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# Endovascular therapy for vasospasm secondary to subarachnoid hemorrhage: A meta-analysis and systematic review

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ABSTRACT

Endovascular therapy has been used as an alternative treatment for vasospasm following subarachnoid hemorrhage. The effectiveness and safety of endovascular therapy are still controversial. We performed a systematic review and meta-analysis to identify any advantage of endovascular therapy over traditional medical treatment. We systematically reviewed related English publications by searching PubMed, Ovid, Cochrane library, and Web of Science up to May 2017.The risk ratios (RR) and 95% confidence intervals (CI) were synthesized with fixed effect model. Subgroup analyses and sensitivity analyses were conducted to check the robustness the result. Publication bias was measured with funnel plot. Eight cohort studies were included, receiving a mean score of 7 on the Newcastle-Ottawa Scale. The overall effect (RR 1.01, [95% CI 0.80–1.26]) found no significant difference in the outcome between the endovascular treatment and control groups but with heterogeneity ($Chi^2 = 18.07$, $p = 0.01$, $I^2 = 61\%$). Subgroup analyses stratified by country, year of publication, treatment modality, follow-up time, and sensitivity analysis by excluding the most biased study yielded the same result (RR 1.19, [95% CI 0.94–1.52]), with rare heterogeneity ($Chi^2 = 4.21$, $p = 0.65$, $I^2 = 0$). Funnel plot was visually symmetric in sensitivity analysis. Despite good performance in reversing vasospasm in previous studies, endovascular therapy did not show superiority to traditional medical treatment in improving patient outcomes. Further randomized controlled studies are needed to elucidate this issue.

## 1. Introduction

Cerebral vasospasm secondary to subarachnoid hemorrhage (SAH) was mainly responsible for the mortality and morbidity in patients surviving initial hemorrhage. Vasospasm was regarded as an independent predictor of poor outcome after SAH [1], making it reasonable that preventing or reversing cerebral vasospasm could result in a better outcome. Prophylactic balloon angioplasty was less studied since a multicenter, randomized clinical trial found no clinical outcome improvement in SAH patients after prophylactic balloon angioplasty [2]. The medical treatment modality consisted of triple-H therapy (hypervolemia, hypertension, and hemodilution) and intravenous nimodipine. For refractory vasospasm to traditional medical treatment, endovascular therapy was commonly used as salvage management. Moreover, with wider use, endovascular therapy gradually became an alternative treatment for vasospasm, challenging traditional medical treatment. Kimball et al. summarized articles referring to endovascular therapy and proposed that it may be indicated in the event of failed medical management or concern for medical complications [3]. Recently, Patel et al. reported that noncompliant balloon angioplasty reversed angiographic vasospasm in 97% of cases without procedural morbidity or mortality [4], making it an effective and safe measure. Many studies[5–9] had compared the effect of endovascular therapy with traditional medical treatment on the outcomes of patients with cerebral vasospasm but achieved inconsistent results.

Endovascular therapy, composed of transluminal balloon angioplasty (TBA) and intra-arterial vasodilator (IAV), was implemented alone or in combination to treat vasospasm following SAH. IAV, also known as pharmacologic angioplasty, was used to dilate distal arteries, while mechanical balloon angioplasty served to expand proximal vessels. However, the superiority of endovascular therapy over conventional medical therapy remains controversial, which impeded its use in the guideline (Class 2b, Level B evidence) [10]. Therefore, we conducted a systematic review to identify whether endovascular therapy held an advantage over traditional treatment in improving the outcomes of patients with vasospasm following SAH.

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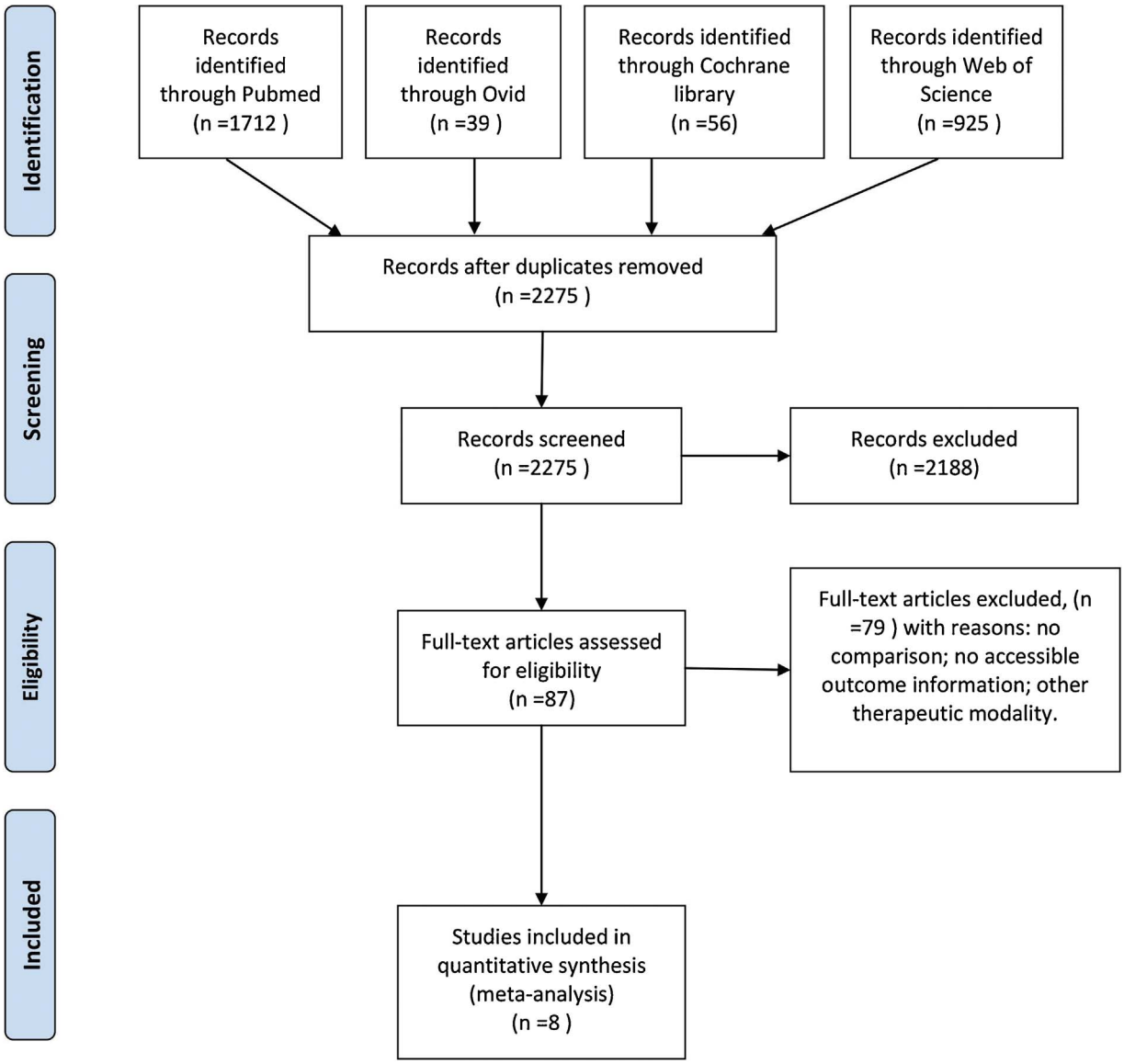


**Fig. 1.** Flow diagram of literature search.

## 2. Material and methods

### 2.1. Search strategy

We attempted to conduct this review based on the reporting of meta-analysis of observational studies in epidemiology [11]. Through searching PubMed, Ovid, Cochrane Library, and Web of Science from their starting dates to May 2017, we systematically reviewed related English publications. MeSH and keywords were used in combination: "endovascular intervention," "endovascular therapy," "angioplasty," "intra arterial," "subarachnoid hemorrhage," and "vasospasm." We also manually screened reference lists of included studies and other reviews.

### 2.2. Study selection

We included studies meeting the following criteria: (1) described patients with vasospasm following SAH; vasospasm can be verified by angiography, clinical manifestation, transcranial Doppler; (2) endovascular therapy was the main treatment, including TBA, IAV, or a combination of both; (3) compared with the control group, which received no endovascular therapy; (4) had definite recorded endpoint in both groups. Studies were excluded if they (1) conducted research on prophylactic endovascular management and (2) considered vasospasm secondary to other reasons. If the same population in different studies totally or partially overlapped, we selected only the study with the largest sample number.

The main endpoint was poor outcome at the last follow-up, defined by a score of 1–3 on the Glasgow Outcome Scale. Secondary endpoints included blood velocity of treated vessel, recurrence of vasospasm, and delayed cerebral infarct. Two investigators (Z.Y. and X.H.) independently evaluated inclusion criteria for searched articles, and if divergence existed, they negotiated and consulted a third author (C.Y.) to achieve consensus.

### 2.3. Data extraction

From included articles, we used data-extracted forms to collect information about authors, years of publication, locations of trial, treatment modality, follow-up time, treatment complication, management and occurrences of endpoints in both groups, and sources of funding. Additionally, we tried to contact authors to obtain access to accurate information.