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Systematic Review of Treatment for Unruptured Intracranial Aneurysms: Clipping Versus Coiling

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ABSTRACT

AIM: To compare endovascular coiling and surgical clipping for the evaluation of clinical outcomes in patients with unruptured intracranial aneurysms.

MATERIAL and METHODS: We searched MEDLINE, EMBASE, the Cochrane Library and three Chinese domestic electronic databases, namely, Wanfang, CNKI and VIP for studies published between January 1990 and January 2018. We included controlled clinical studies comparing clinical outcomes between surgical clipping and endovascular coiling treatments. Two researchers extracted the data and assessed the quality of the studies, and a meta-analysis was performed using RevMan 5 software.

RESULTS: We analysed a total of 23 controlled clinical studies including 117,796 cases. Meta-analysis demonstrated similar ischaemia rates between clipping and coiling with an odds ratio [OR] of 1.36 (95% CI: 0.77–2.40). The occlusion rate and bleeding risk were higher with clipping than coiling; the pooled ORs were 5.31 (95% CI: 3.07–9.19) and 2.39 (95% CI: 1.82–3.13), respectively. In addition, clipping resulted in a longer hospital stay (OR = 2.90, 95% CI: 2.14–3.65) than coiling did. Patients who underwent clipping had a higher short-term mortality (OR = 1.99, 95% CI: 1.70–2.33) and neurological deficit rate (OR = 2.05, 95% CI: 1.73–2.44) compared with those who underwent coiling. However, 1 year mortality and deficit rate were similar for both clipping and coiling, with pooled ORs of 0.75 (95% CI: 0.41–1.38) and 0.94 (95% CI: 0.53–1.67), respectively. Funnel plots did not demonstrate a publication bias, with the exception of ischaemic outcome, and sensitivity analysis showed consistent results.

CONCLUSION: Our study demonstrates that coiling is associated with a lower rate of occlusion, shorter hospital stay, lower bleeding risk and lower short-term mortality and morbidity compared with clipping. In terms of ischaemic risk, 1 year mortality and morbidity, coiling and clipping bear a similar risk. In addition, we speculate that surgical clipping may have a better outcome than endovascular coiling in the long term especially in young patients. Further research is needed to confirm our conclusion.

KEYWORDS: Unruptured intracranial aneurysms, Surgical clipping, Endovascular coiling, Systematic review

INTRODUCTION

Unruptured intracranial aneurysms (UIAs) have been detected more frequently since the development of non-invasive and high-resolution imaging techniques, such as magnetic resonance angiography and computed tomography angiography. The prevalence of UIAs in the general population is estimated to be 3.2% (95% CI: 1.9%–5.2%) according to Vlak et al. research (45); however, patients still have a risk of aneurysm rupture, which can lead to poor prognosis (15). There are currently two treatment approaches for intracranial aneurysms: surgical clipping and endovascular coiling. Clipping is a standard and valid treatment for aneurysms. Endovascular coiling is less invasive and has become an increasingly popular method of treatment since 1995 when detachable coils were invented to treat aneurysms

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(49). For this study, we performed a systematic review and meta-analysis in order to compare the two methods. Because no randomised controlled trials (RCTs) on this topic exist, we pooled controlled clinical studies to compare the safety and efficacy of the two methods. Although a systematic review of these treatment methods for UIAs has been published (37), we have included many more studies and performed different analyses in the current review. Therefore, we believe the quality of evidence for each main outcome is stronger than in the previous study.

MATERIAL and METHODS

Inclusion and Exclusion Criteria

We included randomised and non-randomised controlled clinical trials comparing the efficacy and safety of surgical clipping versus endovascular coiling in patients with UIAs. Studies were limited to Chinese- and English-language reports published between January 1990 and January 2018. We excluded studies that were published repeatedly, and those with overlapping data were included only once. In addition, we excluded studies with <10 cases in one group.

Search Strategies

We retrieved controlled clinical trials from PubMed, EMBASE, the Cochrane Library and three Chinese domestic electronic databases: Wanfang, CNKI and VIP. We performed searches for the following keywords and MeSH terms: 'unruptured aneurysm', 'nonruptured aneurysm' and 'grade 0 aneurysm'. The Boolean operator 'OR' was used to connect these terms. In addition, we examined the references of the selected articles. The search procedures are presented in Figure 1.

Data Extraction

Two independent reviewers conducted the search and evaluated the quality of the studies. Experts were consulted to reach a consensus in cases of disagreement. Data extracted from the publications included study design, patient age, sex, race, hospital location, length of follow-up and intervention outcomes including mortality, bleeding, ischaemia, occlusion of aneurysm, deficit and duration of hospital stay.

Quality of Evidence Assessment

We assessed the quality of evidence of the included studies according to the *Cochrane Handbook of Systematic Reviews Version5.1.0.* The main items included randomisation, allocation concealment and blinding. Quality of evidence was rated as A, B or C. Two reviewers independently evaluated the quality of the evidence, and any disagreements were resolved by discussion and consensus.

Statistical Analysis

The meta-analysis was performed using Review Manager, version 5.0 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, 2014). Heterogeneity between studies was tested using the I^2 statistic and was considered statistically significant if the I^2 value was >50%. Funnel plots were used to visually estimate publication bias. We used the fixed effects model if there was no heterogeneity and the random effects model if there was heterogeneity. P<0.05 was considered statistically significant. In addition, we performed sensitivity analysis to assess the robustness of the synthesis of results in the meta-analysis.

RESULTS

A total of 23 eligible controlled clinical studies including 117,796 cases were included in our meta-analysis. Among these studies, two were prospective single centre, three were prospective multicentre, nine were retrospective single centre

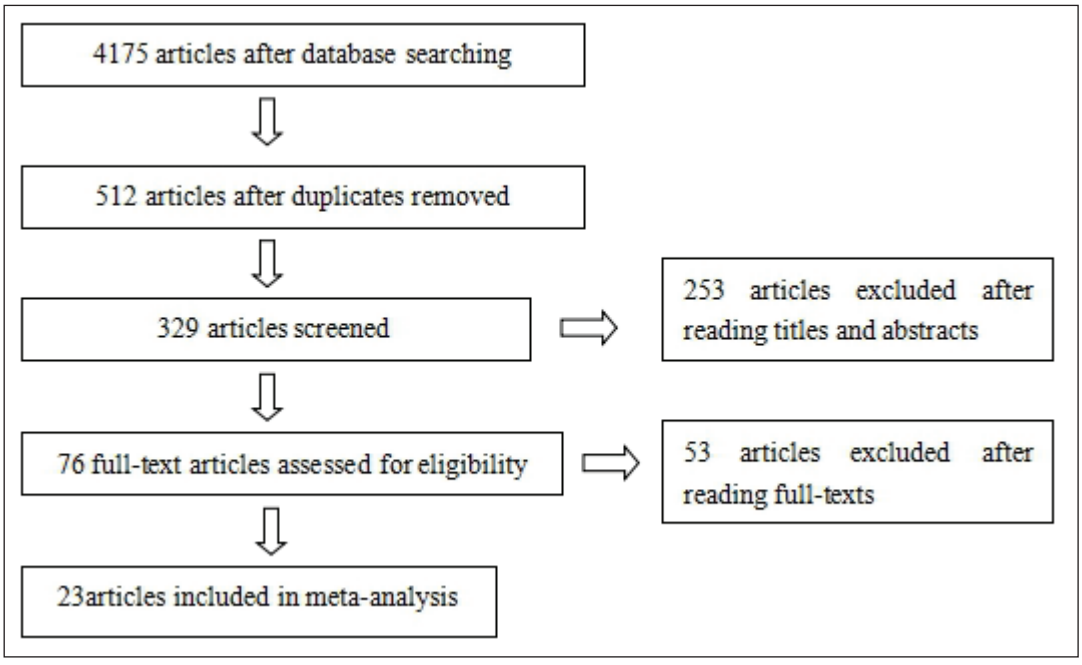

Figure 1: Process of searching and selection of articles for this study.

Table I: Characteristics of the Included Studies

Study	Country	Study type	Clipping case	Coiling case	Outcome	Follow-up
Lot G. et al., 1998 (28)	France	PS	25	83	death, deficit	1 year
Johnston SC. et al., 2001 (18)	USA	RM	1699	370	death, hospital stay	discharge
Wiebers DO. et., 2003 (47)	ISUIAI	PM	1917	451	death, deficit	1 month, 1 year
Manabe H. et al., 2004 (29)	Japan	RS	93	16	death, occlusion, deficit, hospital stay	1 month
Brilstra EH. et al., 2004 (3)	Netherlands	PM	32	17	death, bleeding, occlusion, ischaemia, deficit	1 year
Shen JK. et al., 2005 (38)	China	RS	19	28	death, deficit	discharge
Solheim O. et al., 2006 (39)	Norway	RS	44	31	death, occlusion, bleeding, ischaemia, deficit	3 months
Iwamuro Y. et al., 2007 (16)	Japan	RS	78	54	death, ischaemia, deficit, hospital stay	3 months
Gerlach R. et al., 2007 (9)	Germany	PS	94	39	death, bleeding, occlusion, ischaemia, deficit	6 months
Higashida RT. et al., 2007 (13)	USA	RM	1881	654	death, deficit, cost, hospital stay	discharge
Kim JE. et al., 2010 (20)	South Korea	PM	846	824	death, deficit	1 month
Alshekhlee A. et al., 2010 (1)	USA	RM	3738	3498	death, bleeding, hospital stay	discharge
Brinjikji W. et al., 2011 (4)	USA	RM	29918	34125	death, complications	discharge
Lawson MF. et al., 2012 (27)	USA	RM	6611	7439	death, deficit	discharge
McDonald JS. et al., 2013 (30)	USA	RM	1380	1380	death, complications	discharge
Kunz M. et al., 2013 (25)	Germany	RS	363	200	death, deficit, hospital stay	discharge, 13 months
Lai LT. et al., 2013 (26)	Australia	RM	3098	2824	bleeding, seizure	discharge
Fu CT. et al., 2014 (8)	China	RS	40	15	death, deficit	discharge
Dammann P. et al., 2014 (6)	Germany and Switzerland	RM	87	16	death, occlusion, ischaemia, deficit	discharge, 1 year
Duan Y. et al., 2014 (7)	USA	RS	69	56	hospital stay cost	2 months
Jalbert JJ. et al., 2015 (17)	USA	RM	4357	7942	death, deficit, hospital, stay	30-days
Song J. et al., 2015 (40)	South Korea	RS	558	566	death, bleeding, ischaemia, seizure, deficit	1 month 6 months
Suzuki M. et al., 2015 (41)	Japan	RS	141	80	death, complications	discharge

RS: *Retrospective single centre;* ***RM:*** *Retrospective multicenter;* ***PM:*** *Prospective multicenter;* ***PS:*** *Prospective single centre.* ***ISUIAI:*** *International Study of Unruptured Intracranial Aneurysms Investigators.*

and nine were retrospective multicentre studies. Baseline characteristics of these studies are outlined in Table I.

However, not all 23 studies were blinded, and there was no information on randomisation or allocation concealment. Hence, the quality of all 23 studies combined was rated C.

Outcomes

1. Ischaemia

Eight studies investigated ischaemia outcome following clipping and coiling treatments. Ischaemia was described in the different studies as a hypodense lesion on computed tomography scan, ischaemic stroke, ischaemic events and ischaemic complications. The odds ratios (ORs) for ischaemia in each study were 1.57 (95% CI: 0.27–9.04) for Brilstra 2004; 0.07 (95% CI: 0.04–11.60) for Solheim 2006; 1.12 (95% CI: 0.28–4.45) for Gerlach 2007; 1.63 (95% CI: 0.48–5.59) for Iwanuro 2007; 2.99 (95% CI: 2.14–4.19) for McDonald 2013; 1.39 (95% CI: 0.78–2.49) for Kunz 2013; 0.43 (95% CI: 0.12–1.59) for Dammann 2014 and 0.34 (95% CI: 0.03–3.25) for Song 2015. Pooled ischaemia rates were 8.1% for clipping and 3.6% for coiling. Because heterogeneity was detected (I^2 = 56%, p=0.02), a random effects model was used. The pooled OR was 1.36 (95% CI: 0.77–2.40) (Figure 2), and the difference was not statistically significant (p>0.05). Therefore, the ischaemic risks of clipping and coiling are comparable.

2. Occlusion of aneurysms

Five studies investigated the occlusion of aneurysms following clipping and coiling treatment. All studies used angiography for this particular outcome assessment. Gerlach 2007 defined occlusion as no aneurysm filling. Brilstra 2004, Manabe 2004, Solheim 2006 and Dammann 2014 described it as successful or complete isolation or occlusion of the aneurysm. The ORs for occlusion in each study were 6.75 (95% CI: 0.65–69.97) for Brilstra 2004; 7.45 (95% CI: 2.23–23.89) for Manabe 2004; 5.50 (95% CI: 1.55–19.74) for Solheim 2006; 7.33 (95% CI: 2.54–21.20) for Gerlach 2007 and 2.61 (95% CI: 0.86–7.88) for Dammann 2014. The pooled occlusion rates were 88.2% for clipping and 65.3% for coiling. The fixed effects model was used because no heterogeneity was found (I^2 = 0%, p=0.68). The pooled OR was 5.31 (95% CI: 3.07–9.19) (Figure 3), and the difference was statistically significant (p<0.05). Therefore, the occlusion rate for clipping is higher than for coiling.

3. Bleeding

Bleeding outcome was assessed in seven studies, and data were overlapped in two studies. These studies described bleeding as intracranial haemorrhage and haemorrhagic complications including subdural, epidural, subarachnoid and intraventricular haemorrhage. The ORs for each study were 6.16 (95% CI: 0.31–120.99) for Brilstra 2004; 0.70 (95% CI: 0.04–11.60) for Solheim 2006; 4.85 (95% CI: 0.26–89.94) for Gerlach 2007; 1.75 (95% CI: 1.23–2.50) for Alshekhlee 2010; 3.77 (95% CI: 2.36–6.02) for Lai 2013 and 1.52 (95% CI: 0.25–9.16) for Song 2015. The fixed effects model was used as little heterogeneity was detected (I^2 = 39%. p=0.15). The pooled bleeding rates were 2.5% for clipping and 1.0% for coiling, and the pooled OR was 2.39 (95% CI: 1.82–3.13) (Figure 4), which was a statistically significant difference (p<0.05). Therefore, the risk of bleeding from clipping is higher than from coiling.

4. Duration of hospital stay

The duration of hospital stay was evaluated in eight studies. Studies by Johnston 2001, Manabe 2004 and Iwanuro 2007 did not provide variance of the data, and several studies may have had overlapping data. Consequently, we performed a pooled analysis with four studies. The ORs in each study were 2.90 (95% CI: 2.46–3.34) for Higashida 2007; 2.70 (95% CI: 2.14–3.26) for Kunz 2013; 1.94 (95% CI: 1.20–2.68) for Yifei Duan 2014 and 3.90 (95% CI: 3.44–4.36) for Jalbert 2015. As heterogeneity was detected (I^2 = 87%, p<0.0001), the random effects model was used. The pooled lengths of hospital stay

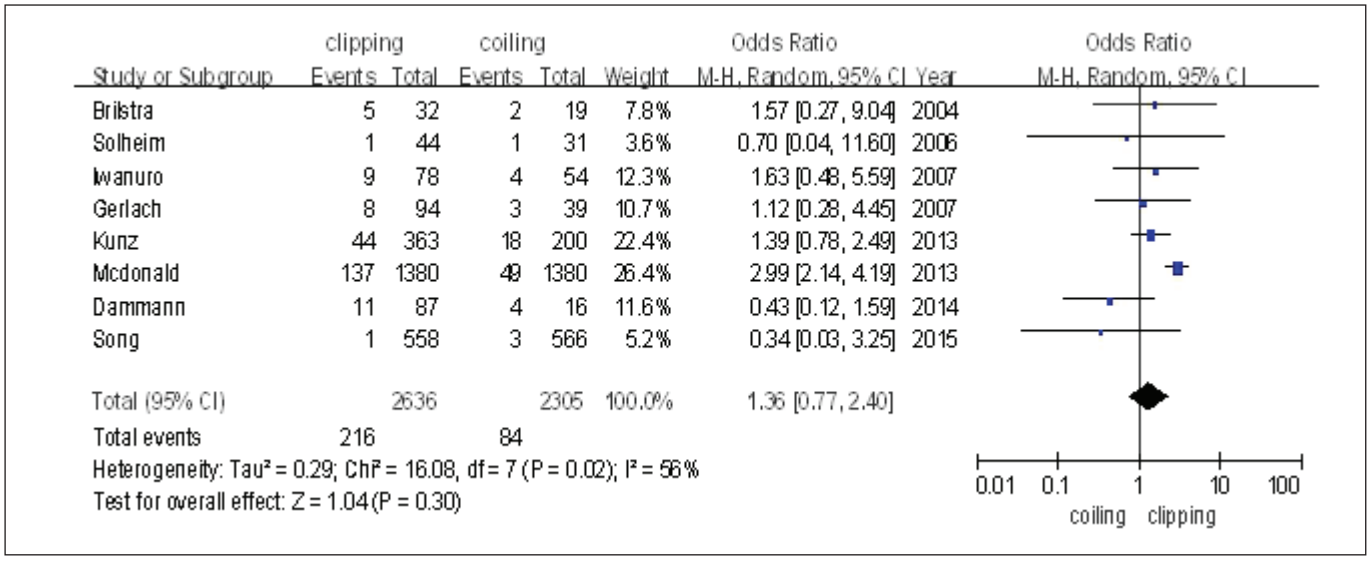

Figure 2: Risk of ischaemia for clipping versus coiling.

were 7.7 days for clipping and 4.1 days for coiling, and the pooled OR was 2.90 (95% CI: 2.14–3.65) (Figure 5) with a statistically significant difference ($p<0.05$). Therefore, the duration of hospital stay is longer for clipping than for coiling.

5. Mortality

Mortality rates of patients who underwent clipping and coiling were reported in 17 studies. Data were overlapping in several studies; thus, we used subgroup analysis to better compare the death rate. The studies were divided into two groups including a short-term group (follow-up for 1 month or until discharge) and a 1 year group (follow-up for 1 year). The short-term group included 10 studies. The fixed effects model was used as there was no heterogeneity (I^2 = 17%). The ORs

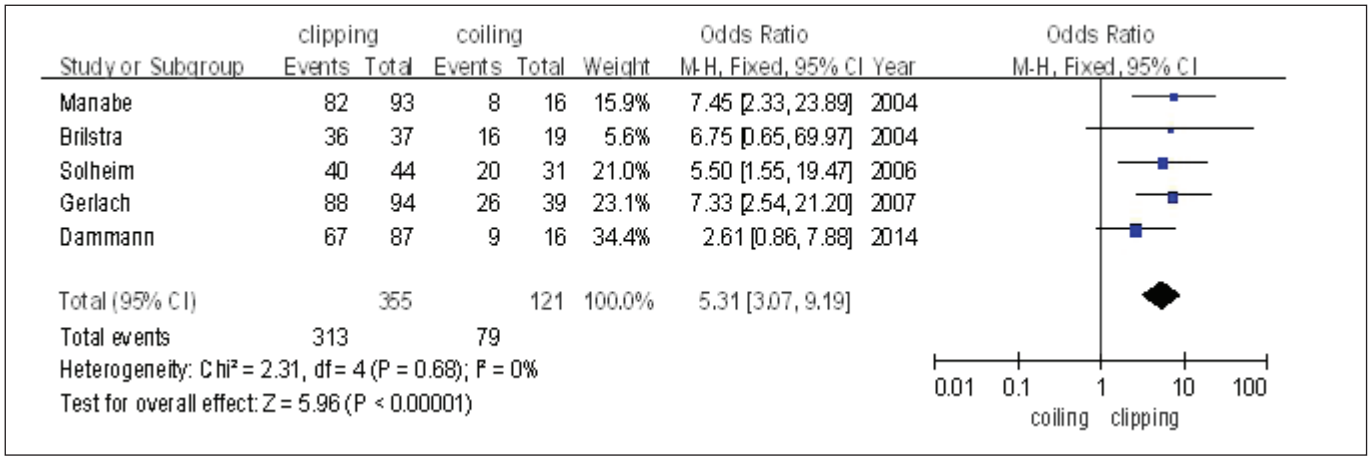

Figure 3: Occlusion rate for clipping versus coiling.

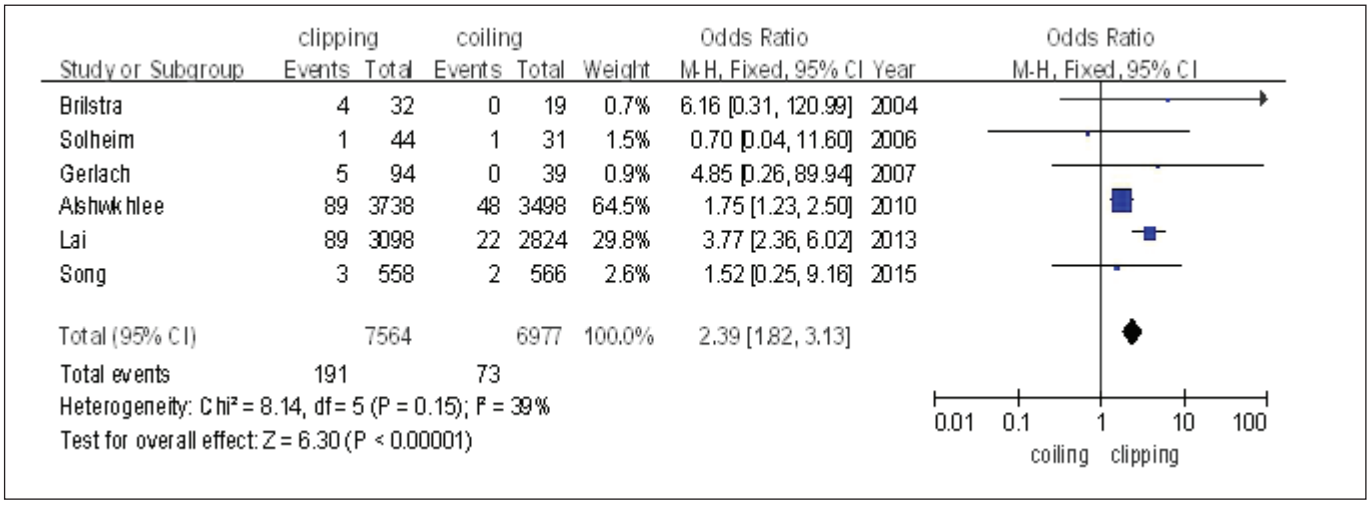

Figure 4: Risk of bleeding for clipping versus coiling.

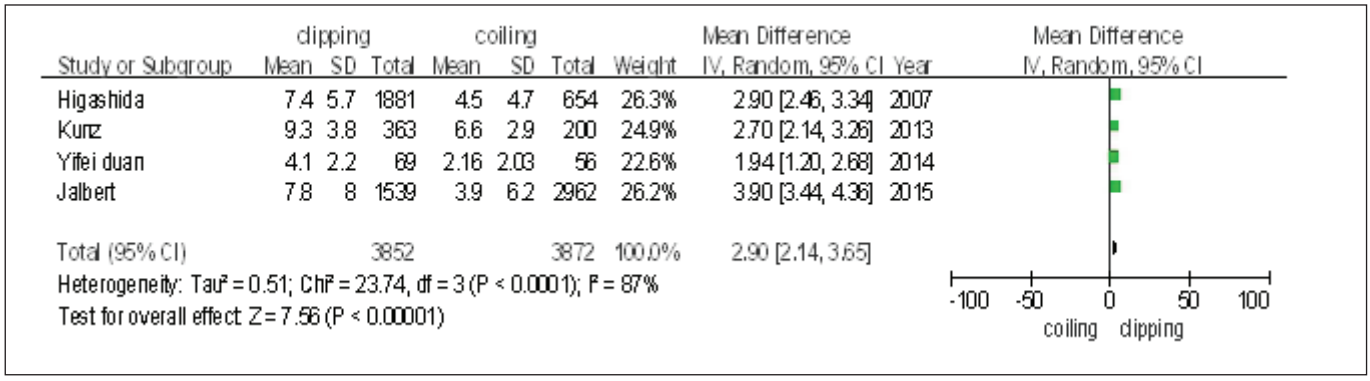

Figure 5: Hospital stay for clipping versus coiling.

in each study were 6.62 (95% CI: 1.61–27.21) for Johnston 2001; could not be estimated for Manabe 2004; 5.89 (95% CI: 0.22–154.48) for Jiankang Shen 2005; 1.46 (95% CI: 0.24–8.78) for Kim 2010; 2.84 (95% CI: 1.71–4.72) for Alshekhlee 2010; 1.84 (95% CI: 1.55–2.18) for Brinjikji 2011; could not be estimated for Dammann 2014; 2.01 (95% CI: 0.09–44.38) for Changtao Fu 2014; 5.09 (95% CI: 0.24–106.26) for Song 2015 and 0.19 (95% CI: 0.01–4.65) for Suzuki 2015. The pooled OR was 1.99 (95% CI: 1.70–2.33) (Figure 6), and the difference was statistically significant ($p<0.05$). Therefore, the pooled mortality for clipping is 1.27%, which is statistically higher than 0.61% for coiling.

The 1 year group included three studies. We used the fixed effects model as there was no heterogeneity. The ORs in each study were 0.75 (95% CI: 0.41–1.38) for Wibers and could not be estimated for Lot 1998 and Dammann 2014 (Figure 7), and the difference was not statistically significant ($p>0.05$). The pooled mortality rates were 2.2% and 2.5% for clipping and coiling, respectively, which were not significantly different.

6. Deficits

Patient quality of life after clipping and coiling treatments was reported in 14 studies. Data were overlapping in several studies. The modified Rankin scale (mRS) and Glasgow Outcome Scale (GOS) were used. Deficits were considered in patients who scored 3, 4 or 5 points on the mRS or 2 or 3 points on the GOS. They were also considered in patients with severe disability or permanent deficits or in those who were discharged to a long-term facility. In a subgroup analysis, eight studies reported short-term deficit rates (follow-up for 1 month or until discharge). The ORs in each study were 1.84 (95% CI: 1.11–3.04) for Wiebers 2003; 1.50 (95% CI: 0.07–30.47) for Manabe 2004; 3.47 (95% CI: 0.57–21.23) for Shen 2005; 1.34 (95% CI: 0.54–3.36) for Kim 2010; 2.22 (95% CI: 1.83–2.69) for Lawson 2012; 1.14 (95% CI: 0.11–11.85) for Fu 2014; 0.25 (95% CI: 0.04–1.63) for Dammann 2014 and 0.61 (95% CI: 0.14–2.55) for Song 2015. The pooled short-term deficit rates were 4.7% and 2.1% for clipping and coiling, respectively. Because no heterogeneity was found ($I^2 = 29\%$, $p=0.20$), the fixed effects model was used. The pooled OR

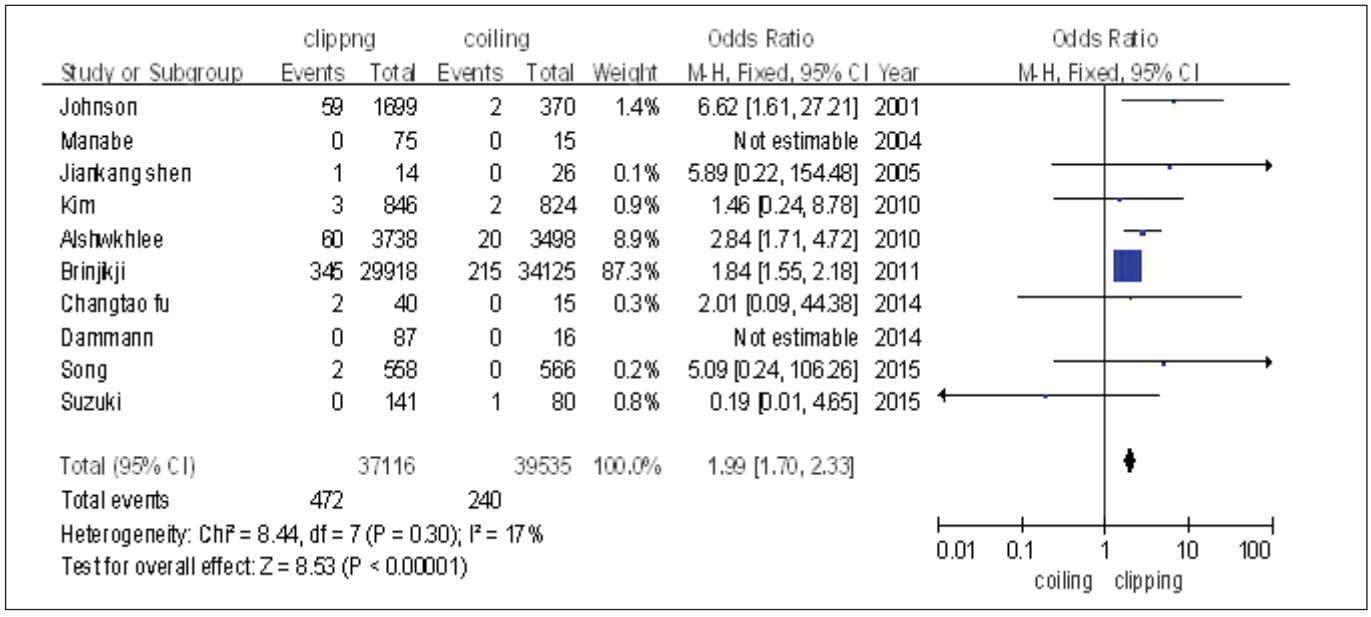

Figure 6: Short-term death rate for clipping versus coiling.

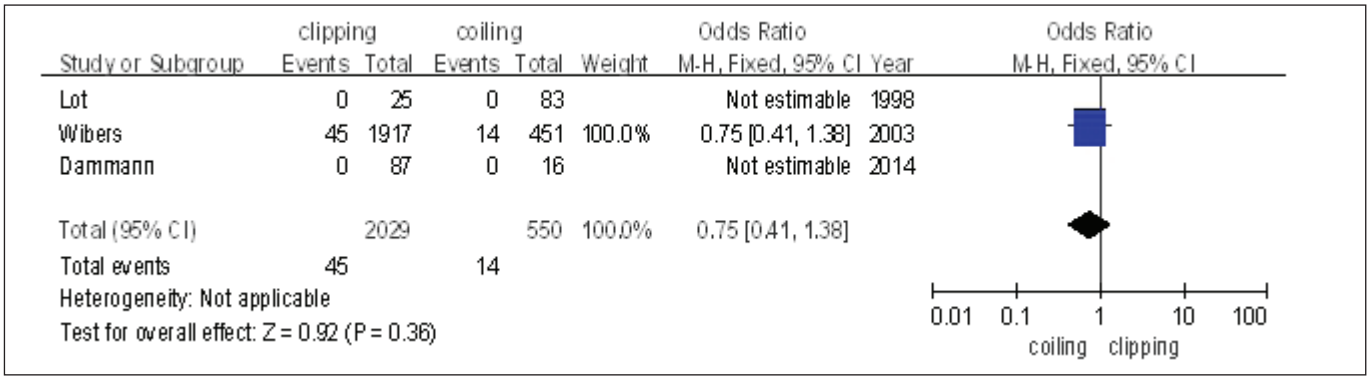

Figure 7: 1 year death rate for clipping versus coiling.

was 2.05 (95% CI: 1.73–2.44) (Figure 8) with a statistically significant difference (p<0.05). Therefore, the short-term deficit rate for clipping is higher than for coiling.

Among the included studies, four reported 1 year deficit rates. The ORs in each study were 0.64 (95% CI: 0.03–13.75) for Lot 1998; 1.43 (95% CI: 0.79–2.59) for Wiebers 2003; 0.82 (95% CI: 0.39–1.73) for Kunz 2013 and 0.17 (95% CI: 0.01–2.94) for Dammann 2014. The pooled long-term deficit rates were 1.8% for clipping and 2.5% for coiling. Moreover, the pooled OR was 0.94 (95% CI: 0.53–1.67) (Figure 9), and the difference was not statistically significant (p>0.05). Therefore, the long-term deficit rates for clipping and coiling are comparable.

Assessment of Publication Bias

Publication biases were visually estimated using funnel plots for each pooled outcome. For the ischaemia outcome, the dots appeared discrete and were distributed symmetrically in the funnel plots for the remaining outcomes. Therefore, publication bias may exist for ischaemia outcomes but is negligible for other outcomes.

Sensitivity Analysis

We performed sensitivity analyses to assess the stability of our findings. For each plot, we excluded each study one by one and then re-conducted the pooled study, where we saw an outcome similar to the original results. There were zero events in several groups for the outcomes of bleeding, mortality and deficit (including the long-term and 1 year groups). Next, we changed zero to one in each group and repeated the pooled analysis for each outcome and again saw outcomes similar to the original results. Therefore, we concluded that our results were robust.

DISCUSSION

RCTs are difficult to implement for surgical interventions; therefore, the best evidence typically is provided by observational controlled studies. Kotowski et al. (22) identified 60 studies and performed a systematic review on the clinical outcomes of UIA treatment with coiling and clipping but did not compare the two treatments directly. Ruan et al. (37) included seven studies comparing several factors in regard to coiling

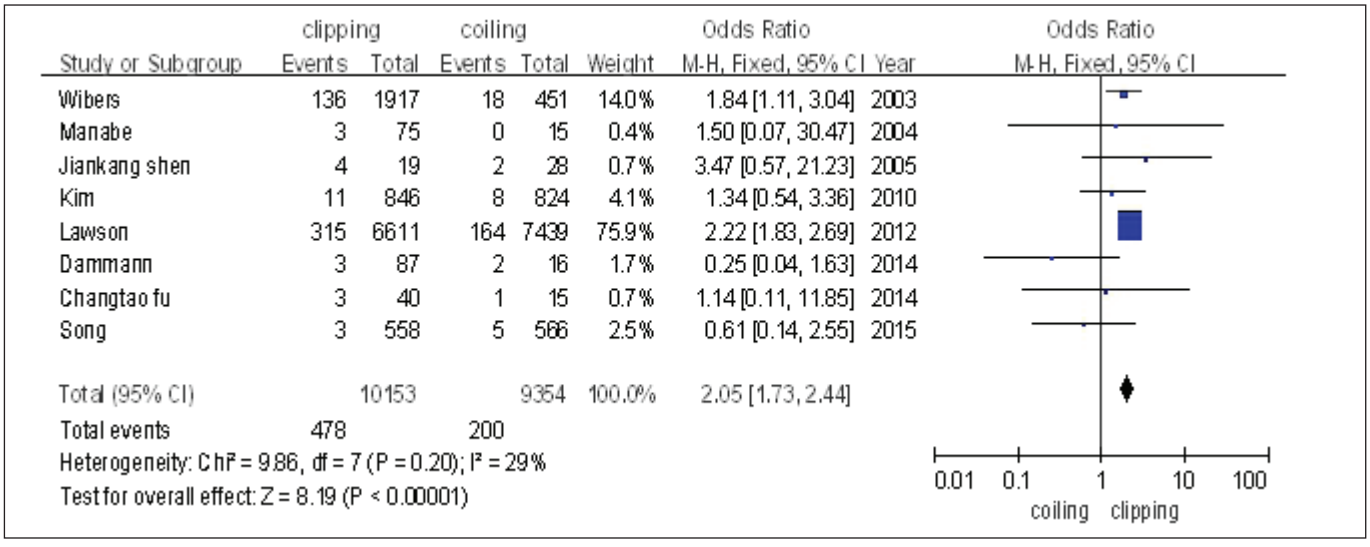

Figure 8: Short-term deficit rate for clipping versus coiling.

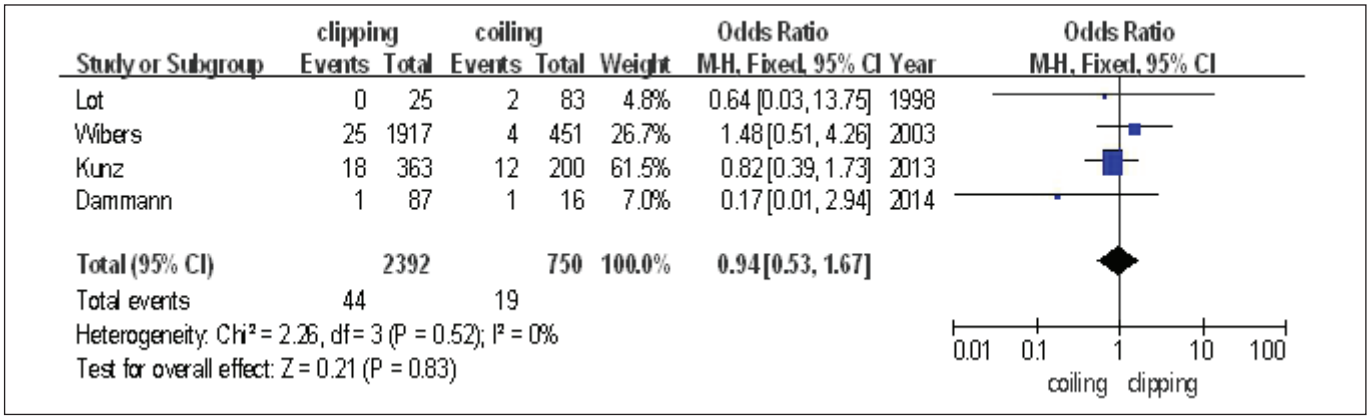

Figure 9: 1 year deficit rate for clipping versus coiling.

and clipping. In the present review, we included even more studies and expanded the sample size, and we performed subgroup analyses. Therefore, we believe our results are more robust compared with previous studies.

We found that coiling had a lower occlusion rate and shorter hospital stay and was associated with lower bleeding risk, short-term mortality and deficit rate. In addition, coiling and clipping showed no significant differences for 1 year mortality and deficit rate in ischaemic risk.

Postoperative ischaemia is a serious complication of both coiling and clipping treatments. For clipping, cerebral ischaemia can result from an intraoperative aneurysm rupture (IAR) (25), or the use of temporary clips (23). With coiling, ischaemia is caused by an embolism from aneurysms; thromboembolism could be caused by either the catheter or the coil mass (35). Emboli are not always related to clots but are sometimes attributed to metallic fragments from Guglielmi detachable coils (12). Severe ischaemia may be caused by inadvertent vessel occlusion from coil migration, coil rupture or other types of failures including coil impingement, dissection or severe vasospasm. Clipping appears to have a lower risk of ischaemia than does coiling. However, IAR is more common (25), and an IAR temporary clip has greater risk factors compared with those for coiling. In the current study, we found that the ischaemic risks for clipping and coiling were comparable (OR = 1.36, CI: 0.77–2.40) ($p>0.05$), which is in accordance with the review by Hokari et al. (14). According to Hokari and Kunz's reports, the rates of cerebral ischaemia are 9% for coiling and 12% for clipping (14,25); thus, both treatments have similar ischaemic risks.

In the International Study of UIAs, aneurysm obliteration was considered complete in 51% of patients, partly successful in 21% and no obliteration in 23% using endovascular techniques (47). Other reports have shown aneurysm occlusion rates of 95% for coiling (46), and 96% for clipping (5). Surgical clipping (clipping of the aneurysm neck) is a classic and sophisticated treatment for aneurysms and is generally considered more reliable than coiling. Endovascular repair of UIA can be limited in a wide range of aneurysms or when branches of the vessel merge into the base of the aneurysm. In a large group of UIA patients who underwent endovascular treatment, the failure rate was 5.7% (11), and reported as high as 29.3% in a smaller series of reports (34). Our meta-analysis showed that the pooled OR was 5.31 (95% CI: 3.07–9.19) with a statistically significant difference ($p<0.05$). The occlusion rate of clipping was statistically higher than for coiling, which is consistent with our general perception. Clipping typically remains easier compared with coiling for complicated aneurysms although surgical clipping may require leaving a small residual neck when aneurysms are partially calcified or have parent or branching vessel involvement in the aneurysm base in order to prevent parent vessel stenosis, especially in large or giant aneurysms (9). Furthermore, a wrapped aneurysm can prevent further bleeding.

Subarachnoid haemorrhage (SAH) may still occur with both surgical clipping and endovascular coiling because of the regeneration of treated aneurysms or new aneurysm formation (43,36). Bleeding, such as SAH, may also be caused by fragile vascular walls after coiling (36), an imperfect clip (44) and surgical complications, including subdural, epidural and subarachnoid bleeding after clipping. Reports have shown that the bleeding rate for clipping was 6% (14), and the rate of SAH was 1.4% 10 years after clipping (44). Complications related to craniotomy have the greatest risk for bleeding. The bleeding rate for coiling has been reported as 0% (19), which was much lower than for clipping. In the current study, the calculated risk of bleeding was 2.5% for clipping and 1.0% for coiling. The pooled OR was 2.39 (95% CI: 1.82–3.13) ($p<0.05$), which is consistent with previous reports. Therefore, the risk of bleeding with clipping appears to be higher than with coiling.

The safety of clipping and coiling treatments has been heavily debated. Two previous meta-analyses reported that mortality from clipping was 1% (21), and 2% (33). A recent meta-analysis reported that mortality with coiling was 1.9% (22). Subgroup analyses in the current study revealed that short-term mortality rates were 1.27% for clipping and 0.61% for coiling. The short-term mortality for clipping was significantly higher than for coiling (OR = 1.99, 95% CI: 1.70–2.33) ($p<0.05$). In addition, long-term mortality rates were 2.2% and 2.5% for clipping and coiling, respectively, which were not significantly different (OR = 0.75, 95% CI: 0.41–1.38) ($p>0.05$). The American Heart Association/American Stroke Association Guidelines revealed that endovascular coiling was associated with reduced procedural morbidity and mortality compared with surgical clipping but had a higher overall risk of recurrence (42). The higher short-term mortality of surgical clipping may be due to treatment invasiveness and complications following craniotomy. Despite these drawbacks, surgical clipping is reported to result in more durable aneurysm occlusion than is coiling, which was supported by a randomised study that found higher recurrence rates after coiling compared with clipping (31). Long-term angiographic follow-up studies have estimated recurrence rates of UIA after coiling up to 24% (32). Therefore, patients were at higher risk for recurrence following a coiling procedure compared with a clipping procedure. Accordingly, the mortality rate for coiling was also higher in the long-term group.

Morbidity rates for clipping and coiling have been reported at 3% (24), and 1% (48), respectively. Subgroup analyses in the current study demonstrated that the deficit rate for clipping was higher than for coiling in the short-term group. In the 1 year group, the deficit rates of clipping and coiling were not statistically different. Complications of craniotomy could cause short-term differences in mortality outcome. Epidemiological studies have also shown that patients with UIAs treated with clipping are more often discharged to long-term care facilities when compared with those treated with coiling (4). The patients who underwent clipping gradually recovered from operational injury over time. However, coiled UIA may still lead to recanalisation and unexpected growth and rupture, resulting in deficits during follow-up (2). Therefore, the deficit rate for coiling was similar to that for clipping.

Traditional treatment with surgical clipping is now being challenged by the less invasive endovascular coiling method. Although coiling reduces patient lesions and has lower short-term mortality and morbidity, it has a lower occlusion rate. Mortality and morbidity in the 1 year group were comparable for clipping and coiling. We speculate that mortality and morbidity in the coiling group may be higher than in the clipping group in the long term (5 years, ≥10 years). Another study revealed that 20.4% of patients with coiled unruptured aneurysms underwent additional hospitalisations for aneurysm repair procedures versus only 8.7% of patients with clipped UIA at long-term (range, 4–12 years) follow-up, and the difference was statistically significant ($p<0.001$) (10). Our results demonstrate that surgical clipping may have a better long-term outcome compared with endovascular coiling especially for young patients. However, further research is necessary to validate our results.

The limitations of our study are apparent. First, all of the studies were observational and no RCTs were identified. Because of ethical requirements of clinical trials, all studies did not apply blinding, randomisation or allocation concealment. Therefore, the combined quality of the 23 included studies was rated C, which is a low level of evidence. Selection bias may inevitably exist in addition to publication bias in ischaemia studies. Therefore, further studies are required, and the results of this systematic review should be interpreted with caution.

CONCLUSION

The present study shows that coiling has a lower occlusion rate and a shorter hospital stay and is associated with a lower risk of bleeding and short-term mortality and morbidity compared with clipping. Coiling and clipping treatments have similar risks for ischaemia and 1 year mortality and morbidity. We speculate that surgical clipping may have a better long-term outcome compared with endovascular coiling especially in young patients. Further research is needed to confirm our conclusion.

AUTHORSHIP CONTRIBUTION

Study conception and design: ZS, YZ, XG, JF, JY, TL, BF
Data collection: ZS, YZ, XG, JF, JY, TL, BF
Analysis and interpretation of results: ZS, YZ, XG, JF, JY, TL, BF
Draft manuscript preparation: ZS, YZ, XG, JF, JY, TL, BF
Critical revision of the article: ZS, YZ, XG, JF, JY, TL, BF
Other (study supervision, fundings, materials, etc...): ZS, YZ, XG, JF, JY, TL, BF
All authors (ZS, YZ, XG, JF, JY, TL, BF) reviewed the results and approved the final version of the manuscript.

REFERENCES

1. Alshekhlee A, Mehta S, Edgell RC, Vora N, Feen E, Mohammadi A, Kale SP, Cruz-Flores S: Hospital mortality and complications of electively clipped or coiled unruptured intracranial aneurysm. Stroke 41:1471-1476, 2010
2. Bavinzski G, Talazoglu V, Killer M, Richling B, Gruber A, Gross CE, Plenk H: Gross and microscopic histopathological findings in aneurysms of the human brain treated with Guglielmi detachable coils. J Neurosurg 91: 284–293, 1999
3. Brilstra EH, Rinkel GJ, van der Graaf Y, Sluzewski M, Groen RJ, Lo RT, Tulleken CA: Quality of life after treatment of unruptured intracranial aneurysms by neurosurgical clipping or by embolisation with coils: A prospective, observational study. Cerebrovascular Diseases 17:44–52, 2004
4. Brinjikji W, Rabinstein AA, Nasr DM, Lanzino G, Kallmes DF, Cloft HJ: Better outcomes with treatment by coiling relative to clipping of unruptured intracranial aneurysms in the United States, 2001–2008. AJNR Am J Neuroradiol 32:1071–1075, 2011
5. Choi SW, Ahn JS, Park JC, Kwon DH, Kwun BD, Kim CJ: Surgical treatment of unruptured intracranial middle cerebral artery aneurysms: Angiographic and clinical outcomes in 143 aneurysms. J Cerebrovasc Endovasc Neurosurg 14:289–294, 2012
6. Dammann P, Schoemberg T, Muller O, Ozkan N, Schlamann M, Wanke I, Sandalcioglu IE, Forsting M, Sure U: Outcome for unruptured middle cerebral artery aneurysm treatment: Surgical and endovascular approach in a single center. Neurosurg Rev 37:643-651, 2014
7. Duan Y, Blackham K, Nelson J, Selman W, Bambakidis N: Analysis of short-term total hospital costs and current primary cost drivers of coiling versus clipping for unruptured intracranial aneurysms. Neurointerv Surg 7:614-618, 2015
8. Fu CT, Chen ZB, Chen XQ, Wang L, Li MC, Xu Z, Wang W: Unruptured intracranial aneurysms: A clinical research of 72 cases. J Clin Surg 22:116-118, 2014
9. Gerlach R, Beck J, Setzer M, Vatter H, Berkefeld J, Du Mesnil de Rochemont R, Raabe A, Seifert V: Treatment related morbidity of unruptured intracranial aneurysms: Results of a prospective single centre series with an interdisciplinary approach over a 6 year period (1999–2005). J Neurol Neurosurg Psychiatry 78:864–871,2007
10. Gonda DD, Khalessi AA, McCutcheon BA, Marcus LP, Noorbakhsh A, Chen CC, Chang DC, Carter BS et al: Long-term follow-up of unruptured intracranial aneurysms repaired in California. J Neurosurg 120:1349-1357, 2014
11. Gonzalez N, Murayama Y, Nien YL, Martin N, Frazee J, Duckwiler G, Jahan R, Gobin YP, Viñuela F: Treatment of unruptured aneurysms with GDCs: Clinical experience with 247 aneurysms. AJNR Am J Neuroradiol 25(4):577–583, 2004
12. Guglielmi G: Generations of Guglielmi detachable coils (letter). AJNR Am J Neuroradiol 18:1195, 1997
13. Higashida RT, Lahue BJ, Torbey MT, Hopkins LN, Leip E, Hanley DF: Treatment of unruptured intracranial aneurysms: A nationwide assessment of effectiveness. J Neuroradiol 28: 146-151, 2007
14. Hokari M, Kuroda S, Nakayama N, Houkin K, Ishikawa T, Kamiyama H: Long-term prognosis in patients with clipped unruptured cerebral aneurysms-increased cerebrovascular events in patients with surgically treated unruptured aneurysms. Neurosurg Rev 36:567–571, 2013

15. Hop JW, Rinkel GJ, Algra A, van Gijn J: Case-fatality rates and functional outcome after subarachnoid hemorrhage: A systematic review. Stroke 28:660–664,1997
16. Iwamuro Y, Nakahara I, Higashi T, Iwaasa M, Watanabe Y, Tsunetoshi K, Munemitsu T, Taha M: Result of neck clipping and coil embolization as a treatment for unruptured aneurysm. Interv Neuroradiol 13 Suppl 1:151–156, 2007
17. Jalbert JJ, Isaacs AJ, Kamel H, Sedrakyan A: Clipping and coiling of unruptured intracranial aneurysms among medicare beneficiaries, 2000to 2010. Stroke 46:2452 -2457, 2015
18. Johnston SC, Zhao S, Dudley RA, Berman MF, Gress DR: Treatment of unruptured cerebral aneurysms in California. Stroke 32:597-605,2001
19. Kim BM, Kim DI, Park SI, Kim DJ, Suh SH, Won YS: Coil embolization of unruptured middle cerebral artery aneurysms. Neurosurgery 68:346–353; discussion 353–354, 2011
20. Kim JE, Lim DJ, Hong CK, Joo SP, Yoon SM, Kim BT: Treatment of unruptured intracranial aneurysms in South Korea in 2006: A nationwide multicenter survey from the Korean Society of Cerebrovascular Surgery. J Korean Neurosurg Soc 47:112-118, 2010
21. King JT Jr, Berlin JA, Flamm ES: Morbidity and mortality from elective surgery for asymptomatic unruptured intracranial aneurysms: A meta-analysis. Neurosurg 81:837–842, 1994
22. Kotowski M, Naggara O, Darsaut TE, Nolet S, Gevry G, Kouznetsov E, Raymond J: Safety and occlusion rates of surgical treatment of unruptured intracranial aneurysms: A systematic review and meta-analysis of the literature from 1990 to 2011. Neurol Neurosurg Psychiatry 84:42-48, 2013
23. Krayenbuhl N, Erdem E, Oinas M, Krisht AF: Symptomatic and silent ischemia associated with microsurgical clipping of intracranial aneurysms: Evaluation with diffusion-weighted MRI. Stroke 40:129–133, 2009
24. Krisht AF, Gomez J, Partington S: Outcome of surgical clipping of unruptured aneurysms as it compares with a 10-year nonclipping survival period. Neurosurgery 58:207-216, 2006
25. Kunz M, Bakhshai Y, Zausinger S, Fesl G, Janssen H, Brückmann H, Tonn JC, Schichor C: Interdisciplinary treatment of unruptured intracranial aneurysms: Impact of intraprocedural rupture and ischemia in 563 aneurysms. J Neurol 260:1304–1313, 2013
26. Lai LT, ODonnell J, Morgan MK: The risk of seizures during the in-hospital admission for surgical or endovascular treatment ofunruptured intracranial aneurysms. Neurosci 20:1498-1502, 2013
27. Lawson MF, Neal DW, Mocco J, Hoh BL: Rationale for treating unruptured intracranial aneurysms: Actuarial analysis of natural history risk versus treatment risk for coiling or clipping based on 14,050 patients in the Nationwide Inpatient Sample database. World Neurosurg 79:472-478, 2013
28. Lot G, Houdart E, Cophignon J, Casasco A, George B: Combined management of intracranial aneurysms by surgical and endovascular treatment. Modalities and results from a series of 395 cases. Acta Neurochir 141: 557-562, 1999
29. Manabe H, Takemura A, Hasegawa S, Nagahata M, Islam S: The choice of treatment method for unruptured cereb.ral aneurysm. Investigation from clinical outcome, angiographical result, duration of hospital stay, and cost for treatment. Interventional Neuroradiology 10 Suppl 1: 143-146, 2004
30. McDonald JS, McDonald RJ, Fan J, Kallmes DF, Lanzino G, Cloft HJ: Comparative effectiveness of unruptured cerebral aneurysm therapies: Propensity scoreanalysis of clipping versus coiling. Stroke 44:988-994, 2013
31. Molyneux AJ, Kerr RS, Birks J, Ramzi N, Yarnold J, Sneade M, Rischmiller J; The ISAT Collaborators: Risk of recurrent subarachnoid haemorrhage, death, or dependence and standardised mortality ratios after clipping or coiling of an intracranial aneurysm in the International Subarachnoid Aneurysm Trial (ISAT): Long-term follow-up. Lancet Neurol 8:427–433, 2009
32. Naggara ON, White PM, Guilbert F, Roy DI, Weill A, Raymond J: Endovascular treatment of intracranial unruptured aneurysms: Systematic review and meta-analysis of the literature on safety and efficacy. Radiology 256:887–897, 2010
33. Raaymakers TW, Rinkel GJ, Limburg M, Algra A: Mortality and morbidity of surgery for unruptured intracranial aneurysms: A meta-analysis. Stroke 29:1531–1538, 1998
34. Raftopoulos C, Goffette P, Vaz G, Ramzi N, Scholtes JL, Wittebole X, Mathurin P: Surgical clipping may lead to better results than coil embolization: Results from a series of 101 consecutive unruptured intracranial aneurysms. Neurosurgery 52:1280–1287, 2003
35. Rordorf G, Bellon RJ, Budzik RE, Farkas J, Reinking GF, Pergolizzi RS, Ezzeddine M, Norbash AM, Gonzalez RG, Putman CM: Silent thromboembolic events associated with the treatment of unruptured cerebral aneurysms by use of Guglielmi detachable coils: Prospective study applying diffusion-weighted imaging. AJNR Am J Neuroradiol 22:5–10, 2001
36. Roy D, Milot G, Raymond J: Endovascular treatment of unruptured aneurysms. Stroke 32:1998–2004, 2001
37. Ruan C, Long H, Sun H, He M, Yang K, Zhang H, Mao B: Endovascular coiling vs. surgical clipping for unruptured intracranial aneurysm: A meta-analysis. Br J Neurosurg 29:485-492,2015
38. Shen JK, Zhao WG, Lin D, Hu JQ, Cheng K, Bian LG, Sun QF: Treatment of unruptured intracranial aneurysms. Chin J Neurosurg 21(4):232-235, 2005
39. Solheim O, Eloqayli H, Muller TB, Unsgaard G: Quality of life after treatment for incidental, unruptured intracranial aneurysms. Acta Neurochir (Wien) 148: 821–830, 2006
40. Song J, Kim BS, Shin YS: Treatment outcomes of unruptured intracranial aneurysm; experience of 1231 consecutive aneurysms. Neurochir (Wien) 157:1303-1310, 2015
41. Suzuki M, Yoneda H, Ishihara H, Shirao S, Nomura S, Koizumi H, Suehiro E, Goto H, Sadahiro H, Maruta Y, Inoue T, Oka F: Adverse events after unruptured cerebral aneurysm treatment a single-center experience with clipping/coil embolization combined units. Stroke Cerebrovasc Dis 24:223-231, 2015

42. Thompson BG, Brown RD, Amin-Hanjani S, Broderick JP, Cockroft KM, Connolly ES, Duckwiler GR, Harris CC, Howard VJ, Johnston S, Claiborne C, Meyers PM, Molyneux A, Ogilvy CS, Ringer AJ, Torner J. Guidelines for the management of patients with unruptured intracranial aneurysms: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 46:2368-2400, 2015
43. Tsutsumi K, Ueki K, Morita A, Usui M, Kirino T: Risk of aneurysm recurrence in patients with clipped cerebral aneurysms: Results of long-term follow-up angiography. Stroke 32:1191–1194, 2001
44. Tsutsumi K, Ueki K, Usui M, Kwak S, Kirino T: Risk of subarachnoid hemorrhage after surgical treatment of unruptured cerebral aneurysms. Stroke 30:1181–1184, 1999
45. Vlak MH, Algra A, Brandenburg R, Rinkel GJ: Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and time period: A systematic review and meta-analysis. Lancet Neurology 10:626 –636,2011
46. Wang B, Gao BL, Xu GP, Xiang C, Liu XS: Endovascular embolization is applicable for large and giant intracranial aneurysms: Experience in one center with long-term angiographic follow-up. Acta Radiol 56:105–113, 2015
47. Wiebers DO, Whisnant JP, Huston J 3rd, Meissner I, Brown RD Jr, Piepgras DG, Forbes GS, Thielen K, Nichols D, O'Fallon WM, Peacock J, Jaeger L, Kassell NF, Kongable-Beckman GL, Torner JC; International Study of Unruptured Intracranial Aneurysms Investigators: Unruptured intracranial aneurysms: Natural history, clinical outcome, and risks of surgical and endovaseular treatment. Lancet 362:103-110,2003
48. Yue W: Endovascular treatment of unruptured intracranial aneurysms. Interv Neuroradiol 17:420–424, 2011
49. Zacharia BE, Ducruet AF, Hickman ZL, Grobelny BT, Badjatia N, Mayer SA, Berman MF, Solomon RA, Connolly ES Jr: Technological advances in the management of unruptured intracranial aneurysms fail to improve outcome in New York state. Stroke 42:2844-2849,2011