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Review

Timing of surgery for aneurysmal subarachnoid hemorrhage: A systematic review and meta-analysis

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ABSTRACT

Introduction: The timing of surgery for aneurysmal subarachnoid hemorrhage influences the outcome, but the optimal timing remains controversial. We conducted a systematic review to clarify whether early surgery was better than late surgery for improving outcome.

Materials and methods: We systematically searched several databases to screen eligible studies. After synthesizing data, an overall effect was shown using a risk ratio (RR) and 95% confidence interval (CI). Subgroup analyses were stratified by multiple variables to control the confounding factors. Sensitivity analyses were applied to check the robustness of the results. Publication bias was measured with Egger's and Begg's tests.

Results: A total of 14 studies were included in the analysis. Compared with late surgery, early surgery significantly decreased the incidence of poor outcome, regardless of whether patients were in good condition (RR, 0.65 [95%CI, 0.50 0.84]; $p = 0.001$) or in poor condition on admission (RR, 0.71 [95%CI, 0.61 0.83]; $p < 0.0001$). Moreover, when patients were in good condition on admission, early surgery also effectively reduced the death rate (RR, 0.61 [95%CI, 0.46 0.82]; $p = 0.001$). Additionally, early surgery reduced the death rate compared with late surgery in patients older than 50 years (RR, 0.49 [95%CI, 0.27 0.89]; $p < 0.002$).

Conclusions: Early surgery was superior to late surgery in reducing a poor outcome and death rate when patients were in good condition on admission, and decreased the incidence of poor outcome when patients were in poor condition on admission. Age was a potential confounding factor, influencing the effect of early surgery. Further study is required on this issue.

1. Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) is a devastating cerebrovascular disease, not only due to the severe effect of initial hemorrhage but also owing to the complicated treatment schemes. Surgical and endovascular treatments have become the mainstay approaches for occluding the aneurysm. Although detachable coil embolization is widely applied, many patients still undergo open craniotomy because not all ruptured aneurysms are amenable to endovascular treatment. The timing of surgical treatment for a ruptured aneurysm is under debate and has experienced a shift from favoring delayed treatment in the 1970s to preferring early treatment in recent years. A nationwide study found that early surgery resulted in unfavorable outcomes [1]. In 1990, the International Cooperative Study demonstrated that early surgery was neither more hazardous nor more beneficial than late surgery. Later, a retrospective study showed that early surgery could benefit patients in good status on admission [2]. Reviewing relevant publications from 1974 to 1998, De Gans et al. found early and intermediate surgical treatment improved outcomes compared with delayed surgery, although the result was derived from an indirect comparison [3].

It was reported that the high mortality and morbidity in the early surgery group was attributed to brain swelling and patients' poor tolerance to the surgery. As microsurgery has developed and neurocritical care has helped patients better tolerate operations, it was unclear whether advanced microsurgery and basic treatment could offset the side effects of early surgery and achieve better outcomes than late surgery. We conducted a systematic review to elucidate whether or not early surgery improves the overall outcomes of patients with aSAH.

2. Materials and methods

2.1. Search strategy

We conducted a comprehensive search through PubMed, Ovid and Web of Science from their inceptions until August 2017. Relevant

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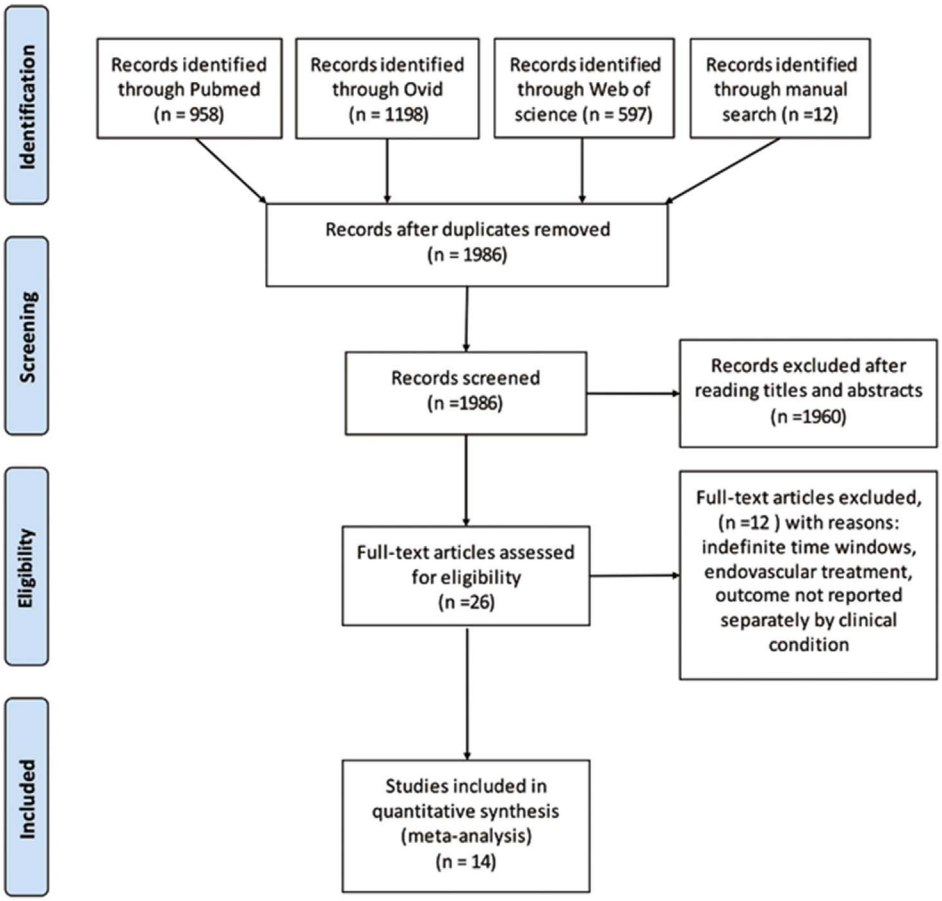

Fig. 1. Flow chart of literature search.

publications in English were screened. In the search process, medical subject headings and keywords were used in combination as follows: "subarachnoid hemorrhage," "subarachnoid hemorrhage," "intracranial aneurysm," "craniotomy," "surgical," "operative," "microsurgical," "time factors," "early," "delay," "timing," "24 h," "48 h" and "72 h"The reference lists of the extracted publications were manually searched. We also attempted to contact the authors of primary studies to obtain further data. This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [4].

2.2. Including criteria

We included studies meeting the following criteria: (1) research on patients with the diagnosis of ruptured intracranial aneurysms; (2) microsurgery as the main treatment for ruptured aneurysms; (3) patients who were assigned to different therapeutic time windows; (4) clinical conditions were recorded on admission or before surgery; (5) overall management outcomes described rather than only the surgical outcomes; (6) outcomes were reported separately by different clinical conditions and different therapeutic time windows. Studies were excluded for reasons as follows: (1) therapeutic time windows were described with items of early and late, rather than exact measurement units of hours or days; (2) reported both surgical and endovascular treatment, from which we could not extract surgical treatment separately.

Two researchers independently screened eligible publications, and differences were resolved by discussion and consensus. When different studies contained overlapping participants partially or totally, we only chose the study with a larger sample size and more detailed information.

2.3. Definitions of outcomes

Good clinical condition on admission or before surgery was defined as I-III class in Hunt and Hess classification (HH), 1–3 score in the World Federation of Neurological Surgeons (WFNS) scale, 13–15 score in the Glasgow Coma Scale (GCS) and the corresponding clinical manifestations described in the studies. The poor clinical condition was opposite the good clinical condition. Early surgery was defined as carrying out the operation within 3 days of aSAH onset. Late surgery was performed 7–10 days after the ictus. Intermediate surgery between these two phases has been proven to lead to an unfavorable outcome in previous reports, as the intermediate time phase corresponds to the peak period of cerebral vasospasm [5–8]. The definition of poor outcome was a 1–3 score in the Glasgow Outcome Scale (GOS), 3–6 in the modified Rankin Scale (mRS) and their corresponding clinical manifestations. To take the greatest advantage of the eligible data, characteristic in more than 95% of patients represented the characteristic of the whole population (i.e., if 95% of participants were in good clinical condition, we considered the whole population to be in good clinical condition).

2.4. Data extraction

Data extraction forms were used to collect pertinent information, including the names of authors, years of publication, study types, duration of studies, female ratio, ratio of anterior circulation aneurysm, clinical condition measurement, outcome measurement, numbers of events of interest and follow-up time.