Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage (Review)

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**Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage (Review)**


This record should be cited as:

This version first published online: 19 October 2005 in Issue 4, 2005.
Date of most recent substantive amendment: 13 June 2005

**ABSTRACT**

**Background**
Patients who have had an aneurysmal subarachnoid haemorrhage (SAH) are at very high risk of rebleeding if the aneurysm is not treated. The standard treatment for several decades has been surgical clipping of the neck of the aneurysm. In recent years, an alternative, the introduction of detachable coils to occlude the aneurysm, has become more common.

**Objectives**
To compare the effects of endovascular coiling versus neurosurgical clipping in patients with aneurysmal subarachnoid haemorrhage.

**Search strategy**
We searched the Cochrane Stroke Group Trials Register (last searched in February 2005). In addition we searched MEDLINE (1966 to January 2004) and EMBASE (1980 to January 2004), and contacted trialists.

**Selection criteria**
We included randomised trials in which endovascular coiling of aneurysms was compared with neurosurgical clipping in patients with SAH who have proven aneurysm.

**Data collection and analysis**
Two authors independently extracted the data and assessed trial quality. Trialists were contacted to obtain missing information.

**Main results**
We identified three randomised trials: two published and one unpublished. The trials included a total of 2272 patients (range per trial: 20 to 2143 patients). Most of the patients were in good clinical condition and had an aneurysm on the anterior circulation. After one year of follow up, the relative risk (RR) of poor outcome for coiling versus clipping was 0.76 (95% confidence interval (CI) 0.67 to 0.88). The absolute risk reduction was 7% (95% CI 4% to 11%). In the worst-case scenario analysis for poor outcome overall, the relative risk for coiling versus clipping was 0.81 (95% CI 0.70 to 0.92) and the absolute risk reduction was 6% (95% CI 2% to 10%). For patients with anterior circulation aneurysm the relative risk of poor outcome was 0.78 (95% CI 0.68 to 0.90) and the absolute risk decrease was 7% (95% CI 3% to 10%). For those with a posterior circulation aneurysm the relative risk was 0.41 (95% CI 0.19 to 0.92) and the absolute decrease in risk 27% (95% CI 6% to 48%).

**Authors’ conclusions**
The evidence comes mainly from one large trial. For patients in good clinical condition with ruptured aneurysms of either the anterior or posterior circulation we have firm evidence that, if the aneurysm is considered suitable for both surgical clipping and endovascular treatment, coiling is associated with a better outcome.
**Plain Language Summary**

Endovascular coiling of ruptured aneurysms in the brain leads to a better outcome than surgical clipping.

Bleeding on the surface of the brain is called a subarachnoid haemorrhage. The bleeding usually comes from the rupture of a weak spot in an artery carrying blood to the brain. This weak spot is like a small balloon, or blister, which is called an aneurysm. The outcome after subarachnoid haemorrhage is generally poor: half the patients die within one month; and of those who survive the initial month, just under half remain dependent on someone else for help with activities of daily living such as walking, dressing, and bathing. One of the risks in patients with subarachnoid haemorrhage is rebleeding. There are two main ways to try to stop this: operative clipping of the neck of the aneurysm or blocking of the aneurysm from inside by endovascular coiling. This review shows that the number of people who survive and are independent in their daily living is higher after coiling than after clipping. The evidence comes mainly from one large trial.

**Background**

Subarachnoid haemorrhage (SAH) is a subset of stroke that has an incidence of approximately 6 to 15 per 100,000 people per year (Linn 1996) and accounts for approximately 5% of all strokes (Bamford 1990). It occurs in relatively young patients: half the patients are younger than 55 years of age (ACROSS 2000); and it carries a poor prognosis. Half the patients die within one month of the haemorrhage and of the patients who survive longer than one month 40% remain dependent (Hop 1997). Because of the poor outcome after the haemorrhage and the young age at which it occurs, the loss of productive life years from SAH is as large as that from ischaemic stroke, which is the most common subset of stroke (Johnston 1998).

In 85% of patients with SAH the cause is rupture of an intracranial aneurysm (Rinkel 1993). About 15% of patients with aneurysmal SAH die before reaching the hospital (Schievink 1995). Those who survive the initial hours after the haemorrhage are at risk of recurrent haemorrhage and secondary cerebral ischaemia. Each of these complications occurs in approximately 30% of patients (Brilstra 2000a). The main goal of treatment in patients with SAH is prevention of these complications. Medical prevention of recurrent haemorrhage is possible by the administration of tranexamic acid. However, this treatment does not improve overall outcome because tranexamic acid increases the risk of secondary cerebral ischaemia or counteracts recovery from the initial ischaemia (Roos 2000; Roos 2000a).

In recent decades the standard way to prevent recurrent haemorrhage has been neurosurgical clipping of the aneurysm. With the introduction of detachable coils to treat the aneurysm, endovascular coiling has becoming increasingly common. In many institutes endovascular coiling has replaced neurosurgical clipping as the treatment of choice, if clipping is technically feasible. The major advantage of endovascular coiling is that a craniotomy is avoided and recovery after the procedure is more rapid. The major disadvantage is that reopening of the aneurysm may occur from impaction of the coils as observed at long-term follow up. Thus, patients need to undergo repeated angiographic follow up. In many observational studies on endovascular treatment in patients with SAH, the risk of rebleeding in the initial weeks after coiling is very low. Also, there does not seem to be an increased risk of secondary ischaemia when compared with no intervention, whereas neurosurgical clipping does increase the risk of secondary ischaemia (Brilstra 1998). The risk of secondary ischaemia is especially increased between the fourth and eighth day after the haemorrhage. If the operation cannot be performed within the initial three days after the haemorrhage, it is usually postponed until after the eighth day. A study on timing of coiling showed no difference in outcome measured at six months according to the timing of coil occlusion after SAH (Baltsavias 2000).

This systematic review of randomised controlled trials compares the outcome after SAH for patients treated by means of endovascular coiling versus neurosurgical clipping.

**Objectives**

To compare the effects of endovascular coiling with those of neurosurgical clipping in patients with aneurysmal SAH by assessing:

1. the proportion of patients who were dead or dependent for activities of daily living at the time of outcome assessment;
2. the proportion of patients with recurrent haemorrhage or secondary ischaemia (with a delayed ischaemic neurological deficit);
3. the proportion of patients with a complication related to the procedures.

**Criteria for Considering Studies for This Review**

**Types of studies**

We sought all randomised trials in which endovascular coiling of intracranial aneurysms was compared with neurosurgical clipping. Only studies with adequate allocation concealment were included.
Types of participants
Patients with aneurysmal SAH in whom the haemorrhage was documented by either computed tomography (CT) scan, magnetic resonance imaging (MRI), or by the presence of xanthochromia in the cerebral spinal fluid in cases with a negative CT; in whom the presence of an intracranial aneurysm had been demonstrated before randomisation by catheter angiography, CT angiography or MRI angiography; and whose aneurysm had been judged suitable for both neurosurgical clipping and endovascular coiling were included in the analysis. Initially we intended to exclude patients who were treated more than 14 days after SAH. However, since the ISAT trial included patients who were treated until 28 days after SAH we changed this exclusion criterion to treatment at more than 28 days after SAH (ISAT).

Types of intervention
Endovascular treatment with detachable coils, and neurosurgical clipping.

Types of outcome measures
To provide an intention-to-treat analysis, we aimed to extract from each trial the outcome at the end of the follow-up period for all patients who were originally allocated to each treatment group.

The main measure of outcome was poor outcome: death or dependence in daily activities (modified Rankin scale 3 to 6 or Glasgow outcome scale (GOS) 1 to 3).

Other outcome measures were:
(1) death from any cause;
(2) secondary cerebral ischaemia, where episodes of clinical deterioration for which no other cause than secondary ischaemia was found were considered probable ischaemia; episodes with clinical deterioration and CT or MRI-proven cerebral infarction were classified as definite ischaemia;
(3) recurrent haemorrhage, where a sudden deterioration leading to death without confirmation of rebleeding by CT, MRI or post-mortem examination was considered a probable recurrent haemorrhage; a sudden clinical deterioration with rebleeding confirmed by CT or post mortem was classified as a definite recurrent haemorrhage;
(4) complications from the intervention (coiling or clipping). A complication was defined as a clinical deterioration observed during the intervention or 24 hours after the intervention.

In addition, we assessed the number of patients with recurrent haemorrhage from the target aneurysm at more than one year after the SAH (as a number per patient years of follow up).

We also assessed the results of treatment in terms of degree of occlusion of the aneurysm directly after treatment and at a follow-up period of one year. Occlusion after endosaccular packing was categorised as:
(1) 100%, occlusion with coils filling the neck;
(2) 90 to 100%, occlusion with neck remnant; and
(3) less than 90% occlusion, which includes any contrast filling within the dome of the aneurism.

If data on angiographic follow up was given for both endovascular and surgically treated patients, we compared the proportions of incompletely occluded aneurysms at the end of the follow-up period.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES
See: Stroke Group methods used in reviews.

Relevant trials were identified in the Cochrane Stroke Group Trials Register, which was last searched by the Review Group Coordinator in February 2005. In addition, we searched MEDLINE (1966 to January 2004) and EMBASE (1980 to January 2004) using the following search strategies.

MEDLINE (Ovid)
1. Subarachnoid Hemorrhage/
2. Intracranial hemorrhages/ or cerebral hemorrhage/ or vasospasm, intracranial/
3. Intracranial Aneurysm/
4. Rupture, Spontaneous/
5. 3 and 4
6. Aneurysm, Ruptured/
7. exp brain/
8. 6 and 7
9. ((subarachnoid or arachnoid) adj6 (heamorrhage$ or hemorrhage$ or bleed$ or blood$).tw.
10. Vasospasm, Intracranial/
11. ((cerebral or intracranial or cerebrovascular) adj6 (vasospasm or spasm).tw.
12. sah.tw.
13. 1 or 2 or 5 or 8 or 9 or 10 or 11 or 12
14. Embolization, Therapeutic/
15. “prosthesis and implants”/ or blood vessel prosthesis/
16. vascular surgical procedures/ or blood vessel prosthesis implantation/
17. (coil$ or Guglielmi$).tw.
18. or/14-17
19. 13 and 18
20. neurosurgical procedures/ or craniotomy/
21. Neurosurgery/
22. aneurysm/su or aneurysm, ruptured/su or intracranial aneurysm/su
23. Subarachnoid Hemorrhage/su [Surgery]
24. clip$.tw.
25. or/20-24
26. 19 and 25
27. limit 26 to human

EMBASE (Ovid)
We also contacted trialists in an effort to identify further published and unpublished studies and scanned the reference list of all relevant publications.

METHODS OF THE REVIEW

Data extraction and trial quality assessment
Two authors (IvdS and MW) independently extracted details of method of randomisation, inclusion and exclusion criteria, blinding of outcome assessment, prognostic factors for outcome (clinical condition on admission, site and size of aneurysm and time interval between SAH and treatment allocation), the definition of outcome measures and the number of patients who were excluded or lost to follow up. Furthermore, we assessed whether intention-to-treat analysis was possible from the published data and if treatment groups were comparable with regard to major prognostic risk factors. In addition, we recorded duration of follow up, the numbers of deaths and patients with poor outcome (dependent in daily life) at the time points used by the trialists, the number of patients with secondary ischaemia or recurrent haemorrhage at the time points used by the trialists, complications from the intervention and technical results of the intervention in terms of degree of obliteration of the aneurysm. Where there was disagreement, both authors reassessed and discussed the article in question together until consensus was reached. We did not use a grading system to assess the quality of trials but performed sensitivity analyses with the exclusion of trials for which the above data were not available. If any patients were excluded or lost to follow up from the analyses, or if any of the necessary data were not available from the publication, we sought further information by contacting the trialists.

Data analysis
The primary and other outcomes were analysed according to the intention-to-treat principle. An estimate of the treatment effect across trials (relative risk (RR) with 95% confidence interval (CI)) was calculated using standard methods for the main outcome measures. We also calculated absolute risk differences with 95% confidence limits. The relative risk and the absolute risk difference were calculated using the Review Manager software, RevMan 4.2, provided by The Cochrane Collaboration. The statistical validity of aggregating the trials was assessed with chi square test statistics for heterogeneity. The Peto method was used to calculate a weighted estimate of the treatment effects across trials (APT 1994). Where this primary analysis suggested a beneficial effect for either treatment, we had specified in our protocol that a secondary analysis would be performed according to the worst-case scenario method. Thus, if data were missing for patients excluded after randomisation or lost to follow up, an analysis was done in which patients in the coiling group with missing follow-up information were assumed to have had a poor outcome and those in the surgical group a good outcome.

Other pre-specified analyses were:
(1) timing of the intervention as early (within 3 days after onset of the SAH); intermediate (within 10 days after onset of the SAH); or late (more than 10 days after the SAH);
(2) timing of the follow-up period, with trials categorized according to time of outcome assessment between (a) one to three months; (b) three to six months; and (c) six to 12 months;
(3) methodological quality of trials with:
- exclusion of studies with insufficient information on inclusion and exclusion criteria;
- exclusion of studies with insufficient data on method of randomisation;
- exclusion of studies with insufficient data on blinding of outcome assessment;
- exclusion of studies with insufficient data on the number of patients who were excluded or lost to follow up;
- exclusion of studies with insufficient data on the definition of outcome events; and
- exclusion of studies with insufficient data on the following prognostic factors (a) clinical condition on admission; (b) size and site of the aneurysm; and (c) time interval between the SAH and treatment allocation.
For secondary ischaemia and recurrent haemorrhage, we performed separate analyses for the combination of probable and definite episodes and for definite episodes alone.

We compared the number of patients with recurrent haemorrhage per patient year of follow up for the period more than one year after the initial haemorrhage.

DESCRIPTION OF STUDIES

We identified two published, unconfounded, randomised trials of endovascular coiling versus neurosurgical clipping for patients with aneurysmal SAH (ISAT; Koivisto 2000) and one unpublished, unconfounded controlled trial of a series of 20 patients randomly allocated to either endovascular or surgical treatment (Brilstra 2000b). The trials recruited patients in the years between 1994 and 2002. No trials were excluded from this review. At present, there are no trials awaiting assessment or any ongoing trials.

Size of trials and treatment modes

The meta-analysis included a total of 2272 randomised patients: 1135 in the endovascular treatment group and 1137 in the surgical treatment group. The largest trial was the International Subarachnoid Haemorrhage Trial (ISAT), which recruited 2143 patients. The other two trials recruited 20 and 109 patients (Brilstra 2000b; Koivisto 2000). The mean age of the patients ranged from 49.5 to 52 years. The randomisation was done within 28 days of the patient ictus.

Inclusion and exclusion criteria

In all trials, SAH was proven either by CT or lumbar puncture, and aneurysms were confirmed by CT-angiography or angiography. After informed consent was obtained, all patients with a ruptured aneurysm that was considered suitable for both clipping and coiling were included if the clinical condition justified treatment. The maximum delay between SAH and treatment was 3 days in the study of Koivisto (Koivisto 2000), 5 days in the study of Brilstra (Brilstra 2000b; Koivisto 2000). The mean age of the patients ranged from 49.5 to 52 years. The randomisation was done within 28 days of the patient ictus.

In the ISAT trial, patients were excluded if they were already participating in another trial (ISAT). In the study of Koivisto, exclusion criteria were defined for patient characteristics as well as for aneurysm characteristics. Patients older than 75 years, with a large haematoma necessitating operation or having a mass effect causing neurological deficit, or with a history of any previous operation for the same aneurysm were excluded. Furthermore, exclusion criteria for the aneurysm concerning size, shape and relationship to adjacent vessel were given (Koivisto 2000). In the study of Brilstra, patients with a fusiform, traumatic or dissecting aneurysm were excluded (Brilstra 2000b).

Outcome measures and follow-up duration

In ISAT, the primary outcome measure was the proportion of patients with a modified Rankin scale score of 3 to 6 (dependency or death) at one year. Secondary outcome measures were rebleeding, quality of life at one year, the frequency of epilepsy, cost-effectiveness, and neuropsychological outcomes. Accrual to ISAT was stopped prematurely, before the planned sample size had been achieved, on the basis of an interim analysis. The Data Monitoring Committee analysed the data on 29 April 2002 and advised the Steering Committee, on the basis of the result, to stop recruitment. The Steering Committee met on 2 May 2002 and decided that recruitment should stop but that follow up must continue. Recruitment ceased immediately (ISAT).

In the study of Koivisto, the primary outcome measurements were the 12-month clinical outcome and 12-month neuropsychological and radiological outcomes. The 12-month clinical outcome was defined by the Glasgow Outcome Scale (GOS), trichotomized into good or moderate recovery (GOS 4 and 5), severe disability and vegetative state (GOS 2 and 3) and death (GOS 1) (Koivisto 2000).

In the study of Brilstra, outcome measures were the proportion of patients with a Rankin score of 3 to 6 (dependency or death), the rates of recurrent haemorrhage and secondary cerebral ischaemia, and the rate of procedural complications at three months (Brilstra 2000b).

METHODOLOGICAL QUALITY

Method of randomisation and data analysis

Two trials used sealed envelopes as the method of randomisation (Brilstra 2000b; Koivisto 2000). In the study of Brilstra, a computer-generated list was used and the sealed envelopes were not within reach of the treating physician. In ISAT, a minimisation algorithm was used to ensure balance between the two groups based on clinical grade, size and location of aneurysm, and extent of extravasated blood on the CT, and allocations were made by telephone call to a central randomisation service (ISAT). In the three trials, appropriate statistical methods were applied to the data analyses.

Outcome assessment and comparability of the treatment groups

Clinical outcome measures

Clinical outcome measures were collected by means of a validated postal questionnaire mailed to the patients in ISAT (ISAT). In the study of Koivisto, the 12-month clinical outcome was evaluated by a single neurosurgeon primarily responsible for treatment or the principal investigator of the study (Koivisto 2000); and in the study of Brilstra, patients or their care givers were interviewed by telephone to assess functional outcome three months after SAH (Brilstra 2000b). Twelve-month clinical outcome was assessed at the outpatients clinic by a neurologist or by a neurosurgeon who had not operated on the patient. No information on secondary cerebral ischaemia was given in the report of ISAT (ISAT). In the
study of Koivisto, secondary ischaemia was not CT or MRI proven, but the diagnosis was based upon clinical signs of ischaemic neurological deficit (Koivisto 2000). In the study of Brilstra, secondary cerebral ischaemia was CT or MRI proven (Brilstra 2000b). In all three trials, rebleeding had to be confirmed by CT.

Data on degree of occlusion after clipping and coiling
For ISAT, the angiographic occlusion on the first follow-up angiography performed after the procedure was reported for 881 of 988 patients allocated to endovascular treatment and alive after one year, and for 450 of 965 patients allocated to surgical treatment alive after one year. In the endovascular group, timing of follow-up angiography was before discharge in 28 patients, before two months in 80 patients, between two to 12 months in 690 patients, between one and two years in 58 patients and after two years in 25 patients. MRI-angiography was used in 47 patients. In the neurosurgical group, timing of follow-up angiography was before discharge in 142 patients, before two months in 61 patients, between two to 12 months in 199 patients and between one and five years in 48 patients (ISAT). In the study of Koivisto, the primary (direct post treatment) as well as final (after one-year follow up) angiographic results of endovascular and surgical treatment of the ruptured aneurysms were given (Koivisto 2000). In the study of Brilstra, direct post-treatment information of completeness of occlusion after treatment was available for all patients; angiographic follow-up information was available for only one of the clipped patients and for six of the eight patients who survived six months after the SAH (Brilstra 2000b).

Comparability of treatment groups
In the three trials analysed, the prognostic factors of gender, age and clinical condition on admission were balanced. Aneurysm location and size were similar for the treatment groups within each of the three studies. However, in ISAT the prognostic determinant time between randomisation and first procedure (that is, the time between SAH and treatment) differed slightly but statistically significantly between the coiled and clipped patients. For those allocated to endovascular treatment the mean interval was 1.1 days (IQR 0 to 1, range 0 to 30), and for those allocated to neurosurgical treatment the mean interval was 1.7 days (IQR 0 to 2, range 0 to 41) (ISAT).

Follow up and completeness of data on follow up
In ISAT, the main outcome measure was assessed at two months, one year and annually thereafter. At one-year follow up, the vital status was known for all included patients. For eight coiled patients and seven clipped patients the disability status was missing at the two-month follow up. At one-year follow up the disability status was missing for 10 coiled patients and 15 clipped patients (ISAT). In the study of Koivisto, clinical and neuropsychological outcome was assessed after 3 and 12 months. No patients were lost to follow up. Mean follow-up duration was 39 months (SD 18 months) (Koivisto 2000). In the study of Brilstra, the main outcome measures were assessed at three months and no patients were lost to follow up at that time. Mean duration of follow up was 25 months (SD 22 months). At a follow-up duration of 12 months, 8 coiled patients and 8 clipped patients were available for analysis. No information on vital status was present for two patients in the endovascular treatment group and two patients in the surgical treatment group (Brilstra 2000b).

RESULTS

Main outcome measures

Poor outcome
At one year, 264 of the 1123 patients allocated to endovascular treatment (24%) and 344 of the 1120 patients allocated to the surgical treatment group (31%) had a poor outcome. All three trials adequately reported on functional outcome at a follow-up time of 12 months. The weighted relative risk (RR) reduction of endovascular coiling versus neurosurgical clipping was 24% (RR 0.76, 95% confidence interval (CI) 0.67 to 0.88). The absolute risk reduction was 7% (95% CI 4% to 11%); this meant that for every 14 (95% CI 9 to 25) patients that were coiled instead of clipped one poor outcome result was prevented. In the worst-case scenario, in which patients whose data were missing in the clipping group were assumed to have had a poor outcome and those in the clipping group were assumed to not have had a poor outcome, the relative risk reduction of coiling versus clipping was 19% (RR 0.81, 95% CI 0.70 to 0.92). The absolute risk reduction by treatment with coils was 6% (95% CI 2% to 10%). The weighted relative risk reduction of endovascular coiling versus neurosurgical clipping at a follow-up duration of two to three months was 29% (RR 0.71, 95% CI 0.63 to 0.81). The absolute risk reduction was 10% (95% CI 7% to 14%).

Case fatality
In the endovascular treatment group, 94 (8.4%) of the 1123 patients had died from any cause within one year versus 116 (10.4%) of the 1120 patients allocated to the surgical treatment group. The relative risk reduction in deaths at one-year follow up for endovascular treatment was 19% (RR 0.81, 95% CI 0.63 to 1.05) compared to clipping. The absolute risk reduction was 2% (95% CI 0% to 4%). The relative risk reduction in death for endovascular coiling versus neurosurgical clipping at two or three months was 12% (RR 0.88, 95% CI 0.66 to 1.2). The absolute risk reduction was 1% (95% CI -1% to 3%).

Secondary cerebral ischaemia
Data on secondary cerebral ischaemia were not available for ISAT. Combining the two small trials, secondary cerebral ischaemia was observed in 29 of 62 patients (47%) allocated to the endovascular treatment group and in 32 of 67 patients (48%) allocated to the surgical treatment group. The weighted relative risk reduction of endovascular coiling versus neurosurgical clipping was 2% (RR 0.98, 95% CI 0.68 to 1.4). The absolute risk reduction was 1% (95% CI -16% to 18%).
**Recurrent haemorrhage**

Nineteen (1.7%) of the 1135 patients allocated to endovascular treatment and 30 (2.6%) of the 1137 patients allocated to surgical clipping suffered from rebleeding before treatment. The risk for pre-procedural rebleeding for endovascular coilings compared to neurosurgical clipping was reduced by 36% (RR 0.64, 95% CI 0.37 to 1.12). The absolute risk reduction was 1% (95% CI 0% to 2%). With regard to post-procedural rebleeding, up to one year after treatment, the relative risk of rebleeding was higher for endovascular treatment. Twenty-nine of the 1135 patients (2.6%) allocated to endovascular treatment and 14 (1.2%) of the 1137 patients allocated to surgical clipping had an episode of rebleeding. The relative risk was 2.0 (95% CI 1.1 to 3.7). The absolute increase in risk was 1% (95% CI 0% to 2%). At a follow-up period of one (ISAT) to three months (Brilstra 2000b; Koivisto 2000) the relative risk for post-procedural rebleeding was 2.7 for coiling versus clipping (95% CI 0.7 to 10). The absolute increase in risk was 0% (95% CI 0% to 1%).

**Complications from intervention**

In ISAT, no information on complications from the interventions was given (ISAT). In the study of Koivisto, information was reported on technical failure and clinical deterioration within 24 hours of the treatment (Koivisto 2000). The study of Brilstra reported on complications from the intervention, defined as clinical deterioration within 24 hours after the intervention (Brilstra 2000b). Complications occurred in 8 (13%) of the 62 patients treated endovascularly and in 8 (12%) of the 67 surgically-treated patients (12%). The weighted relative risk increase with endovascular coilings versus neurosurgical clipping was 5% (RR 1.1, 95% CI 0.44 to 2.5). The absolute risk increase was 1% (95% CI -10% to 12%).

**Death or recurrent haemorrhage at more than one year after the SAH**

**Death**

In the ISAT trial, 20 endovascularly-treated patients and 28 clipped patients died between one year and follow up at five years. In the survival analysis, the proportion of patients alive decreased by 3% in the four-year period after the first year for endovascular patients and by 4% for the clipped patients. This corresponds to a death rate of 7.6 per 1000 patient years for patients treated endovascularly and 10.2 per 1000 patient years for patients treated surgically (ISAT).

In the study of Koivisto, two patients allocated to endovascular treatment died after one year and one patient allocated to surgical treatment died. In survival analyses, the proportion of patients alive decreased by 5% for coiled patients in the three and half year period after the first year of follow up and by 7% for the clipped patients. This corresponded to a death rate of 14.6 per 1000 patient years for patients treated endovascularly and 20.7 per 1000 patient years for patients treated surgically (Koivisto 2000). In the study of Brilstra, a total of 8.7 patient years were available for the coiled patient group and a total of 19.6 patient years were available for the clipped patient group after the one year follow-up period. None of the patients had died during this period of follow up (Brilstra 2000b).

**Recurrent haemorrhage**

In the ISAT trial, seven patients had a recurrent haemorrhage from the target aneurysm after one year (mean follow-up period of four years; 4069 patient years follow up in the endovascular treatment group, 3994 patient years follow up in the surgical treatment group). Six of these patients were in the endovascular group and one was allocated neurosurgery. Additionally, three patients had a recurrent haemorrhage after one year from another aneurysm but no information on the treatment modality of the target aneurysm was given for these patients (ISAT).

In the studies of Koivisto and Brilstra, no rebleeds occurred more than one year after SAH. The mean follow-up period after one year was 27 months in the study of Koivisto (Koivisto 2000) and 13 months in the study of Brilstra (Brilstra 2000b).

**Degree of occlusion after coiling and clipping**

For ISAT, direct post-treatment results and angiographic occlusion on the first follow-up angiography performed after the procedure was given. Direct post-treatment information was based upon the first procedure actually performed, not the original allocation. Of the 1095 patients who were endovascularly treated, coiling failed in 81 patients (7.4%). In 22 of 1012 (2.2%) patients in whom the first treatment was neurosurgical, clipping was not completed or not attempted in 35 patients (3.5%). The aneurysm was successfully wrapped in 14 of these 35 patients. The angiographic occlusion on the first follow-up angiography performed after the procedure was reported for 881 of 988 eligible patients allocated to endovascular treatment and for 450 of 965 eligible patients allocated to surgical treatment. Occlusion was complete in 66% of coiled patients and 82% of the clipped patients; a 90% to 100% occlusion of the aneurysm had occurred in 26% of the coiled patients and 12% of the clipped patients; incomplete occlusion (less than 90%) was found in 7.8% of the endovascularly-treated patients and 5.6% of the surgically-treated patients (ISAT).

In the study of Koivisto, the direct post-treatment results of treatment were available for all patients, as were the one year follow-up angiographic results. In the endovascularly-treated patients, direct post-treatment complete obliteration was achieved in 50% of patients compared with 74% in the surgically-treated patients group. In 35% of the coiled patients an occlusion of 90% to 100% was achieved, compared with 16% of the clipped patients; and in 15% of the clipped patients the aneurysm was less than 90% occluded against 11% of the clipped patients. After one year, occlusion was complete in 77% of coiled patients and 86% of the clipped patients; a 90% to 100% occlusion of the aneurysm had occurred in 19% of the coiled patients and 12% of the clipped patients; incomplete occlusion (less than 90%) was found in 4%
of the endovascularly-treated patients and 2% of the surgically-treated patients. On comparison of incomplete obliteration (less than 100% obliteration) for coiled versus clipped patients during one-year follow up, the relative risk increase was 1.67 (95% CI 1.29 to 2.17) and the absolute risk increase in risk was 13% (95% CI 7% to 19%), both statistically significant. The relative risk for obliteration less than 90% was 1.73 (95% CI 0.97 to 3.1) (P value 0.06) and the absolute increase in risk was 4% (95% CI 0% to 0.07%) (P value 0.03) (Koivisto 2000).

In the study of Brilstra, angiographic follow up was not available for all endovascularly- or surgically-treated patients but immediate post-treatment information was given for all patients. Clipping of the aneurysm was not feasible in one patient and clipping was incomplete in another patient. Immediate post-embolisation angiography showed complete occlusion in five coiled patients and a 90% to 99% occlusion in the other five coiled patients (Brilstra 2000b).

Additional analysis
The timing of the intervention was early in the study of Koivisto (treatment within three days) (Koivisto 2000); early or intermediate in the study of Brilstra (Brilstra 2000b) and early, intermediate or late in ISAT (ISAT). Since we had no information on outcome related to timing of the intervention we could not perform the proposed analysis of outcome measures according to the timing of the intervention.

Sub-analyses based on methodological quality were not necessary because all three trials met all methodological criteria except for the criterion for blinding of outcome assessment.

A subgroup analysis for basilar aneurysms could not be performed since only data for posterior circulation aneurysms were present. Therefore, we performed an analysis for all posterior circulation aneurysms and all anterior circulation aneurysms for which information was available, for ISAT and the study of Koivisto (Koivisto 2000). In the study of Brilstra no patients with posterior circulation were included (Brilstra 2000b). For patients with a posterior circulation aneurysm, the relative risk of poor outcome was 0.41 (95% CI 0.19 to 0.92) and the absolute decrease in risk 27% (95% CI 6% to 48%). For those with an anterior circulation aneurysm the relative risk was 0.78 (95% CI 0.68 to 0.90) and the absolute risk decrease was 7% (95% CI 3% to 10%).

Discussion

Effect of endovascular coiling
The aggregation of the results of all identified studies on endovascular versus surgical treatment in patients with a SAH showed a reduction of poor outcome after treatment by coiling compared with clipping. Even in the worst-case scenario analysis, the reduction of poor outcome in endovascularly-treated patients was still statistically significant. The reduction in case fatality was not statistically significant. The analysis on post-procedural recurrent haemorrhage (up to one-year follow up) showed a significantly higher risk in the coiled patient group but the main outcome measure of poor outcome was ascertained after one year of follow up. Therefore, all instances of rebleeding within the first year after treatment were accounted for in the primary outcome measure.

Methodological issues of the present overview
This overview represents the results of one large trial and two much smaller trials. The results are largely dependent on the largest trial (ISAT) because results are weighted to number of patients and events in each trial. However, the results of the smaller trials were in the same direction for the primary outcome measure. ISAT was stopped prematurely on the basis of an interim analysis. There was no evidence of heterogeneity in any of the analyses.

The treatment and control groups were well balanced regarding baseline characteristics. Peri- and post-procedural management is probably also similar between the two treatment strategies except for the use of platelet aggregation inhibitors. Aspirin is often prescribed after coiling of aneurysms, although the impression is that ISAT investigators from the UK did not use it frequently. In a systematic review antiplatelet therapy reduced the occurrence of secondary ischaemia and tended to improve overall outcome (Dorhout Mees 2003). If indeed use of platelet aggregation inhibitors was greater in the endovascular group this may have contributed to the better outcome after coiling.

We intended to perform a subgroup analysis for patients with a ruptured aneurysm of the basilar artery. However, no specified information on main outcome measures was available for this subgroup of patients. In our subgroup analysis for all posterior circulation aneurysms the relative risk of poor outcome was significantly decreased for endovascular coiling.

Another type of patient that was under-represented in the trials included in the review were patients with aneurysms of the middle cerebral artery (MCA). These aneurysms are often not suitable for coiling. The total number of patients with aneurysms from the MCA was still considerable and the results in patients with MCA aneurysms were in the same direction as in patients with aneurysms at other sites. Therefore, it seems reasonable to assume that the results of this review also hold true for patients with MCA aneurysms and whose anatomy was suitable for either endovascular or surgical treatment. Patients in poor clinical condition were also under-represented. All three randomised trials only included patients whose clinical condition justified treatment by either clipping or coiling and from whom informed consent was obtained, which is more difficult in patients with a poor clinical condition. Because a poor clinical condition at time of admission is an important predictor for poor outcome, the results of this review cannot be directly applied to patients in poor clinical condition for admission. For these patients we have to base our current clinical
decisions on data other than those from a randomised trial. As coiling has the advantage of being less invasive than surgery it also seems the preferred option in patients with poor clinical condition. Given the absence of good evidence on the effectiveness of surgical treatment for this group of patients, there is no good reason to support surgical treatment in these patients either. Keeping all these uncertainties in mind, coiling seems to be the preferred strategy because coiling is less invasive than surgery.

An unanswered question is the long-term durability of aneurysm occlusion after endovascular treatment. Late spontaneous reperfusion of the aneurysm may lead to insufficient protection against recurrent haemorrhages in the future. One should keep in mind, however, that similar uncertainties exist on the long-term occlusion rate of surgically-treated aneurysms. The regrowth of aneurysms close to the surgical clip has been described, with an incidence of approximately 0.5% per year (David 1999; Tsusumi 2001). In addition, de novo formation of aneurysms has been described on locations other than the original aneurysm site. In follow-up studies of patients treated for an aneurysm the rate of development of new aneurysms ranged between 0.8% and 2% per year (David 1999; Juvela 1993; Juvela 2001; Tsusumi 2001). These new aneurysms again may cause a SAH (Wermer 2005). In fact, we are only beginning to gather knowledge on the long-term prognosis and management of patients treated for one or more aneurysms. The presence and rupture of an aneurysm is not an once-in-a-lifetime event but the consequence of a defect in the intracranial vessel wall that can give rise to additional aneurysms later in life.

**AUTHORS’ CONCLUSIONS**

**Implications for practice**

The results of this review mainly draw on evidence from patients in good clinical condition after subarachnoid haemorrhage (SAH). For these patients we now have firm evidence that if the aneurysm is considered suitable for both surgical clipping and endovascular treatment coiling is associated with a better outcome. The evidence comes mainly from one large trial. For patients in poor clinical grades, there is no reliable randomised evidence comparing the risks and benefits of coiling versus clipping. As coiling has the advantage of being less invasive than surgery coiling also seems to be the preferred option in patients with poor clinical condition. A disadvantage of coiling is that aneurysms are more often incompletely treated (90% to 100% obliteration) and carry a risk for reopening. At one-year follow up, the risks of repeated angiography and treatment do not negate the benefits but data on long-term follow up are not yet available.

**Implications for research**

The long-term follow up (more than one year after SAH) of coiled patients with regard to renewed filling of the aneurysm is an unknown but important issue that needs further study. There is no reliable trial evidence to guide treatment in patients with a poor clinical condition. More valuable additional information can be expected from the ISAT study. This includes an analysis on the cost-effectiveness of endovascular treatment versus surgical clipping and the long-term results of both treatments.

**POTENTIAL CONFLICT OF INTEREST**

Dr A Molyneux acts as a medical advisor to the Micrus Corporation, a company which manufactures detachable coils. He also has a stock interest in this company. Dr M Clarke is on the Executive Committee for the ISAT trial.

**ACKNOWLEDGEMENTS**

We thank Drs EH Brilstra and WJJ van Rooij for their contributions to the development of the protocol for this review.

**SOURCES OF SUPPORT**

External sources of support
- Netherlands Hartefoundation NETHERLANDS

Internal sources of support
- NHS Research and Development Programme, UK Cochrane Centre UK
References to studies included in this review

**Bralstra 2000b [published data only]**
Bralstra EH, Lussevele E, on behalf of the SCATO Study Group. Early embolization with coils in patients scheduled for delayed operation after aneurysmal subarachnoid hemorrhage: a randomized pilot study. Unpublished data.

**ISAT [published data only]**


**Koivisto [published data only]**

Additional references

**ACROSS 2000**

**APT 1994**

**Balsavias 2000**

**Bamford 1990**

**Bralstra 1998**

**Bralstra 2000a**

**David 1999**

**Dorhout Mees 2003**

**Hop 1997**

**Johnston 1998**

**Juvela 1993**

**Juvela 2001**

**Linn 1996**

**Rinkel 1993**

**Roos 2000**

**Roos 2000a**

**Schievink 1995**

**Tsumumi 2001**
Wermer 2005


*Indicates the major publication for the study

---

**Tables**

Characteristics of included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Brilstra 2000b</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Blinding: no.</td>
</tr>
<tr>
<td></td>
<td>- Analysis: intention to treat.</td>
</tr>
<tr>
<td></td>
<td>- Excluded patients: 9.</td>
</tr>
<tr>
<td></td>
<td>- Cross-over cases: no.</td>
</tr>
<tr>
<td></td>
<td>- Losses to follow up: at 1 year follow up: 2 patients in the endovascular treatment group and 2 patients in the surgical treatment group.</td>
</tr>
<tr>
<td></td>
<td>- Definition of outcomes: stated.</td>
</tr>
<tr>
<td>Participants</td>
<td>- Location: University Medical Centre Utrecht and St Elisabeth Hospital Tilburg, The Netherlands.</td>
</tr>
<tr>
<td></td>
<td>- Coil: 10 (male 3 (30%)).</td>
</tr>
<tr>
<td></td>
<td>- Clip: 10 (male 3 (30%)).</td>
</tr>
<tr>
<td></td>
<td>- Age range: 35-75.</td>
</tr>
<tr>
<td></td>
<td>- Entry criteria: documented aneurysmal SAH by either CT or DSA within the preceding 4 days, clinical state justifying treatment, aneurysm suitable for both treatment modalities.</td>
</tr>
<tr>
<td></td>
<td>- Comparability of treatment groups: good for major prognostic factors.</td>
</tr>
<tr>
<td></td>
<td>- Clinical grade on admission:</td>
</tr>
<tr>
<td></td>
<td>- Coil: WFNS I: 4; II: 3; III: 1; IV: 2; V: 0.</td>
</tr>
<tr>
<td></td>
<td>- Clip: WFNS I: 4; II: 2; III: 2; IV: 1; V: 1.</td>
</tr>
<tr>
<td></td>
<td>- Aneurysm location:</td>
</tr>
<tr>
<td></td>
<td>- Coil: ACA and Acom: 5; MCA: 1; ICA: 4; posterior circulation: 0.</td>
</tr>
<tr>
<td></td>
<td>- Clip: ACA and Acom: 3; MCA: 2; ICA: 5; posterior circulation: 0.</td>
</tr>
<tr>
<td>Interventions</td>
<td>- Endovascular treatment by means of coils.</td>
</tr>
<tr>
<td></td>
<td>- Surgical treatment by means of clips.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>- Clinical outcomes: dependency and death at 1 year FU, rebleeding, epilepsy, QOL at 1 year and neuropsychological outcomes.</td>
</tr>
<tr>
<td></td>
<td>- Additional measures: cost-effectiveness?</td>
</tr>
<tr>
<td>Notes</td>
<td>- Exclusion criteria: the logistic conditions for early operation could not be fulfilled.</td>
</tr>
<tr>
<td></td>
<td>- Follow-up duration: 3 months and 1 year.</td>
</tr>
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Allocation concealment  A
### Characteristics of included studies (Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>ISAT</th>
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<tbody>
<tr>
<td></td>
<td>- Blinding: unblinded interim data.</td>
</tr>
<tr>
<td></td>
<td>- Analysis: intention to treat.</td>
</tr>
<tr>
<td></td>
<td>- Excluded patients: 131.</td>
</tr>
<tr>
<td></td>
<td>- Cross-over cases: 8 patients.</td>
</tr>
<tr>
<td></td>
<td>- Losses to follow up: at 1 year follow up: vital status known for all patients, for 10 patients in the endovascular treatment group and 15 patients in the surgical treatment group the disability status was missing.</td>
</tr>
<tr>
<td></td>
<td>- Definition of outcomes: stated.</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>- Location: 43 major neurosurgical centres.</td>
</tr>
<tr>
<td></td>
<td>- Coil: 1073 (male to female ratio: 0.6).</td>
</tr>
<tr>
<td></td>
<td>- Clip: 1070 (male to female ratio: 0.6).</td>
</tr>
<tr>
<td></td>
<td>- Age range: 18-87.</td>
</tr>
<tr>
<td></td>
<td>- Entry criteria: documented aneurysmal SAH by either CT or LP within the preceding 28 days, clinical state justifying treatment, aneurysm suitable for both treatment modalities.</td>
</tr>
<tr>
<td></td>
<td>- Comparability of treatment groups: good for major prognostic factors (except for sign difference in time between SAH and treatment).</td>
</tr>
<tr>
<td></td>
<td>- Clinical grade on admission:</td>
</tr>
<tr>
<td></td>
<td>- Coil: WFNS I: 674 (63%); II: 269 (25%); III: 66 (6%); IV: 38 (4%); V: 11 (1%); VI: 15 (1%).</td>
</tr>
<tr>
<td></td>
<td>- Clip: WFNS I: 661 (62%); II: 280 (26%); III: 68 (6%); IV: 36 (3%); V: 9 (1%); VI: 16 (1%).</td>
</tr>
<tr>
<td></td>
<td>- Aneurysm location:</td>
</tr>
<tr>
<td></td>
<td>- Clip: ACA and Acom: 534; MCA: 139; ICA: 348; posterior circulation: 34.</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>- Endovascular treatment by means of coils.</td>
</tr>
<tr>
<td></td>
<td>- Surgical treatment by means of clips.</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>- Clinical outcomes: dependency and death at 1 year FU, rebleeding, epilepsy, QOL at 1 year and neuropsychological outcomes.</td>
</tr>
<tr>
<td></td>
<td>- Additional measures: cost-effectiveness?</td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td>- Exclusion criteria: refused informed consent, if participating in another RCT of a treatment for SAH.</td>
</tr>
<tr>
<td></td>
<td>- Follow-up duration: 2 months and 1 year.</td>
</tr>
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</table>

#### Allocation concealment

<table>
<thead>
<tr>
<th>Study</th>
<th>Koivisto 2000</th>
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<tbody>
<tr>
<td></td>
<td>- Blinding: no.</td>
</tr>
<tr>
<td></td>
<td>- Analysis: intention to treat.</td>
</tr>
<tr>
<td></td>
<td>- Excluded patients: 7416.</td>
</tr>
<tr>
<td></td>
<td>- Cross-over cases: 47.</td>
</tr>
<tr>
<td></td>
<td>- Losses to follow up: at 1 year: no losses to follow up.</td>
</tr>
<tr>
<td></td>
<td>- Definition of outcomes: stated.</td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td>- Location: Kuopio University Hospital, Kuopio, Finland.</td>
</tr>
<tr>
<td></td>
<td>- Coil: 52 (male to female ratio: 0.5).</td>
</tr>
<tr>
<td></td>
<td>- Clip: 57 (male to female ratio: 0.4).</td>
</tr>
<tr>
<td></td>
<td>- Age range: 14-75.</td>
</tr>
<tr>
<td></td>
<td>- Entry criteria: informed consent, SAH from a ruptured aneurysm suitable for both EVT and surgical treatment (based on diagnostic angiographic determinants), SAH in the preceding 3 days.</td>
</tr>
<tr>
<td></td>
<td>- Comparability of treatment groups: good for major prognostic factors.</td>
</tr>
<tr>
<td></td>
<td>- Clinical grade on admission:</td>
</tr>
<tr>
<td></td>
<td>- Coil: Fisher 0-2; 20; 3-5; 32. HUNT and HESS I-II: 31; III: 2; IV-V: 9.</td>
</tr>
<tr>
<td></td>
<td>- Clip: Fisher 0-2; 22; 3-5; 35. HUNT and HESS I-II: 36; III: 14; IV-V: 7.</td>
</tr>
</tbody>
</table>

*Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage (Review)*

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Characteristics of included studies (Continued)

Coil: ACA: 27; MCA: 7; ICA: 12; posterior circulation: 1.
Clip: ACA: 28; MCA: 12; ICA: 12; posterior circulation: 5.

Interventions
- Endovascular treatment by means of coils.
- Surgical treatment by means of clips.

Outcomes
- Clinical outcomes: 12 month clinical, neuropsychological and radiological outcomes.
- Endpoints:
  primary endpoint: rebleeding or death;
  secondary endpoint: refilling of the aneurysm.

Notes
- Exclusion criteria: older than 75 years, presence of large haematoma necessitating surgery, mass effect causing neurological deficit, previous surgery for the ruptured aneurysm.
- Follow-up duration: 3 months and 1 year.

Allocation concealment A

ACA: anterior cerebral artery
Acom: anterior communicating artery
CT: computed tomography
DSA: digital subtraction angiography
EVT: endovascular treatment
FU: follow up
ICA: internal carotid artery
LP: lumbar puncture
MCA: middle cerebral artery
QOL: quality of life
RCT: randomised controlled trial
SAH: subarachnoid haemorrhage
WFNS: World Federation of Neurological Surgeons subarachnoid haemorrhage grading scale

ADDITIONAL TABLES

Table 01. Angiographic occlusion on follow-up angiography during 1st year post-treatment

<table>
<thead>
<tr>
<th>Nr pt per treatment</th>
<th>100% occlusion (%)</th>
<th>90 - 100% occlusion (%)</th>
<th>&lt; 90% occlusion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISAT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>coiling (n = 881)</td>
<td>584 (66%)</td>
<td>228 (26%)</td>
<td>69 (7.8%)</td>
</tr>
<tr>
<td>clipping (n = 450)</td>
<td>370 (82%)</td>
<td>55 (12%)</td>
<td>25 (5.6%)</td>
</tr>
<tr>
<td>Koivisto</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>coiling (n = 52)</td>
<td>40 (77%)</td>
<td>10 (19%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>clipping (n = 57)</td>
<td>49 (86%)</td>
<td>7 (12%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Total</td>
<td>499 (66%)</td>
<td>189 (25%)</td>
<td>65 (8.6%)</td>
</tr>
<tr>
<td>coiling (n = 753)</td>
<td>230 (81%)</td>
<td>42 (15%)</td>
<td>13 (4.6%)</td>
</tr>
<tr>
<td>clipping (n = 285)</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
## Analyses

### Comparison 01. Poor outcome

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 death or dependency at 2 to 3 months</td>
<td>3</td>
<td>2257</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>0.71 [0.63, 0.81]</td>
</tr>
<tr>
<td>02 death or dependency at 12 months after SAH</td>
<td>3</td>
<td>2243</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>0.76 [0.67, 0.88]</td>
</tr>
<tr>
<td>03 worst-case scenario at 12 months</td>
<td>3</td>
<td>2272</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>0.81 [0.70, 0.92]</td>
</tr>
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</table>

### Comparison 02. Secondary cerebral ischaemia

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 2 to 3 months</td>
<td>2</td>
<td>129</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>0.98 [0.68, 1.41]</td>
</tr>
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</table>

### Comparison 03. Recurrent haemorrhage

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 rebleed before treatment</td>
<td>3</td>
<td>2272</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>0.64 [0.37, 1.12]</td>
</tr>
<tr>
<td>02 rebleed post-procedure up to 1 year</td>
<td>3</td>
<td>2272</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>2.00 [1.08, 3.70]</td>
</tr>
<tr>
<td>03 rebleed post-procedure up to 3 months</td>
<td>3</td>
<td>2272</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>2.66 [0.71, 10.00]</td>
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### Comparison 04. Case fatality

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 death from any cause 2 to 3 months</td>
<td>3</td>
<td>2257</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>0.88 [0.66, 1.18]</td>
</tr>
<tr>
<td>02 death from any cause between randomisation and 1 year after SAH</td>
<td>3</td>
<td>2243</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>0.81 [0.63, 1.05]</td>
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</tbody>
</table>

### Comparison 05. Complications from intervention

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 complications from intervention</td>
<td>2</td>
<td>129</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>1.05 [0.44, 2.53]</td>
</tr>
</tbody>
</table>

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Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage (Review)

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Comparison 06. Degree of obliteration

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 non-complete obliteration after 1 year</td>
<td>2</td>
<td>1038</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>1.67 [1.29, 2.17]</td>
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<tr>
<td>02 less than 90% occlusion after 1 year</td>
<td>2</td>
<td>1038</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>1.73 [0.97, 3.09]</td>
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</table>

Comparison 07. Subgroup analysis: aneurysm location

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
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<tbody>
<tr>
<td>01 12 month poor outcome posterior and anterior circulation</td>
<td>4</td>
<td>2226</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>0.76 [0.66, 0.88]</td>
</tr>
</tbody>
</table>

COVER SHEET

Title

Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage

Authors


Contribution of author(s)

IC van der Schaaf: extracted data from the studies included in the review; prepared the analysis and has written the first drafts of the review.
A Algra: participated in writing the grant application; developing the protocol; appraising the quality of studies; data analysis; data interpretation and writing the review.
MJH Wermer: extracted data from the studies included in the review and participated in writing the review.
A Molyneux: gave comments on the protocol and participated in data interpretation and writing the review.
M Clarke: helped editing the text of the review and has written the synopsis.
J van Gijn: participated in writing the grant application; developing the protocol; appraising the quality of studies; data interpretation and writing the review.
GJE Rinkel: participated in developing the protocol; data extraction; appraising the quality of studies; data analysis; data interpretation; writing the review and entering the review into RevMan. Dr Rinkel is the guarantor for this review.

Issue protocol first published: 2001/2
Review first published: 2005/4
Date of most recent amendment: 17 August 2005
Date of most recent SUBSTANTIVE amendment: 13 June 2005

What's New

Information not supplied by author

Date new studies sought but none found

Information not supplied by author

Date new studies found but not yet included/excluded

Information not supplied by author

Date new studies found and included/excluded

Information not supplied by author
**Analysis 01.01. Comparison 01 Poor outcome, Outcome 01 death or dependency at 2 to 3 months**

Review: Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage

Comparison: 01 Poor outcome

Outcome: 01 death or dependency at 2 to 3 months

<table>
<thead>
<tr>
<th>Study</th>
<th>coil n/N</th>
<th>clip n/N</th>
<th>Relative Risk (Fixed)</th>
<th>Weight (%)</th>
<th>Relative Risk (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brilstra 2000b</td>
<td>4/10</td>
<td>5/10</td>
<td>1.2</td>
<td>1.2</td>
<td>0.80 [ 0.30, 2.13 ]</td>
</tr>
<tr>
<td>ISAT</td>
<td>278/1065</td>
<td>392/1063</td>
<td>96.0</td>
<td>96.0</td>
<td>0.71 [ 0.62, 0.80 ]</td>
</tr>
<tr>
<td>Koivisto 2000</td>
<td>10/52</td>
<td>12/57</td>
<td>2.8</td>
<td>2.8</td>
<td>0.91 [ 0.43, 1.93 ]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1127</td>
<td>1130</td>
<td>100.0</td>
<td>100.0</td>
<td>0.71 [ 0.63, 0.81 ]</td>
</tr>
</tbody>
</table>

Total events: 292 (coil), 409 (clip)

Test for heterogeneity chi-square=0.48 df=2 p=0.79 I² =0.0%

Test for overall effect z=5.26 p<0.00001
### Analysis 01.02.  Comparison 01 Poor outcome, Outcome 02 death or dependency at 12 months after SAH

**Review:** Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage

**Comparison:** 01 Poor outcome

**Outcome:** 02 death or dependency at 12 months after SAH

<table>
<thead>
<tr>
<th>Study</th>
<th>coil n/N</th>
<th>clip n/N</th>
<th>Relative Risk (Fixed)</th>
<th>Weight (%)</th>
<th>95% CI (%)</th>
<th>Relative Risk (Fixed)</th>
<th>95% CI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brilstra 2000b</td>
<td>3/8</td>
<td>4/8</td>
<td>1.2</td>
<td>0.75</td>
<td>[0.24, 2.33]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISAT</td>
<td>250/1063</td>
<td>326/1055</td>
<td></td>
<td>95.0</td>
<td>[0.66, 0.88]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Koivisto 2000</td>
<td>11/52</td>
<td>14/57</td>
<td>3.9</td>
<td>0.86</td>
<td>[0.43, 1.72]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>1123</td>
<td>1120</td>
<td>100.0</td>
<td>0.76</td>
<td>[0.67, 0.88]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 264 (coil), 344 (clip)

Test for heterogeneity chi-square=0.12 df=2 p=0.94 $I^2 = 0.0$

Test for overall effect $z=3.83$ p=0.0001

#### Favours coiling  Favours clipping

---

### Analysis 01.03.  Comparison 01 Poor outcome, Outcome 03 worst-case scenario at 12 months

**Review:** Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage

**Comparison:** 01 Poor outcome

**Outcome:** 03 worst-case scenario at 12 months

<table>
<thead>
<tr>
<th>Study</th>
<th>coil n/N</th>
<th>clip n/N</th>
<th>Relative Risk (Fixed)</th>
<th>Weight (%)</th>
<th>95% CI (%)</th>
<th>Relative Risk (Fixed)</th>
<th>95% CI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brilstra 2000b</td>
<td>5/10</td>
<td>4/10</td>
<td>1.2</td>
<td>1.25</td>
<td>[0.47, 3.33]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISAT</td>
<td>261/1073</td>
<td>326/1070</td>
<td></td>
<td>95.0</td>
<td>[0.69, 0.92]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Koivisto 2000</td>
<td>11/52</td>
<td>14/57</td>
<td>3.9</td>
<td>0.86</td>
<td>[0.43, 1.72]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>1135</td>
<td>1137</td>
<td>100.0</td>
<td>0.81</td>
<td>[0.70, 0.92]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 277 (coil), 344 (clip)

Test for heterogeneity chi-square=0.82 df=2 p=0.66 $I^2 = 0.0$

Test for overall effect $z=3.13$ p=0.0002

#### Favours coiling  Favours clipping
**Analysis 02.01. Comparison 02 Secondary cerebral ischaemia, Outcome 01 2 to 3 months**

Review: Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage

Comparison: 02 Secondary cerebral ischaemia

Outcome: 01 2 to 3 months

<table>
<thead>
<tr>
<th>Study</th>
<th>coil n/N</th>
<th>clip n/N</th>
<th>Relative Risk (Fixed)</th>
<th>Weight (%)</th>
<th>Relative Risk (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brilstra 2000b</td>
<td>5/10</td>
<td>4/10</td>
<td>13.0</td>
<td>1.25</td>
<td>1.25 [0.47, 3.33]</td>
</tr>
<tr>
<td>Koivisto 2000</td>
<td>24/52</td>
<td>28/57</td>
<td>87.0</td>
<td>0.94</td>
<td>0.94 [0.63, 1.39]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>62</td>
<td>67</td>
<td>100.0</td>
<td>0.98</td>
<td>0.98 [0.68, 1.41]</td>
</tr>
</tbody>
</table>

Total events: 29 (coil), 32 (clip)

Test for heterogeneity chi-square=0.28 df=1 p=0.60 I²=0.0%

Test for overall effect z=0.11 p=0.9

---

**Analysis 03.01. Comparison 03 Recurrent haemorrhage, Outcome 01 rebleed before treatment**

Review: Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage

Comparison: 03 Recurrent haemorrhage

Outcome: 01 rebleed before treatment

<table>
<thead>
<tr>
<th>Study</th>
<th>coil n/N</th>
<th>clip n/N</th>
<th>Relative Risk (Fixed)</th>
<th>Weight (%)</th>
<th>Relative Risk (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brilstra 2000b</td>
<td>1/10</td>
<td>2/10</td>
<td>6.6</td>
<td>0.50</td>
<td>0.50 [0.05, 4.67]</td>
</tr>
<tr>
<td>ISAT 17/1073</td>
<td>28/1070</td>
<td>28/1070</td>
<td>91.9</td>
<td>0.61</td>
<td>0.61 [0.33, 1.10]</td>
</tr>
<tr>
<td>Koivisto 2000</td>
<td>1/52</td>
<td>0/57</td>
<td>1.6</td>
<td>3.28</td>
<td>3.28 [0.14, 78.86]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1135</td>
<td>1137</td>
<td>100.0</td>
<td>0.64</td>
<td>0.64 [0.37, 1.12]</td>
</tr>
</tbody>
</table>

Total events: 19 (coil), 30 (clip)

Test for heterogeneity chi-square=1.10 df=2 p=0.58 I²=0.0%

Test for overall effect z=1.56 p=0.1
### Analysis 03.02. Comparison 03 Recurrent hemorrhage, Outcome 02 rebleed post-procedure up to 1 year

**Review:** Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid hemorrhage

**Comparison:** 03 Recurrent hemorrhage

**Outcome:** 02 rebleed post-procedure up to 1 year

<table>
<thead>
<tr>
<th>Study</th>
<th>coil n/N</th>
<th>clip n/N</th>
<th>Relative Risk (Fixed) 95% CI (%)</th>
<th>Weight (%)</th>
<th>Relative Risk (Fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brilstra 2000b</td>
<td>0/10</td>
<td>3/10</td>
<td>23.3</td>
<td>0.14</td>
<td>0.14 [0.01, 2.45]</td>
</tr>
<tr>
<td>ISAT</td>
<td>28/1073</td>
<td>11/1070</td>
<td>73.5</td>
<td>2.54</td>
<td>2.54 [1.27, 5.07]</td>
</tr>
<tr>
<td>Koivisto 2000</td>
<td>1/52</td>
<td>0/57</td>
<td>3.2</td>
<td>3.28</td>
<td>3.28 [0.14, 78.86]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1135</td>
<td>1137</td>
<td>100.0</td>
<td>2.00</td>
<td>2.00 [1.08, 3.70]</td>
</tr>
</tbody>
</table>

Total events: 29 (coil), 14 (clip)
Test for heterogeneity chi-square=3.86 df=2 p=0.15 I²=48.1%
Test for overall effect z=2.22 p=0.03

### Analysis 03.03. Comparison 03 Recurrent hemorrhage, Outcome 03 rebleed post-procedure up to 3 months

**Review:** Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid hemorrhage

**Comparison:** 03 Recurrent hemorrhage

**Outcome:** 03 rebleed post-procedure up to 3 months

<table>
<thead>
<tr>
<th>Study</th>
<th>coil n/N</th>
<th>clip n/N</th>
<th>Relative Risk (Fixed) 95% CI (%)</th>
<th>Weight (%)</th>
<th>Relative Risk (Fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brilstra 2000b</td>
<td>0/10</td>
<td>0/10</td>
<td>0.0</td>
<td>Not estimable</td>
<td>Not estimable</td>
</tr>
<tr>
<td>ISAT</td>
<td>8/1073</td>
<td>3/1070</td>
<td>100.0</td>
<td>2.66</td>
<td>2.66 [0.71, 10.00]</td>
</tr>
<tr>
<td>Koivisto 2000</td>
<td>0/52</td>
<td>0/57</td>
<td>0.0</td>
<td>Not estimable</td>
<td>Not estimable</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1135</td>
<td>1137</td>
<td>100.0</td>
<td>2.00</td>
<td>2.00 [1.08, 3.70]</td>
</tr>
</tbody>
</table>

Total events: 8 (coil), 3 (clip)
Test for heterogeneity: not applicable
Test for overall effect z=1.45 p=0.1
## Analysis 04.01. Comparison 04 Case fatality,Outcome 01 death from any cause 2 to 3 months

### Review: Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage

### Comparison: 04 Case fatality

### Outcome: 01 death from any cause 2 to 3 months

<table>
<thead>
<tr>
<th>Study</th>
<th>coil n/N</th>
<th>clip n/N</th>
<th>Relative Risk (Fixed) 95% CI</th>
<th>Weight (%)</th>
<th>Relative Risk (Fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brilstra 2000b</td>
<td>2/10</td>
<td>2/10</td>
<td>2.2 [0.17, 5.77]</td>
<td>1.00</td>
<td>2.2 [0.17, 5.77]</td>
</tr>
<tr>
<td>ISAT</td>
<td>75/1065</td>
<td>84/1063</td>
<td>91.6 [0.66, 1.20]</td>
<td>0.89</td>
<td>91.6 [0.66, 1.20]</td>
</tr>
<tr>
<td>Koivisto 2000</td>
<td>4/52</td>
<td>6/57</td>
<td>6.2 [0.22, 2.45]</td>
<td>0.73</td>
<td>6.2 [0.22, 2.45]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1127</td>
<td>1130</td>
<td></td>
<td>100.0</td>
<td>0.88 [0.66, 1.18]</td>
</tr>
</tbody>
</table>

Total events: 81 (coil), 92 (clip)

Test for heterogeneity: chi-square=0.12 df=2 p=0.94 I²=0.0%

Test for overall effect: z=0.85 p=0.4

---

## Analysis 04.02. Comparison 04 Case fatality, Outcome 02 death from any cause between randomisation and 1 year after SAH

### Review: Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage

### Comparison: 04 Case fatality

### Outcome: 02 death from any cause between randomisation and 1 year after SAH

<table>
<thead>
<tr>
<th>Study</th>
<th>coil n/N</th>
<th>clip n/N</th>
<th>Relative Risk (Fixed) 95% CI</th>
<th>Weight (%)</th>
<th>Relative Risk (Fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brilstra 2000b</td>
<td>2/8</td>
<td>2/8</td>
<td>1.7 [0.18, 5.46]</td>
<td>1.00</td>
<td>1.7 [0.18, 5.46]</td>
</tr>
<tr>
<td>ISAT</td>
<td>85/1063</td>
<td>105/1055</td>
<td>90.9 [0.61, 1.06]</td>
<td>0.80</td>
<td>90.9 [0.61, 1.06]</td>
</tr>
<tr>
<td>Koivisto 2000</td>
<td>7/52</td>
<td>9/57</td>
<td>7.4 [0.34, 2.13]</td>
<td>0.85</td>
<td>7.4 [0.34, 2.13]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1123</td>
<td>1120</td>
<td></td>
<td>100.0</td>
<td>0.81 [0.63, 1.05]</td>
</tr>
</tbody>
</table>

Total events: 94 (coil), 116 (clip)

Test for heterogeneity: chi-square=0.07 df=2 p=0.96 I²=0.0%

Test for overall effect: z=1.59 p=0.1
## Analysis 05.01. Comparison 05 Complications from intervention, Outcome 01 complications from intervention

**Review:** Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage  
**Comparison:** 05 Complications from intervention  
**Outcome:** 01 complications from intervention

<table>
<thead>
<tr>
<th>Study</th>
<th>coil</th>
<th>clip</th>
<th>Relative Risk (Fixed)</th>
<th>Weight</th>
<th>Relative Risk (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>(%)</td>
<td>95% CI</td>
</tr>
<tr>
<td>Brilstra 2000b</td>
<td>3/10</td>
<td>4/10</td>
<td></td>
<td>51.2</td>
<td>0.75 [0.22, 2.52]</td>
</tr>
<tr>
<td>Koivisto 2000</td>
<td>5/52</td>
<td>4/57</td>
<td></td>
<td>48.8</td>
<td>1.37 [0.39, 4.83]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>62</strong></td>
<td><strong>67</strong></td>
<td></td>
<td><strong>100.0</strong></td>
<td><strong>1.05 [0.44, 2.53]</strong></td>
</tr>
</tbody>
</table>

Total events: 8 (coil), 8 (clip)  
Test for heterogeneity chi-square=0.47 df=1 p=0.49 I²=0.0%  
Test for overall effect z=0.12 p=0.9

---

## Analysis 06.01. Comparison 06 Degree of obliteration, Outcome 01 non-complete obliteration after 1 year

**Review:** Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage  
**Comparison:** 06 Degree of obliteration  
**Outcome:** 01 non-complete obliteration after 1 year

<table>
<thead>
<tr>
<th>Study</th>
<th>coil</th>
<th>clip</th>
<th>Relative Risk (Fixed)</th>
<th>Weight</th>
<th>Relative Risk (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>95% CI</td>
<td>(%)</td>
<td>95% CI</td>
</tr>
<tr>
<td>ISAT</td>
<td>242/701</td>
<td>47/228</td>
<td></td>
<td>90.3</td>
<td>1.67 [1.27, 2.20]</td>
</tr>
<tr>
<td>Koivisto 2000</td>
<td>12/52</td>
<td>8/57</td>
<td></td>
<td>9.7</td>
<td>1.64 [0.73, 3.70]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>753</strong></td>
<td><strong>285</strong></td>
<td></td>
<td><strong>100.0</strong></td>
<td><strong>1.67 [1.29, 2.17]</strong></td>
</tr>
</tbody>
</table>

Total events: 254 (coil), 55 (clip)  
Test for heterogeneity chi-square=0.00 df=1 p=0.97 I²=0.0%  
Test for overall effect z=3.87 p=0.0001
### Analysis 06.02. Comparison 06 Degree of obliteration, Outcome 02 less than 90% occlusion after 1 year

Review: Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage

Comparison: 06 Degree of obliteration

Outcome: 02 less than 90% occlusion after 1 year

<table>
<thead>
<tr>
<th>Study</th>
<th>coil n/N</th>
<th>clip n/N</th>
<th>Relative Risk (Fixed)</th>
<th>Weight (%)</th>
<th>Relative Risk (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISAT</td>
<td>63/701</td>
<td>12/228</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Koivisto 2000</td>
<td>2/52</td>
<td>1/57</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>753</td>
<td>285</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 65 (coil), 13 (clip)
Test for heterogeneity chi-square = 0.04 df = 1 p = 0.84 I² = 0.0%
Test for overall effect z = 1.85 p = 0.06

### Analysis 07.01. Comparison 07 Subgroup analysis: aneurysm location, Outcome 01 12 month poor outcome posterior and anterior circulation

Review: Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage

Comparison: 07 Subgroup analysis: aneurysm location

Outcome: 01 12 month poor outcome posterior and anterior circulation

<table>
<thead>
<tr>
<th>Study</th>
<th>coil n/N</th>
<th>clip n/N</th>
<th>Relative Risk (Fixed)</th>
<th>Weight (%)</th>
<th>Relative Risk (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISAT 12 month poor outcome posterior circulation</td>
<td>4/24</td>
<td>15/34</td>
<td></td>
<td>3.7</td>
<td>0.38 [ 0.14, 1.00 ]</td>
</tr>
<tr>
<td>Koivisto 2000</td>
<td>2/6</td>
<td>3/5</td>
<td></td>
<td>1.0</td>
<td>0.56 [ 0.15, 2.12 ]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>30</td>
<td>39</td>
<td></td>
<td>4.6</td>
<td>0.41 [ 0.19, 0.92 ]</td>
</tr>
</tbody>
</table>

Total events: 6 (coil), 18 (clip)
Test for heterogeneity chi-square = 0.22 df = 1 p = 0.64 I² = 0.0%
Test for overall effect z = 2.15 p = 0.03

<table>
<thead>
<tr>
<th>Study</th>
<th>coil n/N</th>
<th>clip n/N</th>
<th>Relative Risk (Fixed)</th>
<th>Weight (%)</th>
<th>Relative Risk (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISAT 12 month poor outcome anterior circulation</td>
<td>245/1038</td>
<td>311/1021</td>
<td></td>
<td>92.3</td>
<td>0.77 [ 0.67, 0.89 ]</td>
</tr>
<tr>
<td>Koivisto 2000</td>
<td>9/46</td>
<td>11/52</td>
<td></td>
<td>3.0</td>
<td>0.92 [ 0.42, 2.03 ]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>1084</td>
<td>1073</td>
<td></td>
<td>95.4</td>
<td>0.78 [ 0.68, 0.90 ]</td>
</tr>
</tbody>
</table>

Total events: 254 (coil), 322 (clip)
Test for heterogeneity chi-square = 0.19 df = 1 p = 0.66 I² = 0.0%
Test for overall effect z = 3.46 p = 0.0005

Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage (Review)  
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