is a dismally deadly disease when treated with full population responsibility. One third of patients present with a large haematoma or severe hydrocephalus necessitating immediate surgery. Mortality and morbidity figures are unattractive when the treatment center functions as primary imaging center and accepts all patients at ultra early phase to prevent rebleeding. Selection and delayed aneurysm occlusion ensure low percentages of management morbidity and mortality – how about the patients who die of acute rebleeding [7] or haematoma and do not get a chance of decent recovery?

Kuopio and Helsinki Aneurysm Registries

Aneurysmal SAH is particularly frequent in Finland. There is a linkage to 19q13.3 in Finnish aneurysm families [17, 20] but the interplay of genetic and acquired risks [10] remains to be solved. The Kuopio and Helsinki Aneurysm Registries (a) support clinical trials [12, 13, 19], (b) collect basic clinical data [5, 6, 16], (c) characterize aneurysm families and collect blood samples [17, 20], and (d) collect aneurysm walls resected after clipping of the neck [4]. The first published prospective randomised study – well before ISAT – compared the outcome with acutely ruptured aneurysm after coiling or clipping at the Kuopio University Hospital in eastern Finland in 1995–1997 [11–13, 19, 21]. Of the 199 patients ($\leq$75 years, $\leq$72 hours from bleeding), only 109 (55%) were randomizable either to endovascular occlusion or to exovascular occlusion – e.g., 37 patients were excluded because of haematoma or mass effect, and 33 because of aneurysm morphology unsuitable for endovascular occlusion [11].

Cellular and molecular biology of the cerebral aneurysm wall is poorly known

Saccular cerebral artery aneurysms are not just pressurized blebs that threaten to leak. *The cellular and molecular biology of the aneurysm wall is poorly under-*

stood because aneurysm sacs have not been resected for research purposes after clipping of the neck. A study of 24 unruptured and 42 ruptured aneurysm walls from the Helsinki Aneurysm Registry and Biomedicum Helsinki showed that the wall becomes unstable before rupture, showing proliferation, apoptosis, intimal hyperplasia, inflammatory cell infiltration, and thrombosis lining the lumen [4]. Consequently, non-invasive microneuroimaging methods are called for to identify aneurysms prone to leak because most aneurysm will not leak ever [8]. Gene expression profiling and proteome analysis of the wall will guide future development of both endovascular and exovascular occlusive techniques.

Successful endovascular occlusion is a wonder of nature – but is it permanent?

Exovascular occlusion of the aneurysm neck by clipping is hydrodynamically effective but it takes craniotomy and microneurovascular dissection to get the job done. Endovascular occlusion is hydrodynamically demanding. The occlusive material must stay in the lumen to induce and guide the fibrotizing wall reaction – with recruitment of circulating cells – to occlude the lumen and the entire base. Arteries adjacent to the aneurysm base must remain patent which further complicates the design of endovascular instrumentation. It is a wonder of nature that mechanical filling of the lumen with metal coils ever results in smooth re-arterialization over the occluded aneurysm orifice. Successful endovascular occlusion owes to the immense maintenance and healing capacity of the cerebral artery wall, the biology of which is incompletely understood. *Angiographically complete occlusion may fail in the long run which necessitates repeated angiographic follow up, a safety protocol that requires a lot of DSA and endosurgeon capacity at the moment.*

Exosurgery vs. endosurgery

In unselected aneurysm populations, e.g. in the total of 400 annual cases of Helsinki and Kuopio, in about 50% the aneurysm's anatomy or the patient's arteries will allow satisfactory endovascular occlusion. Exosurgery – in our opinion – is preferable at present in the following instances:

– large or giant aneurysm
– very small aneurysm
– wide base aneurysm
– large aneurysmal haematoma or severe hydrocephalus
– severely atherosclerotic or tortuous cerebral arteries

Endosurgery of very small, large, and wide base aneurysms will improve with technical development but not at all exclusive of exosurgery.

Restorative exosurgery after failed endosurgery is difficult

Failure in endovascular occlusion is more common than in clipping. Endovascular failure may call for restorative exosurgery in the acute phase (failed occlusion of aneurysm, rupture of aneurysm, occlusion of major artery), or in the long run (failed occlusion). Clipping of the aneurysm neck after failed coiling or stenting is difficult with the risk of parent artery damage and occlusion. Coils may project into the parent artery or into the brain tissue, e.g. into the brain stem from basilar tip or trunk aneurysms. Fibrotizing wall may engulf coils already within two weeks which supports early restorative surgery when coil material has to be removed. However, restorative exosurgery in acute SAH is particularly difficult because brain is swollen and affected by SAH. The overall situation may call for high-flow bypass surgery [18] – a further indication to keep exosurgery running. The stop of low-flow bypass surgery in the 1980's – inefficient in the EC/IC Bypass Study [3] but now under re-evaluation [15] – eroded neurovascular anastomosis skills that have to be acquired again.

Technical aspects of exovascular aneurysm occlusion

In experienced hands, most aneurysms can be ligated quickly and permanently [2] – in a bloodless field with gentle techniques, minimal or no brain retraction, intact vascular anatomy, and minimal or no skull base manipulation. The repertoire should include the following:

– careful opening and closure – preferably under the operating microscope from skin to skin
– slack brain achieved by opening the lamina terminalis or by frontal ventriculostomy
– avoidance of the use of brain retractors
– sharp dissection rather than blunt dissection
– removal of thrombotic tissue from large aneurysms

– speed of action to avoid ischaemic deficits when using temporary clips
– moulding of the aneurysm base with bipolar coagulation when necessary
– reconstruction of the parent arteries with clips when included in the base of aneurysm
– dissection and resection of the aneurysm sac to ensure perfect clip position after clipping
– intraoperative angiography in large and giant aneurysms
– arteriotomy and thrombectomy of major cerebral arteries
– both high-flow and low-flow bypass techniques

Exosurgery training

Comprehensive skills to clip most aneurysms and to perform intracranial arteriotomies and anastomoses are not easily acquired. Less neurosurgeons will take the track with the advent of endosurgery [14]. It takes a lot of passionate work and the learning curve is not short – in the senior author's (JH) hands, the operative time has dropped below one hour in most cases from two hours a decade ago. Taking digital high quality video clips and discussing them with others is extremely healthy – leading exosurgeons should produce comprehensive video libraries and make them widely available. Leading exosurgeons – like concert pianists – may trace back master-apprentice or senior-junior lineages, with professor Yasargil affecting them all [22]. Professor Yasargil emphasizes (a) profound knowledge of microneurosurgical anatomy acquired in cadaveric laboratories [1], and (b) gentle handling of cerebral arteries and veins acquired by performing microvascular anastomoses in rats – vessels of mice are particularly educative. Delicate endomicroscopes and instrumentations are already being developed, but exosurgeons are still married to the dinosauric exomicroscope. The practice of using a mouth-controlled microscope from skin to skin – freeing both hands to operative work – greatly helps to tame the beast.

CT angiography saves time and money

The use of DSA might have biased the ISAT result as the mean allocation-to-treatment interval was 1.1 days in the endovascular group as against unbelievable 1.7 days in the microsurgical group. In acute SAH, CT angiography as the first imaging method spares time and the patient. With ultrarapid CTA, aneurysm patients can be transferred within one hour after their SAH to the exosurgery room [4] or the endosurgery DSA room – or to the future exo-endo-surgery suite. *The problem of coil and clip artefacts in CTA has to be vigorously solved* – present titanium clips may still obscure postoperative CTA. Future refinement of CTA may allow detailed verification of (a) the immediate post clipping anatomy in the aneurysm region, and (b) the follow up for re-filling after endovascular occlusion.

Future neurovascular center

Competent exovascular and endovascular surgeons should form neurovascular teams to discuss and tailor an individual treatment for each patient, including aneurysm patients. One center with a team of five to six surgeons – exosurgeons and endosurgeons working together – could easily occlude all aneurysms diagnosed in Finland per year – some 600 patients. However, SAH patients require a lot treatment before and after the actual imaging and occlusion – taking few hours at most – of the aneurysms. One national center is not conceivable in Finland because of long transfer distances but could be practical in small densely populated nations.

Conclusions

1. Only specialized neurovascular exosurgeons should continue open aneurysm surgery.
2. Competent exovascular and endovascular surgeons should collaborate in population based neurovascular centers, discussing and tailoring an individual treatment for each patient, including aneurysm patients.
3. The cellular and molecular biology of the aneurysm wall as well as the interplay of genetic and environmental riks factors should be elucidated. Biological prevention – avoidance of smoking as a prime example – will improve management results far more than any endovascular or exovascular mechanical approach.

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