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REVIEW

Comparison between clipping and coiling on the incidence of cerebral vasospasm after aneurysmal subarachnoid hemorrhage: a systematic review and meta-analysis

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Abstract Cerebral vasospasm is one of the most important complications of aneurysmal subarachnoid hemorrhage. The effect of aneurysm occlusion technique on incidence of vasospasm is not exactly known. The objective was to analyze surgical clipping versus endovascular coiling on the incidence of cerebral vasospasm and its consequences. Using the MEDLINE PubMed (1966–present) database, all English-language manuscripts comparing patients treated by surgical clipping with patients treated by endovascular coiling, regarding vasospasm incidence after aneurysmal subarachnoid hemorrhage, were analyzed. Data extracted from eligible studies included the following outcome measures: incidence of total vasospasm, symptomatic vasospasm, ischemic infarct vasospasm-induced and delayed ischemic neurological deficit (DIND). A pooled estimate of the effect size was computed and the test of heterogeneity between studies was carried out using The Cochrane Collaboration's Review Manager software, RevMan 4.2. Nine manuscripts that fulfilled the eligibility criteria were included and analyzed. The studies differed substantially with respect to design and methodological quality. The overall results showed no significant difference between clipping and coiling regarding to outcome measures. According to the available data, there is no significant difference between the types of technique used for aneurysm occlusion (clipping or coiling) on the risk of cerebral vasospasm development and its consequences.

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Introduction

Subarachnoid hemorrhage (SAH) caused by intracranial aneurysm rupture is one of the most serious health-care problems [3]. Approximately 10,000 and 30,000 people per year suffer from SAH in Germany [55] and United States of America [21], respectively.

About half of the patients die due to the primary bleeding or to secondary complications and many survivors need rehabilitation [28, 57]. The main complications after a SAH event are rebleeding and cerebral vasospasm [22, 31, 38, 54]. The policy of early aneurysm occlusion has led to progressively lower rates of rebleeding [16, 30, 31, 38, 54]. However, despite the improvements in management of aneurysmal SAH, vasospasm remains an important cause of morbidity and mortality [2, 6, 11, 12, 29, 47, 61].

Although vasospasm incidence ranges from 40% to 70% of aneurismal SAH patients (angiographic vasospasm), it causes symptoms with delayed ischemic neurological deficits (symptomatic vasospasm) in only 17–40% of patients with aneurysmal SAH [1, 8, 9, 32]. Around 50% of patients with symptomatic vasospasm will develop ischemic infarct [42].

The multifactorial pathophysiology of vasospasm is extremely complex and a considerable number of experimental and clinical studies have been performed in order to predict and prevent its occurrence [21].

Since the classic study by Fisher et al. [14] in 1980, who investigated the relationship of the amount and distribution of subarachnoid blood detected by computerized tomography to the later development of cerebral vasospasm, a large

amount of blood has been considered the most common predictive factor for vasospasm after SAH [21, 24]. Others factors as younger age, poor clinical condition on admission, hyperglycemia and smoking habits also have been described as predictive of vasospasm occurrence [4, 21, 24, 37].

Consequently, the reasonable hypothesis that removing subarachnoid blood clots would reduce the vasospasm incidence has been tested in many clinical and experimental studies [20, 26, 49, 60].

Until recently, craniotomy and clipping has been the preferred method of treatment for intracranial aneurysm occlusion [27]. The wide opening and evacuation of blood clots from the Sylvian fissure and cisterns during this procedure are believed to reduce the incidence of vasospasm [63], with some authors believing that the effect is more evident with early clot removal [40, 45, 60].

Although there are studies where the results failed to prove the efficacy of clot removal [26], some authors showed evidence of its role in vasospasm reduction [45, 60, 63], while others suggest that its likely benefit could be overlapped by secondary cerebral lesion caused by brain retraction or a higher incidence of vasospasm triggered by vessel manipulation during surgery [25, 67].

Despite the lower occlusion rates when compared with the classic treatment by craniotomy and clipping, endovascular coiling has become an established alternative for aneurysm treatment with improved outcome in small aneurysms with small necks [46, 64]. However, clot removal is not feasible with endovascular techniques. Therefore, it is reasonable to suppose that the level of potential spasmogens in the CSF might be higher and vasospasm may develop at a higher incidence and severity compared to clipping where the clot removal is accomplished. On the other hand, abluminal vessel manipulation is absent during coiling, which may even lead to a lower incidence of vasospasm after endovascular aneurysm treatment.

Unfortunately, the only multicenter randomized clinical trial comparing neurosurgical clipping and endovascular coiling (ISAT), up to now, did not publish any results regarding to post-treatment vasospasm incidence [46].

Overall, studies comparing patients treated with craniotomy and clipping versus endovascular and coiling have shown conflicting results related to vasospasm incidence. Lower rates of vasospasm have been associated with craniotomy and clipping according to some authors [18]; others associate lower rates with endovascular coiling [66]; while the majority of studies failed to prove a real treatment-dependency concerning to vasospasm developing [8, 34].

The heterogeneity of studies with respect to definition of end points and methodology is the most important factor responsible by controversial results. While some authors have studied angiographic vasospasm and symptomatic vasospasm, others tried to analyze the ischemic infarct caused by vasospasm and its clinical consequences. Furthermore, the wide variety of methods used for vasospasm diagnosis is an aggravating factor in generation of conflicting data.

The main goal of this systematic review is to analyze the available data about the role of aneurysm occlusion technique in regard to the development of cerebral vasospasm and its clinical and radiological consequences.

Methods

Search strategy

The MEDLINE database was the information source used. The following keywords were queried individually or in association: *vasospasm, aneurysm, clipping, coiling, infarct or stroke and subarachnoid hemorrhage*. The included limits were: *English* for language category, *Humans* for study category and *added to MEDLINE in the last 10 years* for the period of publication. Date of latest search: March 2006.

Selection criteria

All clinical trial manuscripts about aneurysmal subarachnoid hemorrhage that included both patients treated by clipping or coiling were analyzed as well as their references. The inclusion criteria were papers whose objective included analysis of vasospasm, symptomatic vasospasm, ischemic infarct and/or delayed ischemic neurological deficit (DIND) due to vasospasm. If the results of work were published in more than one paper, we decided to include only the paper which analyzed the rates of ischemic infarct vasospasm-induced. Manuscripts that included unruptured aneurysms were excluded, since the objective was to analyze vasospasm and its consequences after aneurismal subarachnoid hemorrhage. In order to have an overall analysis, we excluded papers that analyzed specific vessel or vascular territory. Because of the difficulty in defining symptomatic vasospasm in comatose or sedated patients, we excluded studies that analyzed only patients with poor clinical conditions at admission.

Data collection and analysis

Manuscript selection and evaluation of study quality were performed by two authors that independently reviewed the articles for inclusion or exclusion. No disagreements were found. In order to analyze the level of evidence of the articles reviewed, we applied the system classification proposed by Cook et al. [5], which is summarized in Table 1.

Data extracted from eligible studies included the following outcome measures: total vasospasm (symptomatic or asymptomatic measured by angiography or transcranial Doppler-TCD), symptomatic vasospasm, ischemic infarct vasospasm-induced and delayed ischemic neurological deficit (DIND). The number of patients treated with clipping or coiling, as well as the number of each outcome of interest, was recorded. For each study, a relative risk (RR) and confidence interval (CI) were computed as the measure of effect size. A pooled estimate of the effect size was computed using a standard inverse-variance fixed-effect weighting method [50]. The test for heterogeneity between study results was accomplished with a standard chi-square test and *I*-squared statistic using the computer program Review Manager (RevMan), version 4.2 for Windows (The Cochrane Collaboration, 2003, The Nordic Cochrane Centre, Copenhagen).

Results

Nine manuscripts were included and carefully analyzed. Data about these papers are summarized in Table 2.

Description of studies

Concerning study design, four papers were retrospective [4, 23, 52, 66]; four were prospective [8, 15, 18, 34], and from these, one randomized [34]; and one paper was initially retrospective but became prospective during the study [24]. Level I manuscripts were not found. One paper, because of its prospective and randomized analysis, could be classified as level II. The others papers were classified as grade III (prospective but nonrandomized) and grade IV (retrospective).

Regarding aneurysm treatment modality, excepting the prospective and randomized study [33], the decision on how to occlude the aneurysm was based on individual patient analysis in all studies. Consequently, the number of patients who underwent craniotomy and clipping was higher than endovascular and coiling group in almost all papers. There is only one study where endovascular patients were the majority [4]. The number of patients included in each work ranged from 37 to 619.

In addition, it is important to note that in some studies, because of individual case decision, older patients [24, 66], patients clinically believed to have a poor prognosis [23, 24, 52, 66] and aneurysms located in the posterior circulation [23, 52, 66] tended to be treated with endovascular coiling instead craniotomy and clipping.

Among the reviewed articles, only some of them described no difference between their patients groups with respect to age, Fisher grades and clinical condition at admission [4, 8, 24, 34, 66], while others failed in match their clipped and coiled patients [15, 18, 23, 52].

In order to minimize bias, some authors excluded patients with a poor clinical condition at admission (WFNS grades IV and V) [8]. Others included patients Hunt Hess IV and V and recognize that their results were likely influenced by their inclusion due to the difficulty in performing accurate diagnosis of symptomatic vasospasm in such patients [4]. On the other hand, some authors preferred not to exclude but analyze separately results from good and poor grades patients [24, 52].

In three papers, the method used for vasospasm diagnosis was transcranial Doppler (TCD) [4, 15, 18]; angiography was used in one [8]; both TCD and angiography were used for vasospasm diagnosis method in four papers [23, 24, 52, 66] and in one study the method used was SPECT [34].

Among all nine manuscripts reviewed, only five described in their methods an intended clot removal in patients submitted to craniotomy and surgical clipping [8, 18, 24, 52, 66]. The management of SAH was described in eight of nine studies and was comparable for all patients within each paper, except the work conducted by Charpentier et al. [4], whose methods described that only most of their patients were admitted to the neurosurgical intensive care unit, but not all of them.

In one single paper the patients were treated within 48 h after SAH [66]. Three authors treated their patients within 72 h after SAH [4, 8, 18, 34]. Four works described that part of their patients were treated after 72 h [4, 15, 24, 52] and one paper did not describe the timing of clipping or coiling [23].

The follow-up period ranged from the day of discharge up to 12 months. The Glasgow Outcome Scale (GOS) was used for outcome analysis in seven studies [4, 8, 15, 18, 23, 34, 52], while Modified Rankin Score was used in one paper [24].

Table 1 Levels of evidence according to Cook et al. [5]

System classification	
LEVEL OF EVIDENCE	
Level I	Data from randomized trials with low false-positive and low false-negative errors
Level II	Data from randomized trials with high false-positive or high false-negative errors
Level III	Data from nonrandomized concurrent cohort studies
Level IV	Data from nonrandomized cohort studies using historical controls
Level V	Data from anecdotal case series
STRENGTH OF RECOMMENDATION	
Grade A	Supported by level I evidence
Grade B	Supported by level II evidence
Grade C	Supported by level III, IV or V evidence

Table 2 Summary data of the manuscripts that compare the effects of aneurysm occlusion technique (clipping or coiling) in vasospasm incidence

Author [reference] (year)	Study design (level of evidence)	Number of patients	Procedure ratio (clip/coil)	Diagnosis method	Intended clot removal	Procedure timing	SAH treatment	Vasospasm ratio clip vs coil (method)	Symptomatic vasospasm clip vs coil	Ischemic infarct clip vs coil (method)	Neurological deficit clip vs coil	Follow-up	Outcome	Outcome scale
Gruber et al. [18] (1998)	Prospective; nonrandomized (level III)	156	111/45	TCD	Yes	Within 72 h	Homogeneous	ND	ND	21.6% vs 37.7% (CT)	11.7%vs 15.5% (NS)	ND	No difference	GOS
Yalamanchili et al.[66] (1998)	Retrospective (level IV)	37	19/18	TCD and angiography	Yes	Within 48 h	Homogeneous	ND	74% vs 22%	ND	ND	ND	ND	ND
Charpentier et al. [4] (1999)	Retrospective (level IV)	244	99/145	TCD	ND	Within 72 h (only 81%)	Heterogeneous	ND	22.2% vs 17.2% (NS)	ND	ND	6 months	ND	GOS
Koivisto et al. [33] (2002)	Prospective; randomized (level II)	46	24/22	SPECT	ND	Within 72 h	Homogeneous	ND	No difference	No difference (MRI)	ND	3 and 12 months	No difference	GOS; neuro-psychological assessment [a]
Rabinstein et al. [52] (2003)	Retrospective (level IV)	415	339/76	TCD and angiography	Yes	146 patients after day 4	Homogeneous	ND	Higher in clip only in WFNS I–III	ND	Higher in clip only in WFNS I–III	6 months	No difference	GOS
Goddard et al. [15] (2004)	Prospective; nonrandomized (level III)	292	212/80	TCD	ND	22.7% after vasospasm onset	Homogeneous	No difference (TCD)	ND	ND	16.5% vs 13.8% (NS)	4–8 months	No difference	GOS
Dehdashti et al. [8] (2004)	Prospective; nonrandomized (level III)	98	72/26	Angiography	Yes	Within 72 h	Homogeneous	ND	25% vs 15% (NS) WFNS I–III or Fisher I–III (NS)	No difference (CT)	9% vs 7% (NS)	3 and 6 months	No difference	GOS
Hoh et al. [24] (2004)	Retrospective (272); prospective (243) (level III)	515	413/79 + (23 both)	TCD and angiography	Yes	Mean 3rd day	Homogeneous	No difference (TCD + angiography)	No difference	ND	ND	day of discharge	Better in clip (HH= I–III)	Modified Rankin Score
Hoh et al. [23] (2004)	Retrospective (level IV)	619	505/114	TCD and angiography	ND	ND	ND	ND	ND	15% vs 17% (NS) (CT)	ND	6 months	Better in clip	GOS

[a] Published by Koivisto et al. [34]

GOS Glasgow Outcome Scale, *HH* Hunt Hess classification, *ND* not described, *NS* not significant, *SAH* subarachnoid hemorrhage, *SPECT* single-photon emission tomography, *TCD* transcranial Doppler, *WFNS* World Federation of Neurosurgical Societies Classification

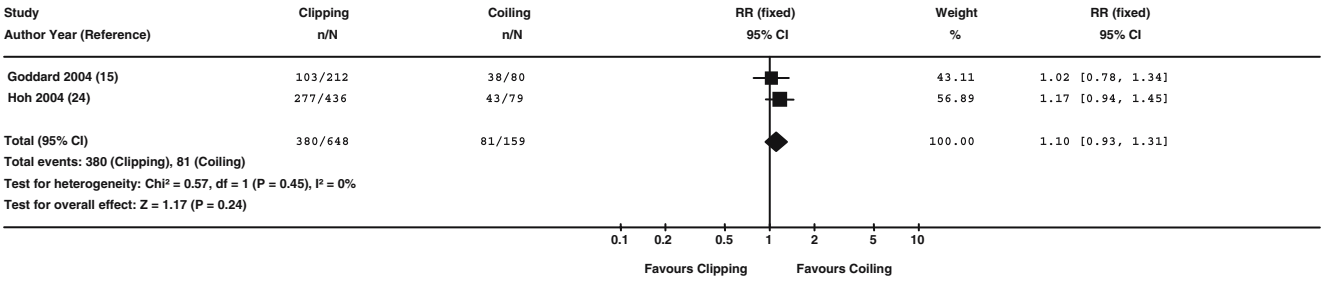

Fig. 1 Meta-analysis graph showing pooled estimate of total vasospasm (asymptomatic and symptomatic) after clipping or coiling technique for aneurysm occlusion. The relative risk (*RR*) for total vasospasm is measured in each study with 95% confidence interval (*95% CI*)

Analysis of vasospasm, symptomatic vasospasm, ischemic infarct and DIND

Overall vasospasm rates (symptomatic and asymptomatic) were analyzed in two studies [15, 24] whose results are illustrated in Fig. 1. Both studies presented no significant difference between clipping and coiling with respect to overall vasospasm (RR 1.10; 95% CI 0.93–1.31).

Symptomatic vasospasm rates were published in six papers [4, 8, 24, 34, 52, 66]. The definition of symptomatic vasospasm in agreement with each study included in this analysis is described in Table 3. Clipping compared with coiling tended to increase the RR of symptomatic vasospasm (RR 3.32; 95% CI 1.34–8.20) in the study published by Yalamanchili et al. [66]. However, after a pooled estimate, no statistically significant result was found (RR 1.21; 95% CI 0.99–1.48). These results are described in Fig. 2.

Four papers presented rates of infarcts caused by vasospasm [8, 18, 23, 34]. The results published by Gruber et al. [18] showed a lesser RR for ischemic infarct vasospasm-induced after surgical clipping (RR 0.57; 95% CI 0.34–0.96). All others studies presented no significant differences between clipping and coiling regarding to infarcts. Consequently, when a pooled estimate was accomplished, the overall result presented no significant differences (RR 0.81; 95% CI 0.59–1.10). Figure 3 demonstrates this analysis.

The analysis of DIND incidence was achieved in four studies [8, 15, 18, 52] and all of them presented no statistically significant difference between clipping and coiling (RR 1.05; 95% CI 0.74–1.49). The statistical analysis can be seen in the Fig. 4.

Discussion

Definition of vasospasm and diagnosis methods

The incidence of vasospasm after SAH varies to a great extent in comparative studies of clipping and coiling for ruptured aneurysm occlusion. This variability is, at least in

Table 3 Definition of symptomatic vasospasm according to each study where this outcome measure was analyzed

Study (Reference)	Definition of symptomatic vasospasm
Yalamanchili et al. [66]	Evidence of neurological decline included any features on the neurological examination consistent with diminished cerebral blood flow, either diffusely or in arterial territory distribution. This included any significant change in sensorium or level of consciousness. Headache alone was not considered an indicator of cerebral ischemia.
Charpentier et al. [4]	Combination of (1) the development of focal neurological signs or deterioration of the level of consciousness , or both, occurring between 3 and 14 days after SAH and (16) an increase in mean TCD velocities of >120 cm/s in the investigated territories. One-point Glasgow Coma Scale decrease was considered as a meaningful deterioration.
Koivisto et al. [33]	The most obvious reason for patient's deterioration. If the patient only gradual deterioration of conscious level or almost constant confusion, with possible confounding factors such as metabolic disorder or a disturbance in the electrolyte balance, the symptoms were classified as possible vasospasm. If the patient clearly developed a sudden neurological deficit or had no confounding factors or other explanation for insidious deterioration, the symptoms were classified as probable vasospasm.
Rabinstein et al. [52]	Documented arterial vasospasm that was consistent with new neurological deficits that presented between 4 and 14 days after the onset of SAH and could not be explained by other causes of neurological deterioration (rebleeding, acute or worsening hydrocephalus, electrolyte disturbances, hypoxia or seizures).
Dehdashti et al. [8]	Development of a nontreatment-related neurological deficit in a delayed fashion which could not be attributed to other causes of neurological deterioration (rebleeding, acute or worsening hydrocephalus, treatment complications, electrolyte disturbance, hypoxia or seizures). Headache alone was not considered an indicator of cerebral vasospasm.
Hoh et al. [24]	Clinical judgment using the following criteria: (1) new or worsening of neurological deficit occurring between days 4 and 14 after SAH, (2) no other identifiable cause for neurological worsening as demonstrated on computed tomographic scan (such as hydrocephalus or bleeding) or otherwise (such as seizure or metabolic disturbance), (3) vasospasm on cerebral angiography, TCD, computed tomographic angiography, or magnetic resonance angiography.

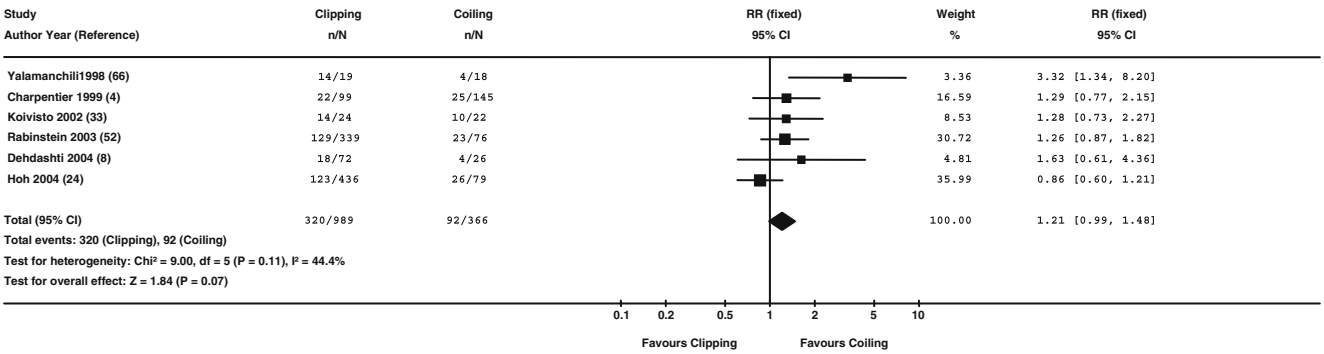

Fig. 2 Meta-analysis graph showing pooled estimate of symptomatic vasospasm after clipping or coiling technique for aneurysm occlusion. The RR for symptomatic vasospasm is measured in each study with 95% CI

part, due to the lack of a uniformly used definition of cerebral vasospasm. Some authors analyze the incidence of angiographic and symptomatic vasospasm, while others analyze ischemic infarcts supposedly caused by vasospasm and its neurological consequences.

The subject is further complicated by a wide range of methods available in order to diagnose vasospasm and ischemic disturbances vasospasm-induced. Although CT or MRI angiography can identify arterial narrowing, conventional angiography is the "gold standard" method for the definitive diagnosis of vasospasm [21]. Some methods use indirect changes suggestive of vasospasm, like an increase of blood flow velocity detected by TCD; while others use imaging techniques to diagnose tissue ischemia resulting from vasospasm, such as positron emission tomography, stable xenon-enhanced computed tomography, single-photon emission tomography and combined diffusion-weight with hemodynamically weighted MRI [21]. More recently, intracerebral microdialysis has been demonstrated as a useful and safe method for detection of brain ischemia in neurointensive care patients with SAH; however, it is time-consuming and there is no evidence that one method is more efficient and reliable than other existing method used for vasospasm detection [10, 51, 56].

Although the sensibility for vasospasm detection in anterior circulation ranges from 53% [7, 36] in the anterior communicating artery to 93% [7, 36] in the middle cerebral artery with specificity up to 100% [59], several studies have been unable to establish a direct correlation between TCD velocities and the onset of neurological deficit caused by ischemic infarct [15, 17, 44]. As well as TCD, SPECT provides information about the cerebral flow, which can be caused or not by vasospasm. SPECT may be normal at the same time that TCD velocities are elevated in individual vessels of patients that remain asymptomatic because of preserved autoregulation and contralateral flow [39]. On the other hand, SPECT may be abnormal in patients who underwent technically successful angioplasty of spastic vessels and normalization of TCD velocities after treatment [39].

Effects of craniotomy and clot removal

The amount of blood after SAH is the most important predictive factor of vasospasm [21]. Consequently, the intended clot removal during neurosurgical clipping is considered by several authors as being responsible for lower rates of vasospasm [40, 45, 60, 63].

Weir [65] studied chronic vasospasm on a primate model and concluded that it is related to the presence of adherent clots along cerebral arteries and, when severe, may lead to cerebral infarction. He stated that clot removal within 48 h following SAH reduces vasospasm intensity; other experimental studies found similar results [62, 68].

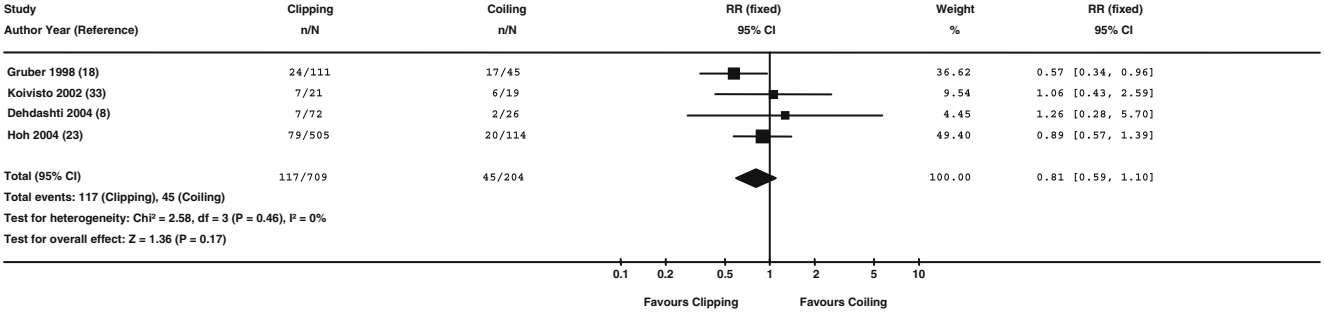

Fig. 3 Meta-analysis graph showing pooled estimate of ischemic infarct after clipping or coiling technique for aneurysm occlusion. The RR for ischemic infarct is measured in each study with 95% CI

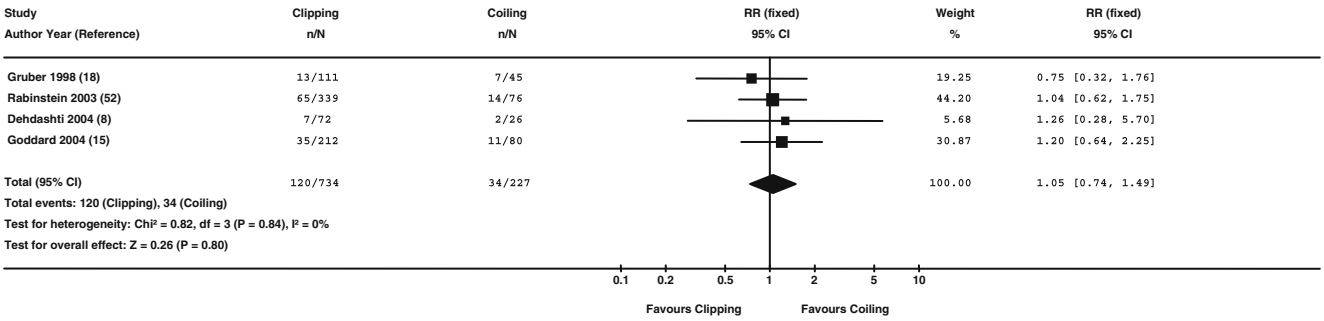

Fig. 4 Meta-analysis graph showing pooled estimate of delayed ischemic neurological deficit (DIND) after clipping or coiling technique for aneurysm occlusion. The RR for DIND is measured in each study with 95% CI

There is experimental evidence that unremoved intracerebral clots can produce focal brain injury by alteration of cerebral perfusion pressure, by increase of local tissue pressure with local microcirculation impairment and by release of spasmogens from the clot [43, 48, 58].

Taneda [60] concluded that early operation combined with radical removal of subarachnoid clots minimizes the overall mortality and morbidity in patients with ruptured intracranial aneurysms by preventing rebleeding and probably by avoiding vasospasm.

On the contrary, some authors suggested that craniotomy results in exacerbation of vasospasm. Contributing factors include the release of blood and its products into subarachnoid space, arachidonic acid and free radicals liberation, and the spastic response of brain arteries to surgical manipulation [13, 66]. In addition, dissection and disruption of brain parenchyma results in the release of lipid peroxides as arachidonic acid that leads to the synthesis of prostaglandins and free radicals [19, 41, 53]. The combination of cerebral manipulation and exposition to blood products results in prolonged and severe vasospasm [35].

Among the manuscripts analyzed, Gruber et al. [18] concluded that a higher infarct rate with endovascular treatment was consequence of unremoved subarachnoid and intracerebral clots, despite absence of significance when patients with Fisher IV and WFNS grade V were excluded from their analysis. On the other hand, Yalamanchili et al. [66] published a higher incidence of vasospasm after clipping instead of coiling and conclude that release of blood and its products associated with vessels manipulation provided by craniotomy, microsurgery and clipping were the likely responsible mechanisms.

Vasospasm, symptomatic vasospasm, ischemic infarct and DIND

The incidence of vasospasm after SAH is approximately 70%. However, signs and symptoms caused by vasospasm occur in up to 40% of these patients [1, 8, 9, 32]. Therefore, although the diagnosis of asymptomatic vasospasm is very important in order to prevent its consequences, the diagnosis of symptomatic vasospasm has a greater value. On the other hand, because of the improvements in neurosurgical intensive care and endovascular techniques, part of patients with symptomatic vasospasm is successfully treated [6]. Consequently, in our point of view, the most important outcome measures are ischemic infarct and delayed ischemic neurological deficit (DIND) vasospasm-induced.

Although some studies included in our analysis have shown higher incidence of vasospasm after clipping or coiling, the methods used in these studies are characterized by low evidence level (levels III and IV). Besides, the only level II evidence study failed to demonstrate any relationship between the type of treatment used for aneurysms occlusion and subsequent development of vasospasm [34].

Despite the possible benefit provided by clot removal during clipping occlusion, our overall results disclosed no statistically significant difference between patients whose aneurysm was occluded by surgical clipping or endovascular coiling with regard to incidence of vasospasm, symptomatic vasospasm, ischemic infarct and DIND.

Limitations of the study

We analyzed nine manuscripts with respect to the effects of treatment modality on vasospasm incidence and the comparison between their results is limited by differences in study design, methodology, definition and diagnosis of vasospasm, timing of treatment, intended clot removal, management of SAH and outcome measures. On the other hand, most of the studies included in our analysis represent the complete sample of aneurysmal SAH admitted at a single neurosurgical center and, therefore, their results provide valuable information.

Because only one manuscript included in our analysis is prospective and randomized, more clinical trials using this methodology must be performed in order to answer this question.

Conclusions

Cerebral vasospasm has a complex multifactorial pathophysiology and complete understanding of why some patients develop symptoms while others do not remains a problem to be solved.

The overall results provided by this meta-analysis disclosed no difference between the types of technique used for aneurysm occlusion, surgical clipping or endovascular coiling, regarding the risk of vasospasm development and its consequences.

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Comments

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The authors have done a state-of-the-art review of an issue of substantial interest recently; that is, whether there is a difference in the

incidence of cerebral vasospasm among patients undergoing neurosurgical clipping compared with those treated by endovascular coiling. They searched the English language literature and used the software available from the Cochrane group, which allows a very structured, comprehensive and rigorous review to be conducted. They concluded, based on review of nine manuscripts, that there is no difference between the treatments in the incidence of vasospasm, symptomatic vasospasm, delayed ischemic neurological deficits or infarction due to vasospasm.

Some of the limitations need to be addressed. The comparison is not based on randomization between clipping and coiling. When the patients are not randomized to clipping or coiling one cannot exclude differences in baseline characteristics that could affect the incidence of vasospasm. Indeed these were present. More posterior circulation aneurysms that may have a lower risk of vasospasm and more poor grade patients in whom vasospasm may be more difficult to detect, were treated by coiling. The diagnosis of large-artery vasospasm is in doubt also because of the methods used in most studies. The gold standard digital subtraction angiography was seldom used. Transcranial Doppler ultrasound is inaccurate and SPECT does not measure vasospasm, it measures cerebral blood flow.

In the end, it is the clinical outcome of the patient that matters. Considering the randomized trials of clipping compared with coiling, there was better outcome in coiled patients in the larger study, although the magnitude of the difference was remarkably small and the follow-up too short to rule out the possibility that long-term complications in the coiled group would negate the early beneficial effects [2, 3]. The studies include only the subset of aneurysms for which both treatments could be applied. Detailed analysis of delayed ischemia has not been presented. Therefore, for suitable aneurysms that can be well-coiled, whether or not delayed ischemia and vasospasm is different between the two treatments does not depend on vasospasm but on the experience of the individuals who do the two treatments at the center where the patient is. Endovascular treatment in experienced hands for small necked aneurysms is at least equal to, if not superior to, surgery. The interesting point is whether the difference between clipping and coiling is due to early or delayed complications of surgery. Vasospasm develops in relation to the volume, persistence and density of subarachnoid blood clot. It is this reviewer's hypothesis that clot clearance actually may be more rapid after coiling than after surgery and that ventricular drainage may be detrimental with regard to clot clearance.

As an aside, Bryce Weir called my attention to a paper published in Japan in 1978 by Takemae and co-workers [4]. This was probably one of the earliest observations of the relationship between initial subarachnoid clot volume after subarachnoid hemorrhage and the risk of vasospasm, preceding Dr. Fisher's widely cited publication by 2 years [1].

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This publication by Dr. de Oliveira and co-workers reviews the incidence of cerebral vasospasm after aneurysmal obliteration with clips or coils. The authors summarized nine articles and concluded that there were no significant differences in symptomatic and asymptomatic vasospasm, vasospasm-induced infarction, and delayed ischemic neurological deficit between clipping and coiling, although the incidence was inclined to be relatively high (RR 1.2; 95% CI 0.99–1.48) after clipping compared with coiling. Theoretically, removal of subarachnoid blood clots through craniotomy can reduce the vasospasm. The authors discussed that this discrepancy would be caused by surgical manipulation; the surgical manipulation may act as the trigger of vasospasm. We agree with this possibility, because a small number of patients who underwent clipping surgery for unruptured intracranial aneurysms developed vasospasm. Neurosurgeons must keep minimum and gentle surgical manipulation, so as not to induce vasospasm.