Embargoed: 00.01hrs London time Friday 25 October 2002

Endovascular coils beat neurosurgery for treating brain haemorrhage

Landmark international trial halted early as analysis reveals risk cut by a quarter

A landmark clinical trial led by UK researchers has shown that patients who suffer a brain haemorrhage from a ruptured aneurysm[1] have a significantly better chance of surviving without disability if they are treated through the blood vessels than if the aneurysm is clipped by surgery. The findings are published today (Friday 25 October) in the Lancet[2].

Inserting special platinum coils via an artery and blocking off the aneurysm reduced the relative risk of dependency or death by nearly a quarter and the absolute risk by nearly seven per cent compared with surgery. Recruitment to the trial was stopped early when it became clear to the independent data monitoring committee that the difference in outcome was so striking.

The International Subacrachnoid Aneurysm Trial (ISAT), funded by the UK's Medical Research Council, is the first large multi-centre randomised study in the world to compare the two methods. It therefore provides doctors with the first clear evidence on which to base treatment decisions. It involves over 2,000 patients in 43 neurosurgical centres in Europe, North America and Australia and is headed by Dr Andrew Molyneux, a consultant neuroradiologist and Mr Richard Kerr, a consultant neurosurgeon, both from the Radcliffe Infirmary in Oxford.

Until the 1990s the only treatment for subarachnoid haemorrhage involved neurosurgery to place a metal clip across the neck of the ruptured aneurysm and prevent further bleeding – a risky invasive procedure despite advances in techniques. Relatively few patients return to a normal lifestyle and many are left with persistent disability. In 1990 the alternative of the detachable platinum coil became available. The coil is introduced into a major artery in the groin inside a catheter and navigated via x-ray guidance into the artery in the neck. An even smaller catheter then places the coil inside the aneurysm to block it off.

"This trial really has produced a groundbreaking result that will change medical practice," said Dr Molyneux. "While it is important to make clear that there will be some patients for whom surgery is still the most appropriate treatment, coiling should be suitable for eight out of 10 people who suffer a subarachnoid haemorrhage from an aneurysm."

The primary objective of the trial was to determine whether endovascular treatment when compared with conventional neurosurgical treatment would cut the proportion of patients either dead or dependent[3] by a quarter one year after the procedure.

One-year follow up data were available on 1,594 patients. Overall, 27.2% were dead or dependent – 30.6% in the neurosurgery arm and 23.7% in the endovascular arm. This represents a 22.6% relative risk reduction and a 6.9% absolute risk reduction in the endovascular arm.

Overall case mortality rates were similar between the two groups, with 10.1% of the neurosurgical group having died and 8.1% of the endovascular group.

"What this means for patients in the future is that, potentially, out of every 100 patients treated around seven could expect to be better off one year on if they received endovascular treatment rather than conventional surgery. For many patients this could mean the difference between a return to normal life or substantial disability," said Mr Kerr.

The study also looked at the risks from late re-bleeding after treatment. After one year and up to seven years the risk was very low.

"To date this suggests that the long-term risks of further bleeding from the treated aneurysm are low with either therapy, although somewhat more frequent with endovascular coiling. We will continue to follow our patients to assess whether the substantial early benefit of coiling continues long term," said Mr Kerr.

The researchers said that although the trial had been a challenge to organise and needed help and co-operation from many colleagues in the centres, it had been essential. The coil had rapidly gained acceptance in some countries, although use varied widely with relatively high use in some countries, including the UK and France, and low use in the USA and Germany. It was important that the technique was tested in a systematic manner before it became standard treatment. ISAT is the first large randomised trial of a new method of treatment compared with surgical management of subarachnoid haemorrhage since the 1960s, as no alternative method of treating ruptured intracranial aneurysm has been available until the 1990s.

The first patient was recruited into the ISAT pilot study in 1994 and the main trial began in 1997 with the aim of enrolling up to 3,000 patients. ISAT's steering committee halted recruitment in May this year at 2,143 patients after an interim analysis by the independent data monitoring committee showed a clear advantage to the coiling technique.

The research team will report in future on other trial objectives – the cost-effectiveness of coiling compared with neurosurgery and the follow-up of patients for the next five years (and subject to further funding, for another five years after that). It will also evaluate the long-term significance of angiographic results. A separate study funded by the Stroke Association will evaluate whether the neuropsychological results are better with coiling.
(ends)

Notes:

[1] **An aneurysm is a bulge in an artery caused by a weakness in the artery wall. If an aneurysm occurring in the brain bursts it causes subarachnoid haemorrhage, a potentially life-threatening condition. Each year between 6 and 8 people out of every 100,000 in most western populations suffer the rupture of an intracranial aneurysm. It is most common in the age range 35 to 60 and women are more at risk then men. More than 30% of patients die within 24 hours of the bleed and a further 25-30% will die within four weeks without some form of surgical intervention.**

Annual number of cases of subarachnoid haemorrhage

UK	Europe	USA	World
6,000	50,000	25,000	600,000

[2] **The International Subarachoid Aneurysm Trial (ISAT). Results of a prospective multicentre randomised trial comparing neurosurgical clipping with endovascular coiling in 2,143 patients with ruptured intracranial aneurysms. Lancet. Vol. 360 No. 9342. Pp 1267-74.**

[3] **Dependency was measured by the Rankin scale at 2 months, 1 year and annually thereafter. This scale is a widely accepted scientific gauge of determining the level of dependency, with a disability score ranging from 0 (no symptoms) to 5 (fully dependent) and 6 (death).**

Further information:

Margaret Willson (media officer)
Tel: +44 (0)1536 772181
Fax: +44 (0)1536 772191
Mobile:+44 (0)7973 853347
Email: m.willson@mwcommunications.org.uk