Timing of aneurysm surgery in subarachnoid hemorrhage: a systematic review of the literature

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Authors' objectives
To compare early, intermediate and late aneurysm surgery after subarachnoid haemorrhage (SAH).

Searching
MEDLINE was searched from 1974 and eleven neurological and neurosurgical journals were manually searched from January to December 1998. The reference lists of all relevant publications were reviewed until no new studies were identified.

Study selection
Study designs of evaluations included in the review
Studies involving a consecutive case series of patients were included. One randomised controlled trial (RCT) and observational studies were included.

Specific interventions included in the review
Operations performed with the use of an intra-operative microscope were eligible. The timing of surgery was defined a priori as early (within 3 days of onset of SAH), intermediate (4 to 7 days after onset), or late (more than 7 days after onset).

Participants included in the review
Patients who were admitted within 72 hours after the onset of SAH were eligible. Patients who were not considered surgical candidates at any time were excluded whenever possible. Neurological condition at admission was classified according to Hunt and Hess (see Other Publications of Related Interest no.1) as either good (H and H Grade I to III) or poor (H and H Grade IV to V) clinical condition. Patients with anterior and posterior circulation aneurysms were included.

Outcomes assessed in the review
Studies of consecutive series of patients that reported outcomes categorised according to the timing of surgery and clinical condition at admission, and reported management results instead of surgical results, were eligible. Studies that reported outcomes after early surgery in patients in good pre-operative neurological condition (H and H Grades I to III) without mention of the clinical condition, were also included. The primary outcomes in the review were the proportion of patients who died or had poor outcomes (defined as death or dependency) at the end of the follow-up period. Dependent was defined as Glasgow Outcome Scale scores of 3 and 2 (see Other Publications of Related Interest no.2). Outcomes reported as 'fair', 'moderate disability' or 'partly dependent' were considered independent.

How were decisions on the relevance of primary studies made?
Two authors assessed the eligibility of the studies.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Two authors independently extracted the following data: year of publication; study period; study design (retrospective or prospective); the number of patients; characteristics of the patients; location of aneurysm; use of nimodipine; planning of time of surgery; duration of loss of consciousness at onset; amount of cisternal blood; neurological
condition at admission; and classification of outcome. Any disagreements in the data extraction were resolved by discussion and consensus reached.

Methods of synthesis
How were the studies combined?
The overall case fatality and poor outcome rates were calculated for early, intermediate and late surgery, and for patients in good and poor condition on admission. The risk ratios (RR) and 95% confidence intervals (CIs) were calculated for early and intermediate surgery, using patients planned for late surgery as the reference category.

How were differences between studies investigated?
The RRs were adjusted for year of publication, mean age, percentage of men, study design, aneurysm location and nimodipine use. The analyses were repeated after excluding the data from the RCT.

Results of the review
One RCT (211 patients) and 10 observational studies (2 prospective and 8 retrospective studies with a combined total of 1,814 patients) were included. There were 2,025 patients in total.

The definitions of timing of surgery used in the individual studies varied. The gender and age distribution were reported in only 3 studies. Only one study mentioned the use of nimodipine, whereas the duration of loss of consciousness and the amount of cisternal blood loss were never mentioned. The early surgery group contained 963 patients, of whom 740 (77%) were in good clinical condition at admission. The intermediate surgery group contained 152 patients, of whom 141 (93%) were in good clinical condition. The late surgery group contained 910 patients, of whom 693 patients (76%) were in good clinical condition.

Data from all 11 studies.
For patients in good clinical condition on admission, the outcomes were statistically improved after early or intermediate surgery than after late surgery. The RR of a poor outcome was 0.41 (95% CI: 0.34, 0.51) for planned early versus late surgery, and 0.47 (95% CI: 0.32, 0.69) for planned intermediate versus late surgery; the RR of death was 0.40 (95% CI: 0.32, 0.51) and 0.26 (95% CI: 0.14, 0.47), respectively. For patients in poor clinical condition on admission, there was no statistically-significant difference in outcomes between early or intermediate surgery versus late surgery. The RR of a poor outcome was 0.84 (95% CI: 0.67, 1.05) for planned early versus late surgery, and 0.54 (95% CI: 0.24, 1.22) for planned intermediate versus late surgery; the RR of death was 0.81 (95% CI: 0.63, 1.05) and 0.46 (95% CI: 0.17, 1.23), respectively.

Data from the RCT (211 patients).
There was a non statistically-significant trend towards a better outcome for patients in the early surgery group than in the late surgery group, but no significant difference in mortality between early and late operations. The RR of a poor outcome was 0.42 (95% CI: 0.17, 1.04) for planned early versus late surgery, and 1.07 (95% CI: 0.56, 2.05) for intermediate versus late surgery.

The results were similar after adjusting the RR for year of publication, study design and aneurysm location, and after excluding the RCT (no data provided).

Authors' conclusions
This meta-analysis suggests that both early and intermediate surgical treatment improve outcome after aneurysmal SAH, particularly for patients in good clinical condition on admission. However, this impression is derived only from indirect comparisons between different cohorts of patients. Sound evidence on the best timing of surgery is lacking. Observational studies with better methods are needed and, ideally, a new RCT.

CRD commentary
The aims were stated and the inclusion criteria were defined in terms of the participants, intervention and outcome. Eligible studies were not restricted by study design. The search was limited to one database supplemented by handsearches of several relevant journals published in 1998. The methods used to select the studies were described, but no details were provided of the keywords used and it was not reported whether any language restrictions were applied. Relevant data were extracted and tabulated, and the methods used to extract the data were described. The data were apparently pooled across the studies without any assessment of between-study heterogeneity in the outcomes. However, the influence of various factors (including study design) on the results was explored. As the authors correctly state, results from the indirect comparisons reported in the review should be interpreted with caution.

**Implications of the review for practice and research**

**Practice:** The authors state that there is no sound evidence favouring early or late surgical treatment after aneurysmal rupture.

**Research:** The authors state that observational studies with better methods and, ideally, a new RCT are needed. They further state that future observational studies should describe patients admitted within 72 hours after onset of SAH and operated on at standard intervals; that reports must contain data on neurological condition at admission, other prognostic factors and overall management results; and that the outcomes must be related to neurological conditions at admission, the timing of surgery, the duration of loss of consciousness at onset, and the type of SAH confirmed by computed tomography.

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