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Endovascular coiling versus surgical clipping for the treatment of unruptured cerebral aneurysms

Direct comparison of procedure-related complications

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Abstract

Background: Endovascular coiling and surgical clipping are routinely used to treat unruptured cerebral aneurysms (UCAs). However, the evidence to support the efficacy of these approaches is limited. We aimed to analyze the efficacy of endovascular coiling compared with surgical clipping in patients with UCAs.

Method: A systematic search of 4 databases was conducted to identify comparative articles involving endovascular coiling and surgical clipping in patients with UCAs. We conducted a meta-analysis using the random-effects model when $I^2 > 50\%$. Otherwise, a meta-analysis using the fixed-effects model was performed.

Results: Our results showed that endovascular coiling was associated with a shorter length of stay (WMD: −4.14, 95% CI: (−5.75, −2.531), $P < .001$) and a lower incidence of short-term complications compared with surgical clipping (OR: 0.518; 95% CI (0.433, 0.621); $P < .001$), which seems to be a result of ischemia complications (OR: 0.423; 95% CI (0.317, 0.564); $P < .001$). However, surgical clipping showed a higher rate of complete occlusion after surgery, in both short-term (OR: 0.179, 95% CI (0.064, 0.499), $P = .001$) and 1-year follow-ups (OR: 0.307, 95% CI (0.146, 0.646), $P = .002$), and a lower rate of short-term retreatment (OR: 0.307, 95% CI (0.146, 0.646), $P = .002$). Meanwhile, there was no significant difference in postoperative death, bleeding, and modified Rankin Scale (mRS) > 2 between the 2 groups.

Conclusions: The latest evidence illustrates that surgical clipping resulted in lower retreatment rates and was associated with a higher incidence of complete occlusion, while endovascular coiling was associated with shorter LOS and a lower rate of complications, especially ischemia.

Abbreviations: CIs = confidence intervals, IAs = intracranial aneurysms, LOS = length of stay, mRS = Modified Rankin Scale, ORs = odds ratios, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses, RCT = randomized controlled trial, RDs = rate differences, SAH = subarachnoid hemorrhage, UCAs = unruptured cerebral aneurysms, WMD = weighted mean difference.

Keywords: endovascular coiling, surgical clipping, unruptured cerebral aneurysms

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1. Introduction

Subarachnoid hemorrhage (SAH) accounts for approximately 5% of all stroke cases, and in addition to rapidly increasing morbidity rapidly, an increasing trend in the youth rate is obvious.[1] Based on clinical experience, the most common precipitating factor for SAH is ruptured cerebral aneurysms, with morbidity of 9 per 100 000 people.[2] Although a few researchers have reported a stroke rate of approximately 2% per year, which indicates a decline over the past 2 decades, the rate of SAH decrease was smaller than that of stroke.[2] Furthermore, the prevalence of unruptured cerebral aneurysms (UCAs) ranges from 1.7% to 3.1% in the aggregate population;[3] UCAs lead to rupture or death within 1 month for 50% of patients, and incapacitation appears in 40% of patients who survive more than 1 month.[4,5] Therefore, UCAs require timely attention, by using traditional craniotomy aneurysm clipping and interventional embolization, to prevent them from rupturing. Due to its microinvasive nature, the use of endovascular coiling is increasing at a rapid pace,[6,7] and several investigations have found that the clinical results of endovascular coiling are superior to those of clipping for treating UCAs.[8,9] Endovascular coiling avoids a craniotomy and a large incision, which shortens healing time and reduces the incidence of perioperative complications.[10–12] Zhang et al[13] deemed that the hospital stay following interventional therapy was much shorter than that for surgical clipping. However, the intensive promotion of emerging implantable devices, such as coils and stents, might lead to an excessive financial burden and procedure-related complications.[13] On the other hand, a large number of studies have demonstrated that surgical clipping is associated with better durability in aneurysmal obliteration, even though clipping is more invasive.[10,11,14] In this regard, we conducted a meta-analysis to compare the safety and efficiency between endovascular coiling and surgical clipping in patients with UCAs.

2. Materials and methods

Our review work was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[15]

2.1. Data sources and searches

The search for comparative articles involving endovascular coiling and surgical clipping in patients with UCAs was conducted by 2 authors (Q-LJ and X-KK) using electronic databases including Cochrane Library, Medline (1966–2019.7), PubMed (1966–2019.7), and EMBASE (1980–2019.7). The MeSH search terms were as follows: "unruptured aneurysms, endovascular coiling, surgical clipping." Meanwhile, we manually checked the reference lists of the retrieved articles to search for other potential qualifying trials until no more articles could be identified.

2.2. Inclusion and exclusion criteria

Identified studies from the literature search were then further evaluated for inclusion. Inclusion criteria were as follows: population: participants with UCAs; intervention: included endovascular coiling and surgical clipping for treating UCAs; comparison: results about the treatment-related complications are provided; outcome measures: 1 of 10 endpoints length of stay (LOS), postoperative bleeding, death, complications, ischemia, vasospasm, hydrocephalus, completed occlusion, modified Rankin Scale (mRS) > 2, and retreatment were accessed); and full-text studies officially published in English.

Studies were excluded if they evaluated the outcomes between endovascular coiling and surgical clipping without reporting our specified study outcomes in the 2 groups; they were study designs other than clinical studies, such as case reports/series (< 10 patients), reviews, letters to editor, and meta-analyses; they studied animals instead of humans; or the data was unbalanced between the patient populations.

2.3. Data extraction and endpoints

We assigned 2 reviewers (X-KK and Q-LJ) to independently complete this part. A third author joined the extraction process in cases of disagreement. Basic demographic information (age, sex, diagnosis, number of included cases, and outcomes) was extracted. The primary study endpoint measurements were those relevant to surgical safety (postoperative bleeding, death, and short-term complications especially for ischemia, vasospasm, and hydrocephalus). The secondary endpoint was a composite of complete occlusion and postoperative mRS > 2, which were associated with procedural efficiency. Other outcomes of interest were the composite of LOS and retreatment. The clinical outcomes that appeared in the hospital or within 30 days were defined as short-term outcomes.

2.4. Statistical analysis

Stata version 11.0 was applied for the statistical analyses. The heterogeneity was assessed with the help of the I^2 statistic. I^2 values lower than 50% were regarded as indicative of low heterogeneity, and a fixed-effects model was used. Otherwise, a random-effects model was applied. For dichotomous outcomes (postoperative bleeding, death, complications, ischemia, vasospasm, hydrocephalus, completed occlusion, mRS > 2, and retreatment), the odds ratios (ORs) or rate differences (RDs) with 95% confidence intervals (CIs) were used for analysis. Alternatively, the weighted mean difference (WMD) combined with the 95% CI was used for continuous outcomes (LOS).

3. Results

3.1. Search results

A total of 4253 studies were identified by searching the electronic databases; there were 2826 articles after removing duplicates, and 1311 articles were excluded according to our preplanned eligibility criteria by reviewing the title and full abstract. There were 83 studies excluded after scanning the full text. Finally, 25 articles were eligible for quantitative synthesis. Figure 1 describes more information about the searching process.

3.2. Quality assessment and study characteristics

The Newcastle-Ottawa Scale (NOS) was used to evaluate the quality of the included non-RCT (randomized controlled trial). One RCT was regarded as high quality with a Jadad score of 5. The quality scores for all articles are shown in Table 1. A total of 25 studies,[16–40] including 129,317 participants, were included in our meta-analysis. Of these 129,317 patients with UCAs, 72,010 were assigned to the endovascular coiling group, and 57,307 were assigned to the surgical clipping group; the sample size for each included study varied from 41 to 64,043. The studies were from the USA, Germany, Netherlands, Canada, China, Japan, Norway, Korea, France, and Switzerland. Table 2 describes the study characteristics in more detail.

3.3. Primary endpoints

A total of 15 articles reported data on the risk of postoperative death. The results show that the risk of death within 30 days was not significantly greater in the endovascular coiling group (OR: 1.411; 95% CI (0.875, 2.276); $P=.157$, Fig. 2), and no significant difference was found in the subgroup of patients who died in hospital (RD: −0.004; 95% CI: (−0.012, 0.004); $P=.378$). Similarly, 13 articles showed a differential risk of postoperative bleeding between endovascular coiling and surgical clipping groups, but the risk of periprocedural bleeding was not significantly different between the 2 groups, either in the short-term (RD: −0.002; 95% CI (−0.005, 0.001); $P=.133$,

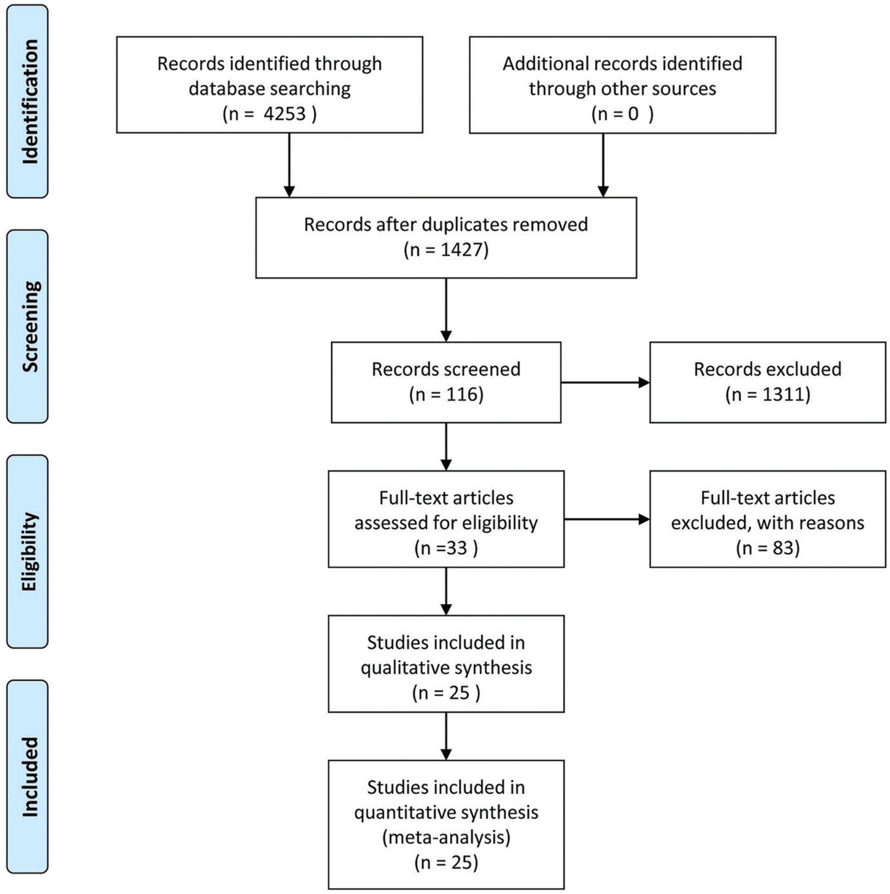

Figure 1. Flowchart of the study selection process.

Table 1

Quality assessment scores of the included studies.

Author, year	Design	Jadad scale			
		Randomization	Blinding	Cohort	Total scores
Darsaut et al, 2017	**Randomized controlled trial**	**2**	**2**	**1**	**5**
		Newcastle-Ottawa Scale			
		Selection	**Comparability**	**Exposure**	**Total scores**
Bekelis et al, 2016	Prospective cohort study	3	2	3	8
Brilstra et al, 2003	Prospective cohort study	3	2	2	7
Brinjikji et al, 2011	Retrospective cohort study	3	2	2	7
Dammann et al, 2014	Retrospective cohort study	3	2	3	8
Diaz et al, 2014	Retrospective cohort study	3	2	1	6
Duan et al, 2014	Retrospective cohort study	3	2	1	6
Erdem et al, 2011	Prospective cohort study	3	2	3	8
Frontera et al, 2012	Retrospective cohort study	3	2	3	8
Gerlach et al, 2007	Prospective cohort study	3	2	3	8
Huang et al, 2019	Retrospective cohort study	3	2	2	7
Iwamuro et al, 2007	Retrospective cohort study	3	2	1	6
Jalbert et al, 2015	Retrospective cohort study	3	2	2	7
Jang et al, 2015	Retrospective cohort study	3	2	2	7
Kim et al, 2018	Retrospective cohort study	3	2	3	8
Lad et al, 2013	Retrospective cohort study	3	2	2	7
Lot et al, 1998	Retrospective cohort study	3	2	2	7
Mcdonald et al, 2013	Prospective cohort study	3	2	3	8
Nanda et al, 2013	Prospective cohort study	3	2	3	8
Pandey et al, 2007	Retrospective cohort study	3	2	3	8
Regli et al, 1999	Prospective cohort study	3	2	2	7
Solheim et al, 2006	Retrospective cohort study	3	2	2	7
Suzuki et al, 2015	Retrospective cohort study	3	2	2	7
Yang et al, 2019	Retrospective cohort study	3	2	3	8
Johnston et al, 2019	Retrospective cohort study	3	2	2	7

Table 2

Overview of included studies.

Author	Country	Years	Type of study	Participants (n)		Gender (F/M)		Age (mean ± standard)		Location of aneurysms
				Coil	Clip	Coil	Clip	Coil	Clip	
Bekelis et al	USA	2016	Prospective	6120	2585	4490/1630	1960/625	72.7	70.5	Mixture
Dammann et al	Germany	2014	Retrospective	16	87	10/6	65/22	54	53.7	MCA
Diaz el al	USA	2014	Retrospective	40	25	NA	NA	NA	NA	MCA
Erdem et al	Germany	2011	Prospective	21	108	NA	NA	NA	NA	MCA
Jang et al	Korea	2015	Retrospective	25	286	NA	NA	NA	NA	MCA
Regli et al	Switzerland	1999	Prospective	13	32	NA	NA	NA	NA	MCA
Brilstra et al	Netherlands	2003	Prospective	19	32	15/4	23/9	51	50	Mixture
Brinjikji et al	USA	2011	Retrospective	34125	29918	NA	NA	56.1 ± 29.4	53.2 ± 25.7	Mixture
Darsaut et al	Canada	2017	RCT	70	66	53/17	41/25	57	56	Mixture
Duan et al	USA	2014	Retrospective	49	65	38/11	49/16	57.6	52.2	Mixture
Frontera et al.	USA	2012	Retrospective	33	36	27/6	29/7	55	54	Mixture
Gerlach et al	Germany	2007	Prospective	37	81	27/10	59/22	48.2	47.6	Mixture
Huang et al	China	2019	Retrospective	37	45	23/14	30/15	52.7 ± 9.6	49.8 ± 11.2	Mixture
Iwanuro et al	Japan	2007	Retrospective	54	78	NA	NA	NA	NA	Mixture
Jalbert et al	USA	2015	Retrospective	7942	4357	6260/1682	3326/1031	72.47	70.77	Mixture
Kim et al	Korea	2018	Retrospective	14 634	11 777	NA	NA	NA	NA	Mixture
Lad et al.	USA	2013	Retrospective	4407	3596	3343/1064	2751/845	54	53	Mixture
Lot et al	France	1998	Prospective	293	102	NA	NA	NA	NA	Mixture
Mcdonald et al	USA	2013	Prospective	3551	1388	2776/775	1019/369	58 (50–67)	55 (47–63)	Mixture
Nanda et al	USA	2013	Prospective	66	74	51/15	53/21	54.3 ± 10.5	55.07 ± 11.12	Mixture
Pandey et al	USA	2007	Retrospective	28	13	22/6	7/6	58.2	47.4	Distal anterior
Solheim et al	Norway	2006	Retrospective	31	44	22/9	30/14	54.2 ± 12.1	55.2 ± 8.4	Mixture
Suzuki et al	Japan	2015	Retrospective	80	141	61/19	106/35	61.9	59.6	Mixture
Johnston et al	USA	1999	Retrospective	255	2357	NA	NA	NA	NA	Mixture
Yang et al	China	2019	Retrospective	64	14	44/20	10/4	74.09 ± 3.88	73.28 ± 2.81	Mixture

Note. F = female, M = male, MCA = middle cerebral artery, NA = not available, RCT = randomized controlled trial.

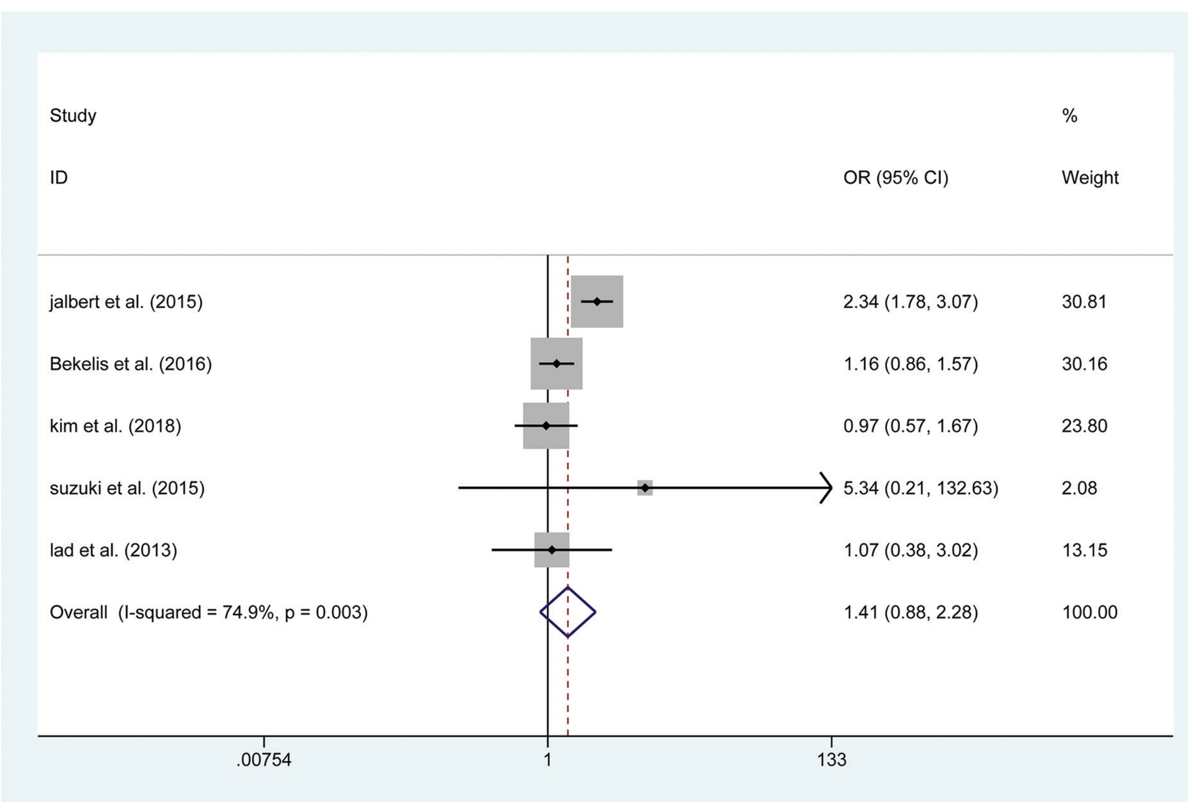

Figure 2. Forest plot of odds ratio (OR) of death within 30 days with endovascular coiling versus surgical clipping.

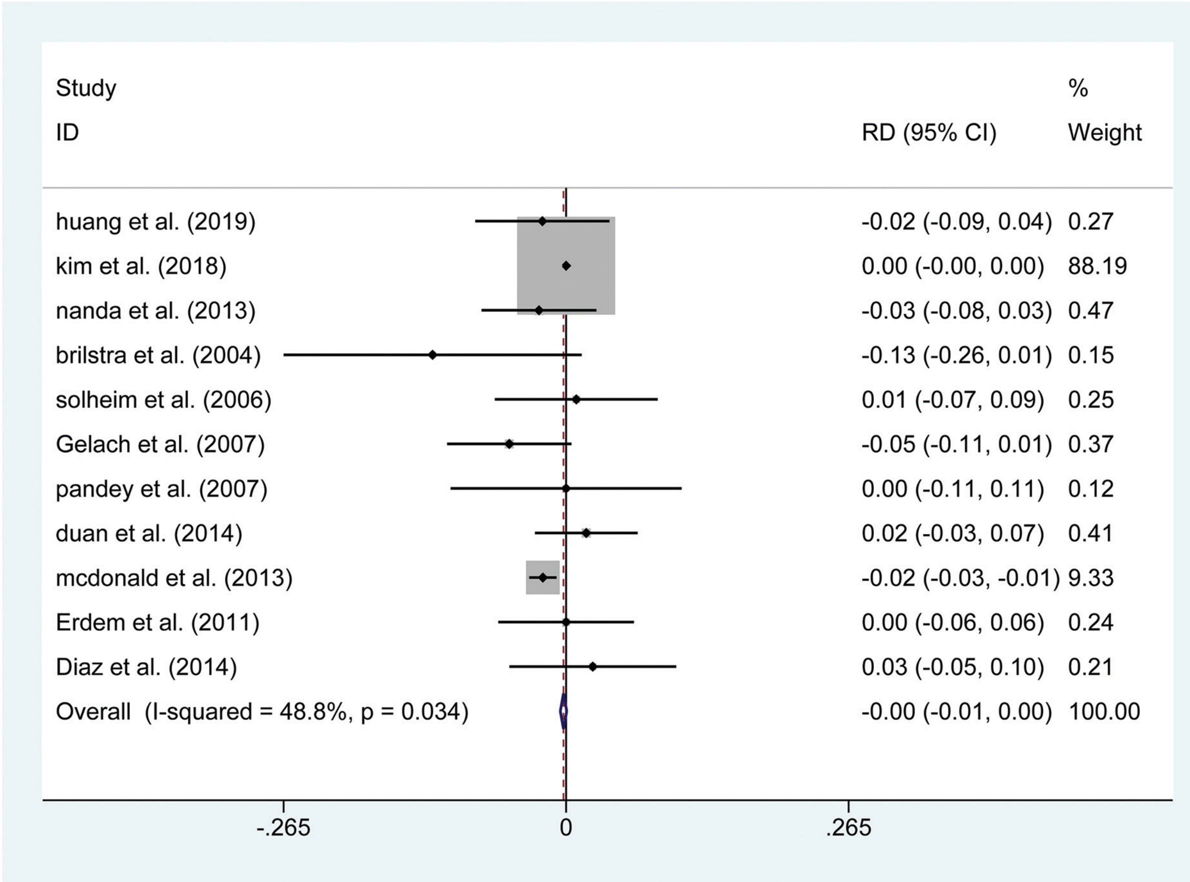

Figure 3. Forest plot of rate difference (RD) of periprocedural bleeding at short-term follow with endovascular coiling versus surgical clipping.

Fig. 3) or at the 1-year follow (OR: 0.568; 95% CI (0.072, 4.459); $P=.590$). Thirteen studies assessed the short-term rates of procedural complications in 84,612 patients and found that endovascular coiling was associated with a lower incidence of complications compared with surgical clipping (4.60% versus 7.0%; OR: 0.518; 95% CI (0.433, 0.621); $P<.001$, Fig. 4), which seemed to be derived from ischemia (4.01% versus 9.08%; OR: 0.423; 95% CI (0.317, 0.564); $P<.001$, Fig. 5) rather than from vasospasm (5.32% versus 0%; RD: 0.060; 95% CI (0.000, 0.120); $P=.048$) and hydrocephalus (1.24% versus 1.38%; OR: 0.901; 95% CI (0.789, 1.030); $P=.127$) (Table 3).

3.4. Secondary endpoints

The secondary endpoint, relevant to the efficiency of the procedure, was a composite of postoperative complete occlusion and mRS > 2. Similar to the results described above, 10 articles mentioned the incidence of postoperative mRS > 2, and pooling the data with a fixed-effects model revealed that there was no significant difference between the 2 groups in the rate of mRS > 2 at both short-term (OR: 0.753, 95% CI (0.361, 1.569), $P=.449$) and 1-year follow-ups (OR: 0.807, 95% CI (0.426, 1.529), $P=.511$). Furthermore, 9 studies focused on the postoperative complete occlusion rate. Pooling the results demonstrated that endovascular coiling had a lower rate of complete occlusion after surgery, in both short-term (OR: 0.179, 95% CI (0.064, 0.499), $P=.001$; Fig. 6) and 1-year follow-ups (OR: 0.307, 95% CI (0.146, 0.646), $P=.002$; Fig. 7).

3.5. Other outcomes of interest

We extracted the LOS value from 8 included articles. Significant heterogeneity was observed ($I^2=99.4\%$, $P<.001$), and a random-effects model was used to show that the LOS was shorter in patients treated with endovascular coiling than in those treated with surgical clipping (WMD: −4.14, 95% CI: (−5.750, −2.531), $P<0.001$; Fig. 8). Similarly, 6 articles mentioned the rates of retreatment; the data was pooled by a random-effects model to reveal that there was a significant difference in the rate of short-term retreatment between the 2 groups (OR: 3.969, 95% CI: (2.110, 7.466), $P<.001$; Fig. 9).

4. Discussion

UCAs are extremely common, with an approximate prevalence of 2% to 5%. They are increasing in their diagnosis owing to the extensive use of noninvasive imaging. Two kinds of treatment are involved in the current options to occlude UCAs. Endovascular coiling is a minimally invasive treatment in which UCA occlusion is completed through the blood vessel, while surgical clipping contained a craniotomy and clip placement on the lesion vessel to occlude UCAs. Although endovascular coiling and surgical clipping are used to prevent UCA rupture, there was no certain evidence of clinical safety and efficiency for either procedure. We conducted this meta-analysis to evaluate the clinical benefit between endovascular coiling and surgical clipping in patients with UCAs.

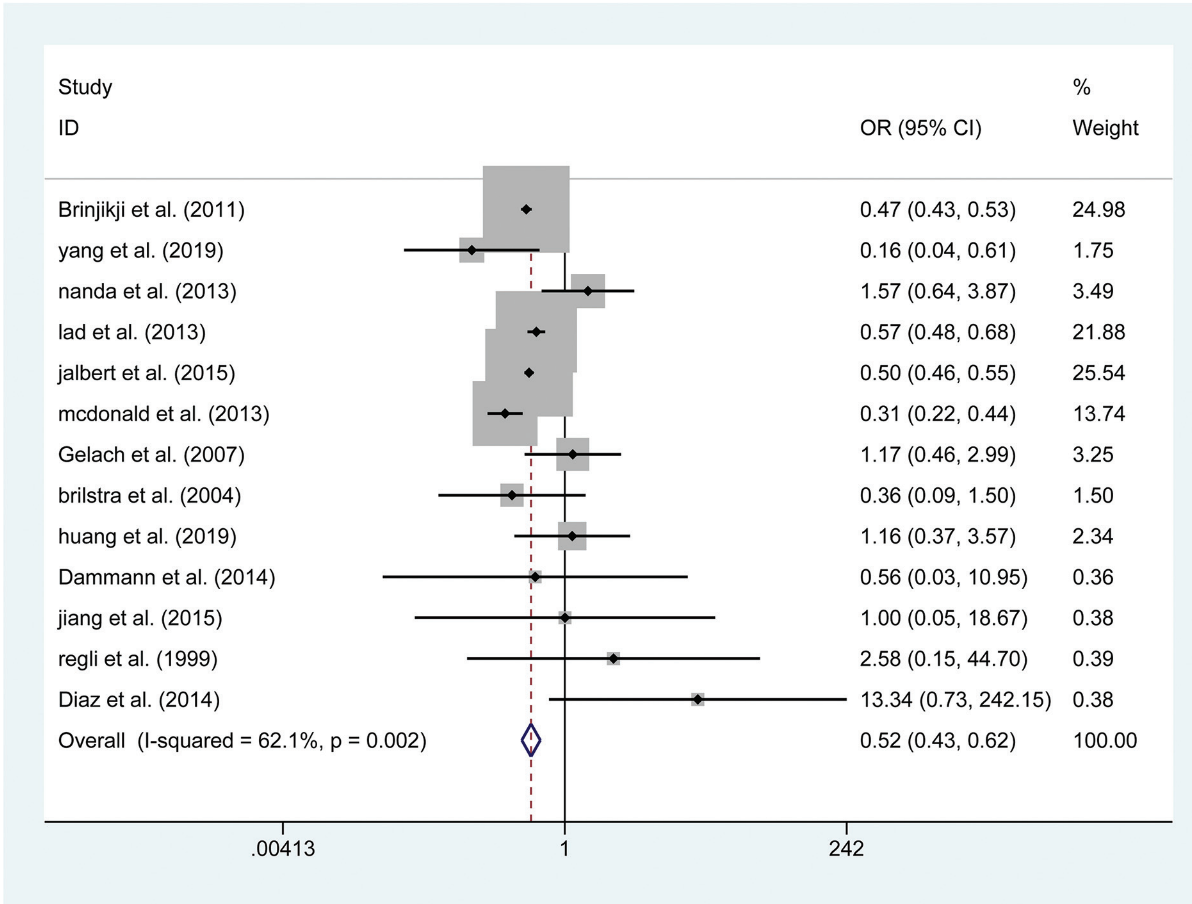

Figure 4. Forest plot of odds ratio (OR) of postoperative complication at short-term follow with endovascular coiling versus surgical clipping.

The primary endpoints were related to the safety in the 2 groups. Similar to the result from a previous meta-analysis,[41] our results demonstrated that the pooled effect estimate of death within 30 days and death in the hospital was 1.411 (95% CI (0.875, 2.276)) and −0.004 (95% CI (−0.012, 0.004)), respectively, revealing that no significant difference was found in the incidence of mortality between the subgroup that died within 30 days and the subgroup that died in the hospital. Reassuringly, the incidence of bleeding at the short-term follow-up was similar between the 2 treatment groups; the postoperative bleeding rate was 1.65% in patients treated with endovascular coiling compared with up to 1.93% in patients treated with surgical clipping, and these bleeding rates were similar at the 1-year follow-up. Moreover, several publications,[42,43] including our own, have shown endovascular coiling to be related to a lower rate of complication compared with surgical clipping (OR: 0.518; 95% CI (0.433, 0.621); $P<.001$), which seems to have derived primarily from ischemia. It has been reported that cerebral ischemia is caused by emboli escaping from aneurysms, and SAH could occur subsequently after an ischemic event.[44,45] Furthermore, it has been documented that endovascular coiling was associated with a higher rate of thromboembolic events with both the coil mass and catheter as a potential thromboembolic causes,[46] which is not the case with surgical clipping. Therefore, endovascular coiling may bear a higher risk of ischemia compared with surgical clipping.

The secondary endpoints referred to the effectiveness of the 2 treatments. In our study, we regarded postoperative complete occlusion and mRS > 2 as measures of surgical effectiveness. Gelach et al[35] reported that the incidence of postoperative complete occlusion was 66.7% in the endovascular group (n = 39), while it was significantly higher (93.6%) in the surgical clipping group (n = 94). Brilstra et al[34] found that endovascular coiling (16/33) was related to a lower complete occlusion rate than the surgical clipping group (36/37, $P<001$). Similar to previous publications, the results of this meta-analysis illustrated that surgical clipping could increase the complete occlusion rates compared with those in the endovascular group. Meanwhile, the present meta-analysis demonstrated that surgical clipping was not associated with a higher rate of mRS > 2 than endovascular coiling for the treatment of UCAs in both short-term (OR: 0.753, 95% CI (0.361, 1.569), $P=.449$) and 1-year follow-up (OR: 0.807, 95% CI (0.426, 1.529), $P=.511$).

Although no significant difference in procedural retreatment rates was found in previous studies, different results were observed in our study (endovascular coiling 19.0% vs. surgical clipping 8.3%). This may be due to the higher rate of emboli escaping from aneurysms. Additionally, we compared the results of LOS and revealed a significantly shorter LOS in UCA patients treated by endovascular coiling than in those treated with surgical clipping, because endovascular coiling is a minimally invasive treatment without a craniotomy. However, a significant

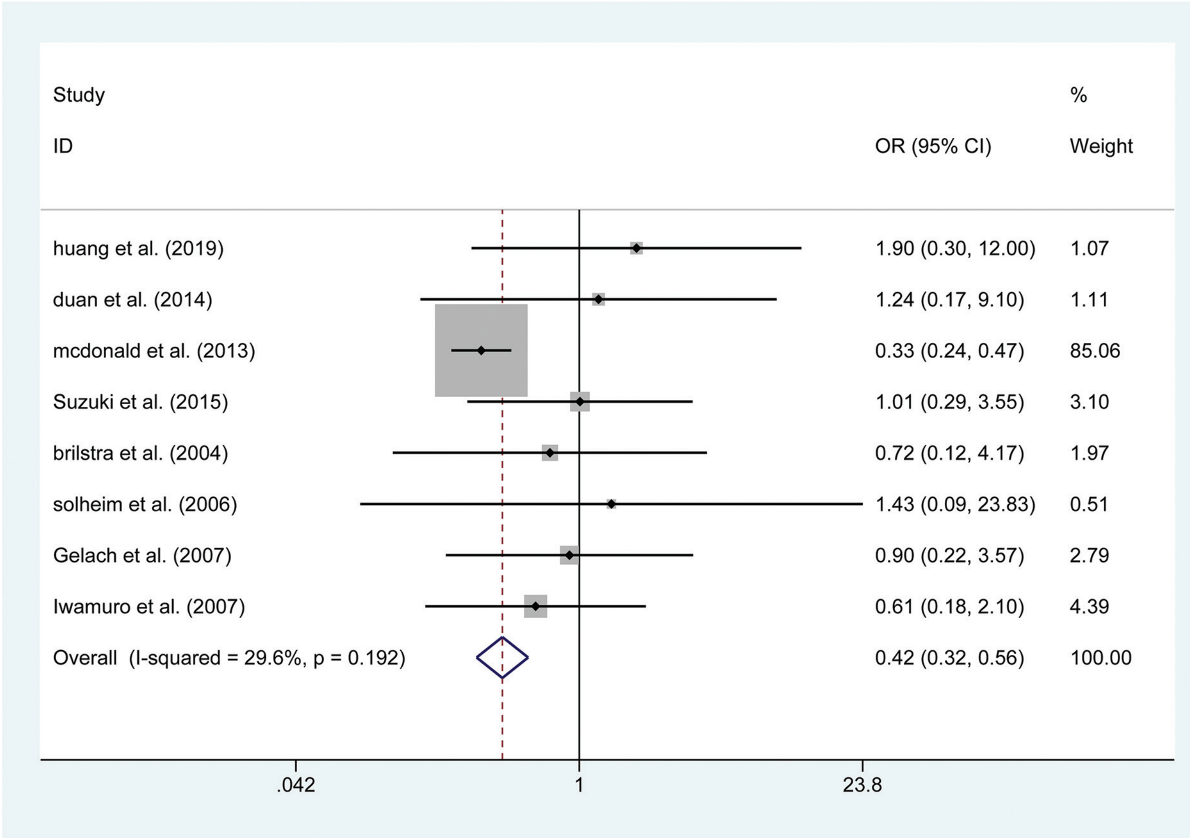

Figure 5. Forest plot of odds ratio (OR) of postoperative ischemia at short-term follow with endovascular coiling versus surgical clipping.

heterogeneity was observed ($I^2=99.4\%$, $P<.001$), this resulted from the different treatment strategies of different research institutions. The present study has several potential limitations. The current study only compares 10 outcomes relevant to complications of the 2 interventions due to the relatively limited data with the same long-term follow-up period. Some heterogeneity was found among the included studies, and we were unable to perform a subgroup analysis based on patient characteristics.

Table 3

Results of meta-analysis comparison of coil and clip for the treatment of patients with unruptured IAs.

		Groups		Overall effect			Heterogeneity	
Outcome	**Studies**	**Coil**	**Clip**	**Effect estimate**	**95% CI**	***P* value**	**I^2 (%)**	***P* value**
Length of stay	8	28,910	18,966	−4.14	(−5.75, −2.531)	**<.001**	99.4%	<.001
Retreatment	6	5361	8871	3.969	(2.110, 7.466)	**<.001**	58.2%	.035
Completed occlusion								
Short-term	7	228	373	0.179	(0.064, 0.499)	**.001**	70.9%	.002
One-year follow	3	130	135	0.307	(0.146, 0.646)	**.002**	0.0%	.639
Postoperative complications	13	46,390	38,222	0.518	(0.433, 0.621)	**<.001**	62.1%	.002
Short-term vasospasm	2	94	87	0.06	(0.000, 0.120)	**.048**	28.2%	.238
Short-term ischemic	8	1694	1883	0.423	(0.317, 0.564)	**<.001**	29.6%	.192
Short-term hydrocephalus	4	35,624	31,450	0.901	(0.789, 1.030)	.127	2.4%	.380
Postoperative bleeding								
Short-term	11	16,346	13,661	−0.002	(−0.005, 0.001)	.133	48.8%	.034
One-year follow	2	89	84	0.568	(0.072, 4.459)	.590	0.0%	.685
Postoperative death								
In hospital	9	40,509	41,828	−0.004	(−0.012, 0.004)	.378	83.5%	<.001
Within 30 days	5	27,974	14,343	1.411	(0.875, 2.276)	.157	74.9%	.003
Post-operative mRS > 2								
Short-term	3	182	206	0.753	(0.361–1.569)	.449	0.0%	.859
One-year follow	9	345	528	0.807	(0.426, 1.529)	.511	0.0%	.800

Note. CIs = confidence intervals, IAs = intracranial aneurysms.

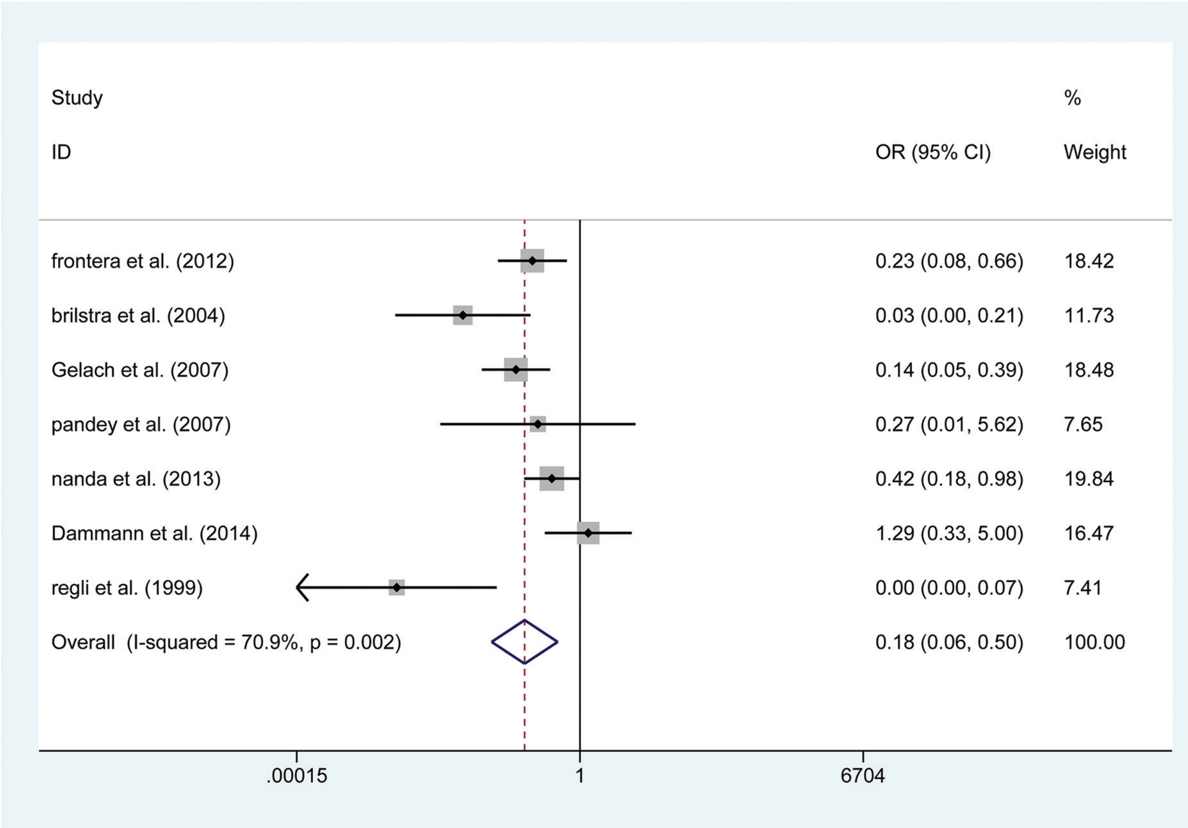

Figure 6. Forest plot of odds ratio (OR) of postoperative completed occlusion at short-term follow with endovascular coiling versus surgical clipping.

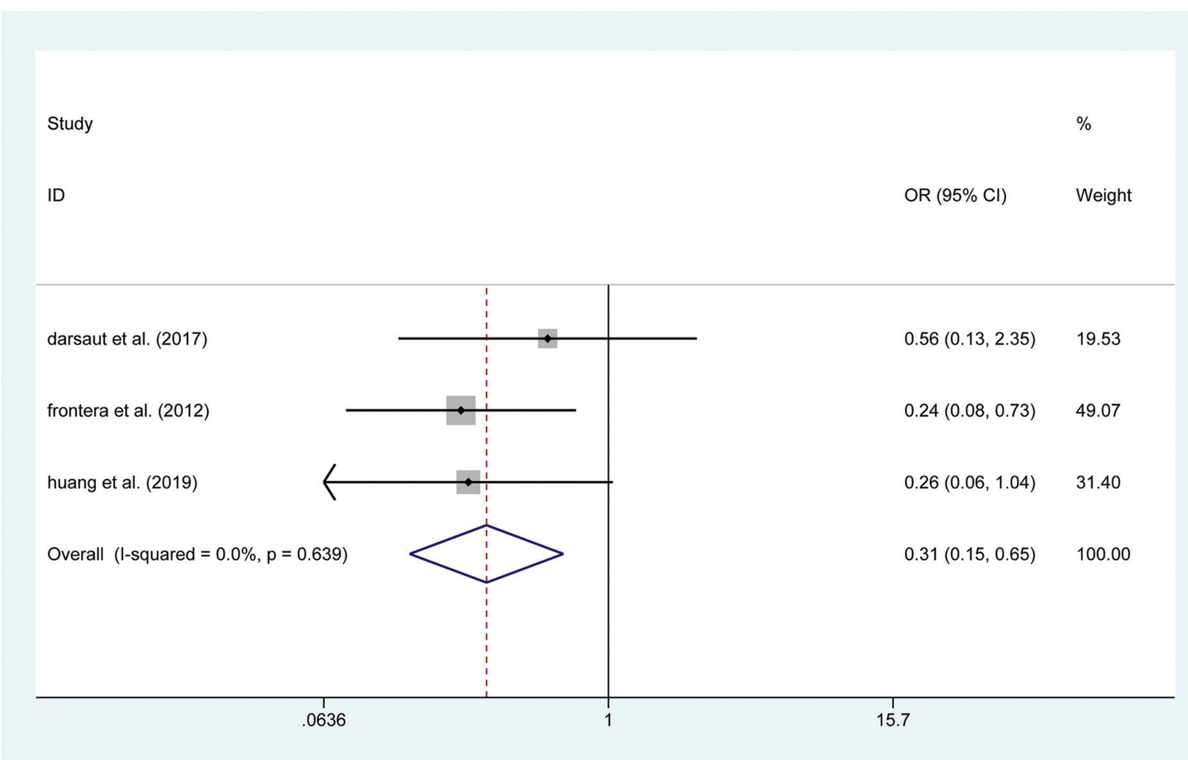

Figure 7. Forest plot of odds ratio (OR) of postoperative completed occlusion at 1-year follow with endovascular coiling versus surgical clipping.

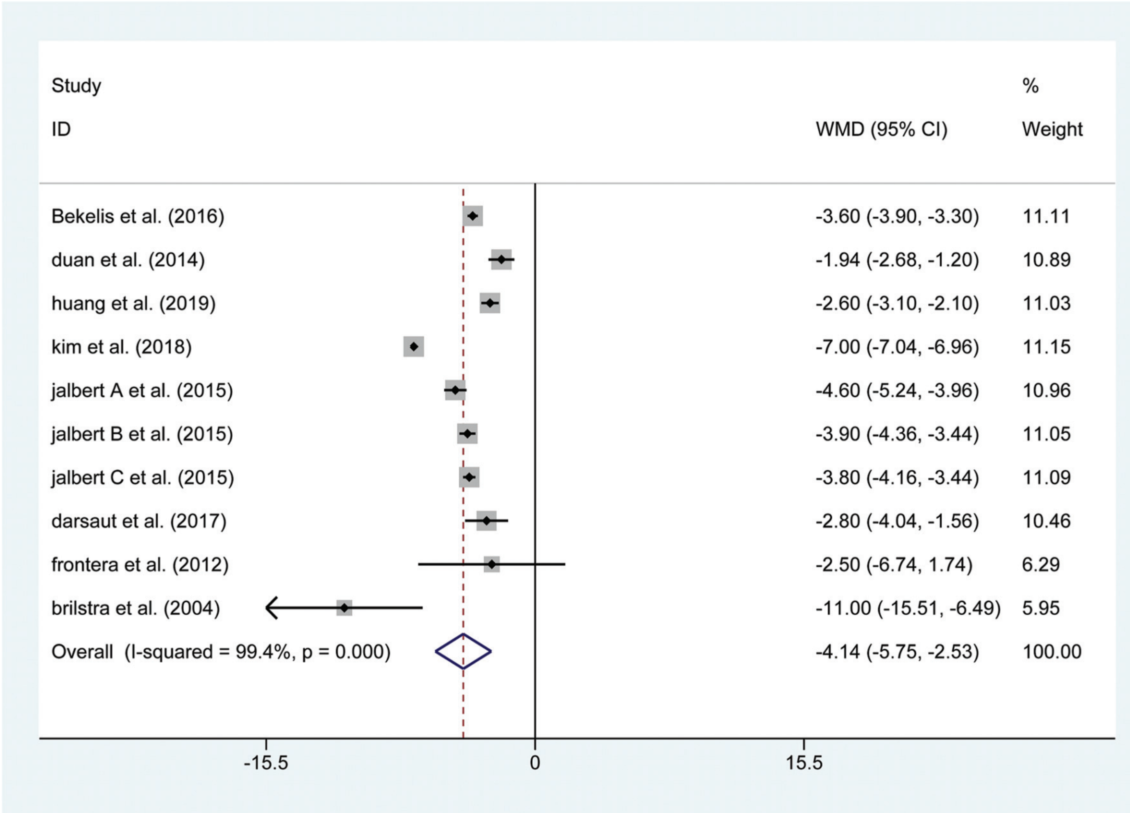

Figure 8. Forest plot of weighted mean difference (WMD) of the length of stay with endovascular coiling versus surgical clipping.

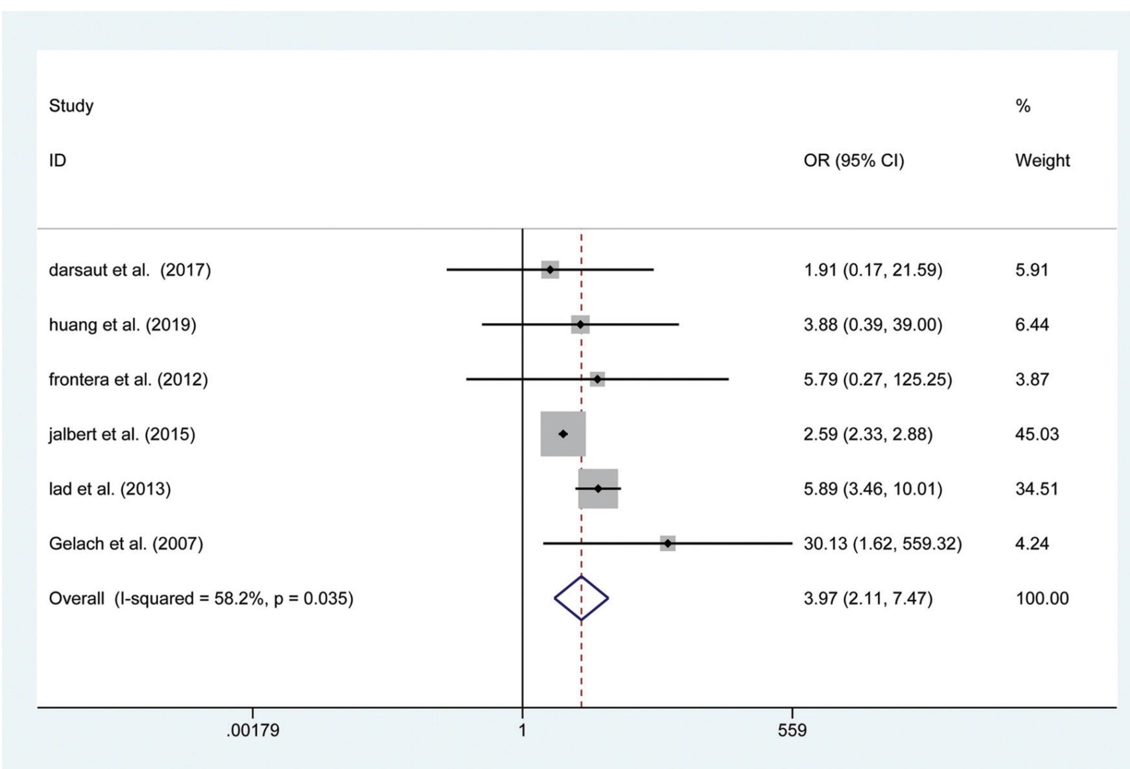

Figure 9. Forest plot of odds ratio (OR) of postoperative retreatment at short-term follow with endovascular coiling versus surgical clipping.

5. Conclusion

The latest evidence illustrates that surgical clipping resulted in lower retreatment rates and was associated with a higher incidence of complete occlusion, while endovascular coiling was associated with shorter LOS and a lower rate of complications, especially ischemia.

Author contributions

Data curation: Wei Wei.
Formal analysis: Yi lei, Wei Wei.
Investigation: Yi lei, Wei Wei.
Methodology: Yi lei.
Software: Yi lei.

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