ISAT: The International Subarachnoid Aneurysm Trail

Lessons and Update

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The long term follow up of patients entered in the ISAT trial continues to give insight into a number of important research questions.

What is the natural history of early rebleeding?

There was a marked variation in time taken from ictus to both randomisation and to treatment seen between ISAT centres with a range of 0-28 days. During this period they were 50 rebleeds seen in the 2143 patients. This allowed a conditional risk can be calculated for the first 15 days post ictus; day 1-9 fluctuates around 1% per day but on day 10 the rate of rebleeding suddenly increases to 4.14% and then from day 11-15 fluctuates around 2-3%. However it should be noted that only a few bleeds were recorded on any day.

Does early treatment of the aneurysm by clipping or coiling increase the chance of poor outcome?

This is the converse question. It has long been argued by neurosurgeons that delayed treatment is of benefit in older sicker patients so does early treatment result in poorer outcome (table 1).

Table 1 The risk of poor outcome from neurosurgery and endovascular treatment performed early 0-2 days, 3-6 days or late 7+ days post ictus.

	0-2 days	3-6 days	7+ days
Endovascular (% with bad outcome)	21	21	31
N	468	326	209
Neurosurgery (% with bad outcome)	29	27	32
N	415	288	281

There is no significant difference in the number of poor outcomes in those treated late and those treated early. So it does *not* appear that early treatment by either modality increases the risk of poor outcome. It should be noted, however, that there was an increased number of elderly and sicker patients in the 7+ group treated by neurosurgery. Treatment in those whom it is clinically feasible should therefore not be delayed in patients who can be treated.

What are the risks of recurrent subarachnoid haemorrhage both in treated aneurysms and de novo aneurysms?

The risk of rebleeding from a cerebral aneurysm per year is higher in endovascular treated patients at 0.21% per year as opposed to 0.08%

per year for neurosurgery treated patients. The overall risk of bleeding is 0.15% per year for all patients. Increase in rebleeding rate in endovascular patients does not affect the overall ISAT result. The cumulative mortality (Kaplan Meier) curves show that the early benefit

from endovascular treatment is maintained at 7 years. This may be related to the fact that patients who rebled from an endovascular treated aneurysm (9 patients) had half the mortality rate of those who rebled following surgery all whom died (3 patients) (table 2).

Table 2 **Rebleeding of treated and other aneurysms after 1 year.**

			<i>Rebleeding Aneurysm</i>			Total
			Target	Other known An	de Novo An	
Endovascular	Count		9	4	3	16
	% within Row		56.3%	25.0%	18.8%	100.0%
	% within Column		75.0%	80.0%	60.0%	72.7%
Neurosurgery	Count		3	1	2	6
	% within Row		50.0%	16.7%	33.3%	100.0%
	% within Column		25.0%	20.0%	40.0%	27.3%
Total	Count		12	5	5	22
	% within Row		54.5%	22.7%	22.7%	100.0%
	% within Column		100.0%	100.0%	100.0%	100.0%

Conclusions

The rebleeding risk after 1 year from a coiled aneurysm is about 0.12% per year.

The risk of death or disability from rerupture is approximately half this rate at 0.07% per year. (> 1:1000).

The risk of bleeding from another or new aneurysm is similar at 0.07%.

The risk of treatment small aneurismal remnants must be carefully weighed against these very small risks.

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