Turk Neurosurg 31(3):301-309, 2021

Review

Received: 10.08.2020
Accepted: 16.11.2020

DOI: 10.5137/1019-5149.JTN.31887-20.3

Published Online: 16.04.2021

Clipping Versus Coiling in Ruptured Basilar Apex Aneurysms: A Meta-Analysis

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ABSTRACT

AIM: To assess the results, effectiveness, safety, and potentials of coiling and clipping of ruptured basilar apex aneurysms.

MATERIAL and METHODS: Included in this study were articles comparisons of outcomes of endovascular coiling and clipping of ruptured basilar apex aneurysms, published in the full-text form (from 1960 to March 31, 2020). Collected variables included: first author's name, country, study period covered, publication year, the total number of patients and follow-up, the early postoperative mortality rate (PostOp-Mo) (30 days from the selecting treatment), permanent neurological deficit (PND), late mortality (LateMo) (after 1 month) and re-intervention (ReInt) (requiring surgery or coiling), for both groups. Outcomes reported by the eligible articles should be evaluated at least 6 months after subarachnoid hemorrhage or intervention (clipping or coiling).

RESULTS: After the preliminary searching, 210 articles were established to be nominees for further investigation. After the application of exclusion and inclusion criteria, there were 9 eligible articles left. The total number of patients was 582 (241 in the clipping group and 341 in coiling). Regarding PostOp-Mo, PND, and LateMo the final results demonstrated no potential significant difference between the two groups. Regarding the subgroup of patients with the ReInt the findings illustrated a statistically significant difference among the two groups [OR 2.33, CI 95%, (1.62– 3.09), Chi^2=0.59 and p=0.001] with no heterogeneity (p=0.79 and I^2=-69.27%).

CONCLUSION: Management complications, recurrences, and reintervention are considerably more frequent in endovascularly treated BX aneurysms.

KEYWORDS: Basilar apex aneurysms, Basilar tip aneurysms, Intracranial aneurysms, Posterior circulation aneurysms, Clipping

INTRODUCTION

In general, vertebrobasilar aneurysms account for at least 5-16% of all intracranial aneurysms and basilar artery apex (BX) aneurysms counting bifurcation or basilar tip and basilar artery-superior cerebellar artery (BA-SCA) aneurysms represent 50% of them (45).

BX aneurysms are anatomically located in one of the most challenging surgical working areas due to their deep and difficult-to-reach position, in addition to their locality to significant cerebrovascular structures (3,5). Lack of microsurgical knowledge in conjunction with the improvement of new endovascular instruments (with lower reported comorbidities and mortality) has decreased open microsurgical clipping of these aneurysms. Therefore, it has been established a directing predisposition for endovascular treatments rather than open microsurgery (11).

Furthermore, two of the landmark multicentered studies (the International Subarachnoid Aneurysm Trial – ISAT and the Barrow Ruptured Aneurysm Trial – BRAT have reported (23,26), when technically possible, that endovascular management

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of posterior circulation aneurysms present better rapid neurological outcome when compared to microsurgery, however, correlated with a certain higher risk of recurrence (which translates into a longer follow-up) than surgical management (16,18,28,35).

Moreover, microsurgical treatment of BX aneurysms is favored by the following factors: large aneurysm size, wide neck, complex morphology, partial thrombosis, incorporation of branching vessels, young patient age, and long life expectancy as well as previously failed endovascular treatment (13,16,28,35,38). Therefore, the identification of a proper subset of patients who could benefit from any of these treatment modalities is required.

Thus, this detailed study aims to assess the results, effectiveness, and potentials between coiling and clipping of ruptured BX aneurysms, and to try to clarify the decision-making process while choosing a treatment modality for patients harboring ruptured BX aneurysms.

MATERIAL and METHODS

Literature Search Strategy

A research protocol was designed to include all characteristics of the conduct of this study. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) were applied for the establishment of protocol and manuscript design (10). The research of the literature was carried out using the Cochrane, Pubmed, and Medline databases (last search on March 31, 2020). To avoid main alterabilities relating to operative procedures, a time filter was applied excluding articles older than 1997. Appropriate keywords and the terms that were sourced from Medical Subject Headings (MeSH) are follows: basilar apex aneurysms; basilar tip aneurysms; intracranial aneurysms; clipping; posterior circulation aneurysms; coiling.

Additionally, we restricted our study to clinical studies and trials, classical articles, multicenter studies, and controlled clinical trials. Also, the references of the investigated publications were manually sourced to recognize other potential eligible manuscripts that would be pertinent. This procedure was reviewed until no further articles were found.

Inclusion and Exclusion Criteria

The PICO (population, intervention, comparison, other) criteria were used to finally be included or excluded for each study: 1. population- limited to patients with ruptured single BX aneurysms; 2. intervention: only microsurgical and endovascular management were used for the treatment of BX aneurysms; 3. comparison: to evaluate the outcomes between the two methods, to refer only to standard coiling technique without extra modified apparatus (such as stent-assisted coiling), to show at least one of the assessed outcomes, for our research to be more homogenized; 4. other: the full-text article was published in English; all articles referring to human adults.

The final aim was to collect a homogenous pool of manuscripts, including prospective and retrospective studies, which would highlight the results of the clipping and coiling of BX aneurysms. Manuscripts were removed from the article pool, when mainly paid attention to reintervention, systematic reviews, case reports, co-morbidities, irrelevant outcome, unestablished techniques, or one of the two methods and all those which established assorted or uncertain results, being dispensed between posterior and anterior circulation. The final article pool enclosed 9 articles (3,7,11,16,22,27,28,35,40) (Table I), which fulfilled our inclusion criteria and were considered appropriate for this meta-analysis (Figure 1).

Data Extraction and Outcomes

Two of the authors independently performed data from the eligible articles. The subsequent general information was

Table I: Design and Baseline Characteristics of Included Trials

Trial, year	Sample size		Mean Age (year)		Percentage of males		PostOp Mo		PND		LaMo		ReInt	
	Clip	Coil	Clip	Coil	Clip	Coil	Clip	Coil	Clip	Coil	Clip	Coil	Clip	Coil
Darsaut TE et al. 2018 (7)	2	2	60.1	58	37	39	0	0	0	1	0	0	0	0
Bohnstedt BN et al. 2017 (3)	24	151	46.8	54.1	23.4	28.6	0	4	1	7	2	7	0	20
Sekhar LN et al. 2013 (35)	24	39	48.8	57.6	0	0	0	0	4	8	0	0	0	12
Jin SC et al. 2009 (16)	28	32	53.6	53.7	16	79	0	6	6	15	0	0	0	9
Taha MM et al. 2006 (40)	8	6	60.2	60.2	28.6	30	0	0	1	2	0	0	0	0
Nagashima H et al. 2004 (27)	76	41	60	54.5	0	0	0	0	17	2	0	1	10	27
Lusseveld E al 2002 (22)	44	44	44.2	47	41	44	5	2	8	3	0	0	0	0
Gruber DP et al. 1999 (11)	15	11	51.4	53.2	33	32	1	0	4	1	0	0	0	4
Nakabayashi K et al. 1997 (28)	20	15	52	52	37	45	2	0	3	1	0	1	0	1

PostOpMo: *Postoperative mortality,* ***PND:*** *Permanent neurologic deficit,* ***LaMo:*** *Late mortality,* ***ReInt:*** *Re-intervention.*

collected: study design, publication year, sample size, first author name, outcomes, and other pertinent data such as: literature quality scores and patient characteristics (39). The articles were prepared and assessed in view of the appropriated criteria (inconsistency was decided through discussion with a third co-author).

In order to compare both treatment modalities, we collected outcome measurements such as early postoperative mortality (within the first 30 days after treatment), permanent neurological deficit (focal or global neurological deficit present after discharge), late mortality (> 30 days after treatment), and the need for re-intervention (either for previously coiled or previously clipped aneurysms). Outcomes reported by the eligible articles should be evaluated at least 6 months after subarachnoid hemorrhage or intervention (clipping or coiling).

Additionally, to decrease the risk of bias in eligible articles, we used a quality assessment tool (Newcastle Ottawa Scale (NOS) (15,39) (Table II).

Statistical Analyses

Statistical analyses were performed using the Stata software (version 16.0 Stata Corp, TX, USA). We estimated the treatment effects using the calculation of the odds ratio (OR), with a 95% interval of confidence (CI) for each study individually. OR were termed as the probability of an incident taking place in the coiling group, separated by the probability of a similar incident occurring in the clipping group. Chi-square test (Chi^2) was used for the detection of heterogeneity ($p<0.10$ or I^2 >50% support heterogeneity. OR values <1 support microsurgical management of the aneurysm (15).

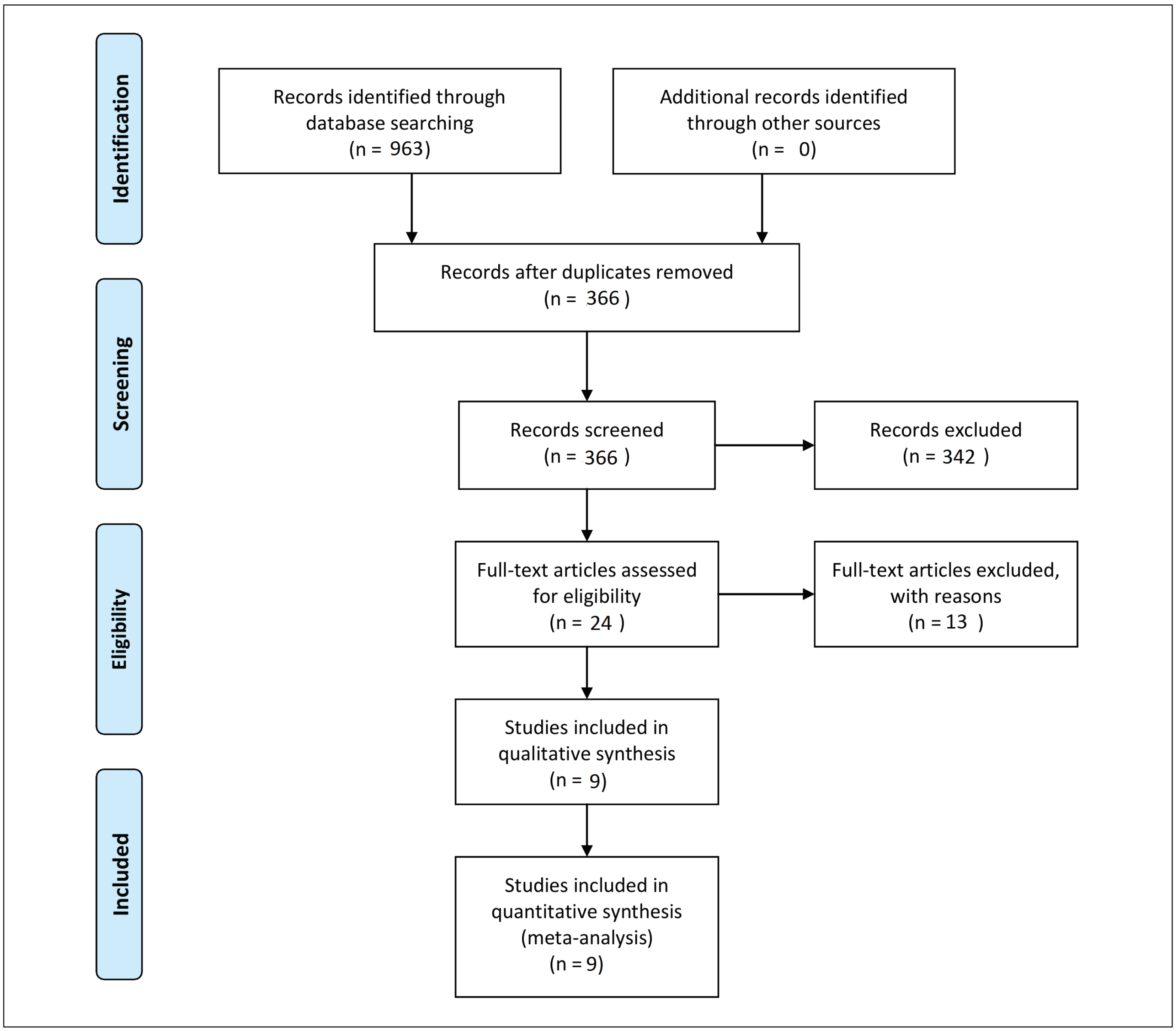

Figure 1: Flow chart.

Table II: Newcastle-Ottawa Scale (NOS) Quality Assessment of Final Article Pool

Trial, year	Study design	Newcastle-Ottawa Scale			
		Selection	Comparability	Exposure	Total Scores
Darsaut T et al. 2018 (7)	Retr	3	3	2	8
Bohnstedt B et al. 2017 (3)	Prosp	3	3	2	8
Sekhar LN et al. 2013 (35)	Retr	2	3	2	7
Jin SC et al. 2009 (16)	Retr	3	3	3	9
Taha M et al. 2006 (40)	Retr	2	3	2	7
Nagashima H et al. 2004 (27)	Retr	3	3	3	9
Lusseveldet E et al. 2002 (22)	Retr	3	3	2	8
Gruber D et al. 1999 (11)	Retr	2	3	3	8
Nakabayashi K et al. 1997 (28)	Retr	3	3	3	9

Retr: *Retrospective,* ***Prosp:*** *Prospective.*

Table III: Meta-Analysis Results

Outcome	Trial	Groups		Overall Effect			Heterogeneity	
		Clip	Coil	Effect Estimate	CI 95%	p	I^2 (%)	p
PostOp Mo	9	8	12	0.17	-0.85–1.19	0.74	-214.0	0.96
PND	9	44	40	0.22	-0.72–0.29	0.40	46.0	0.06
LaMo	9	2	9	0.29	-0.51–1.08	0.48	-9.5	0.50
ReInt	7	10	73	2.36	1.62–3.09	**0.001**	-69.2	0.79

I^2: *Shows the percentage of total variation across studies that is due to heterogeneity rather than chance,* ***CI:*** *Confidence interval,* ***PostOp Mo:*** *Postoperative mortality,* ***PND:*** *Permanent neurologic deficit,* ***LaMo:*** *Late mortality,* ***ReInt:*** *Re-intervention*.

Assessment of Heterogeneity

We assessed heterogeneity by inspecting the graphs and the use of x2, p-value, and I^2 statistics. As the recommendation of the Cochrane Statistical Methods Group (24), a significance level of P-value of heterogeneity was set at 0.1. We interpreted the I^2 value of 50% or greater as high heterogeneity. In the case of heterogeneity, we investigated the reason.

The interstudy heterogeneity was assessed using the Higgins I^2 statistics. The pooled estimates were summarized using the random-effects model and the fixed-effects model otherwise. The results were visualized using OR forest plots. Sensitivity analysis was performed in agreement with the leave-one-out method. Funnel plots were used to demonstrate the potential publication bias.

RESULTS

Search Strategy

A total number of 210 potentially eligible articles were found. After applying all inclusion and exclusion criteria, nine remaining articles were included in the final manuscript pool (3,7,11,16,22,27,28,35,40). In total, this meta-analysis included 582 patients, among them 241 underwent clipping and 341 underwent coiling (Table I).

Early Postoperative Mortality

Of the total group of patients, 20 of the deceased patients were reported as early postoperative mortality (eight patients within the clipping group, and 12 patients in the coiling group) Table I summarizes patients' demographics and complications. However, regarding the total and final results no potential significant difference existed between both groups [OR 0.17, CI 95%, (-0.85– 1.19), Chi^2=0.32 and p=0.74], with no heterogeneity (p=0.96 and I^2=-214.01%) (Figure 2) (Table III).

Permanent Neurological Deficits (PND)

A total of 84 patients suffered from PND, subdivided as follows: 44 patients (clipping group) and 40 patients (coiling group). In this parameter, no significant difference existed between the two groups [OR 0.22, CI 95%, (-0.72– 0.29), Chi^2=1.85 and p=0.40]. A sensitivity analysis was employed using a funnel plot for PND, however, no statistically significant superiority favoring the coiling group in respect to the clipping group existed. This subset had a moderate heterogeneity ($I^{2)}$, and thus low publication bias (p=0.06 and I^2=46%) (Figure 3A, B).

Late Postoperative Mortality

Late postoperative mortality reports were available from seven of the nine retrieved articles. Of this pool of articles,

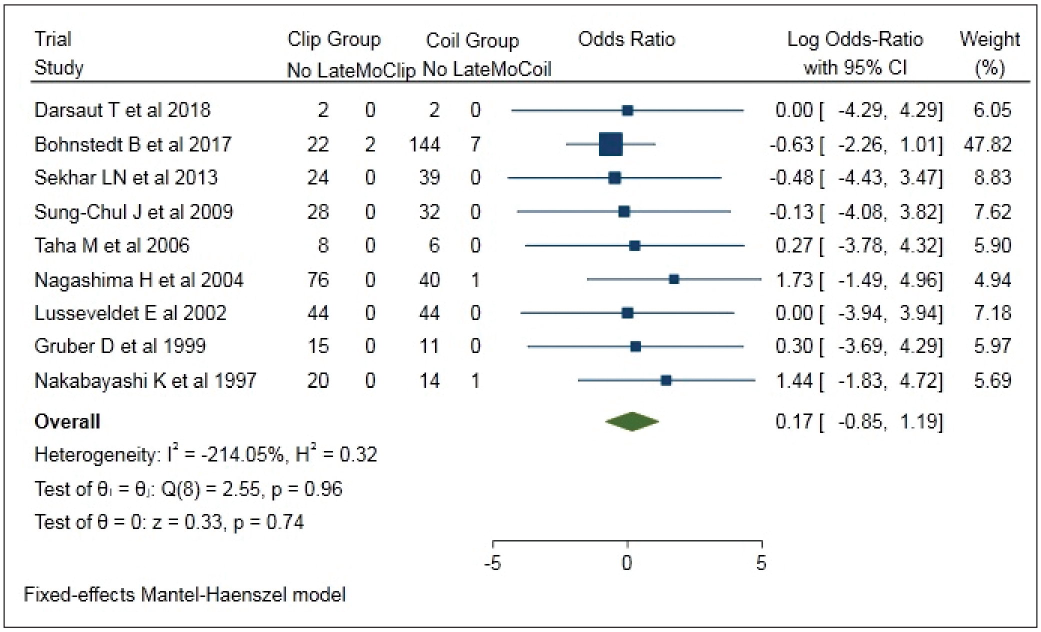

Figure 2: Forest Plot Postoperative Mortality (PostOpMo): Results demonstrate no statistical significant difference between Surgical Clipping and Coiling groups (Odd ratio -[OR 0.17, CI 95%, (-0.85– 1.19), Chi^2=0.32 and p=0.74], with no heterogeneity (p=0.96 and I^2=-214.01%).

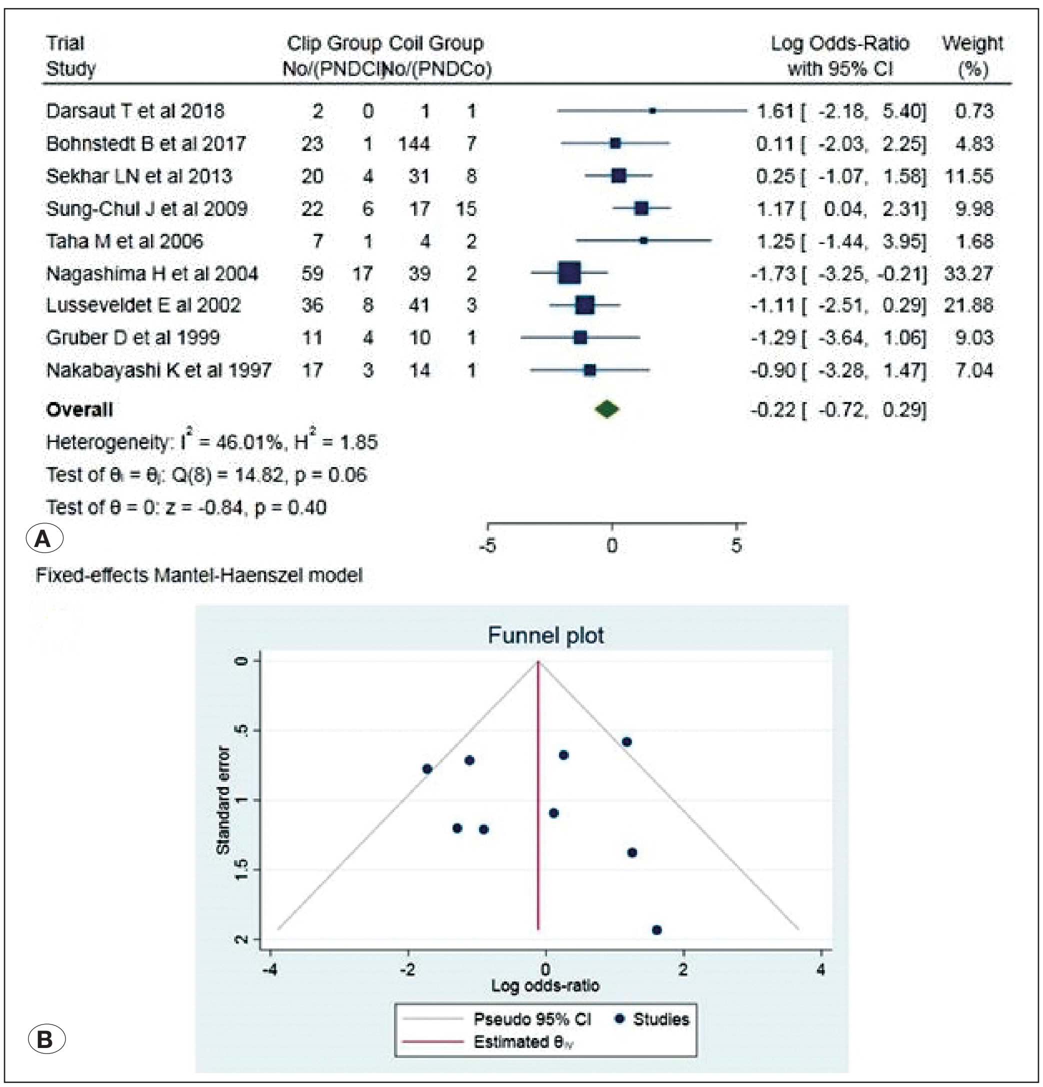

Figure 3: A) Forest Plot Permanent Neurologic Deficit (PND): Results demonstrate no statistically significant difference between the two groups [Odd Ratio-OR 0.22, CI 95%, (-0.72– 0.29), Chi^2=1.85 and p=0.40].

B) Funnel Plot, testing the sensitivity with funnel plot for PND there was no statistically significant superiority of coiling group, with a moderate heterogeneity and thus low publication bias (p=0.06 and I^2=46%).

we identified 11 as late mortality, nine in the coiling group, and two within the clipping group. The results of this sub-analysis demonstrated no significant difference between the two groups [OR 0.29, CI 95%, (-0.51– 1.08), Chi^2=0.91 and p=0.48] with no heterogeneity (p=0.50 and I^2=-9.50%) (Figure 4).

Reintervention

Of the total (n=83) of patients, 73 patients of the coiling group needed reinterventions due to recurrence, whereas the remaining 10 patients requiring reintervention belonged to the clipping group. Regarding this parameter, a statistically significant difference existed between the two groups [OR 2.33, CI 95%, (1.62– 3.09), Chi^2=0.59 and p=0.001] with no heterogeneity (p=0.79 and I^2=-69.27%) (Figure 5A), highlighting the effectiveness of clip occlusion. The funnel plot analysis of this parameter displayed a better dispersion, with very low publication bias (Figure 5B).

DISCUSSION

BX aneurysms represent 5-8% of all brain aneurysms and about 50% of all posterior circulation aneurysms (4,9,44). In general, these aneurysms have poorer outcomes compared to anterior circulation aneurysms and rupture more frequently (45). Therefore, it required more decisive action to treat while managing these aneurysms.

Ruptured BX aneurysms can be managed either by open microsurgical clip placement or through the endovascular process. The recognized disadvantage of open surgical management is its penetration leading to tissue damage and increased surgical morbidity, which seems to be overcome by endovascular procedures, but at the risk of a higher recurrence rate as compared to open surgery (3,7,8,11,13,35,38,40).

Many researchers have estimated treatment results of endovascular and microsurgical management, however, as BX aneurysms are less common than other aneurysm origins, their favorable treatment still remains questionable (1). Therefore, we evaluated the available literature to identify possible benefits of each treatment modality (coiling and clipping) and tried to elucidate a best-practice evidence-based plan while managing patients with ruptured BX aneurysms.

Mortality Rate

Since the introduction of open surgical clip placement and before the acquisition of the microscope, the surgical mortality rate of vertebrobasilar aneurysms was up to 37%, however, after the introduction of microsurgical techniques and microscope, these values decreased to 6-10% (14). Moreover, with the incorporation and advancement of endovascular techniques, these previous percentages have been further reduced to 4 – 8% approximately (19,20,30). Despite these facts, our study demonstrated no superiority between coiling or clipping of ruptured BX aneurysms. This is in line with a previously reported large randomized study, where after a year of treatment (long-term follow-up) no difference between outcomes existed (37). Additionally, it is important to mention that poor preoperative clinical grade and large size of ruptured BX aneurysms are associated with poor outcome, and these patients achieve a better clinical outcome in only 50% of the cases (11).

Morbidity

The main benefit of endovascular management (coiling) over open microsurgery (clipping) is that it is less invasive, thus reducing the risks of procedural-related morbidity (3,11). In our study, no statistical difference existed between these two treatment modalities in a long-term follow-up (Figure 3A, B). These findings are in concordance with several other

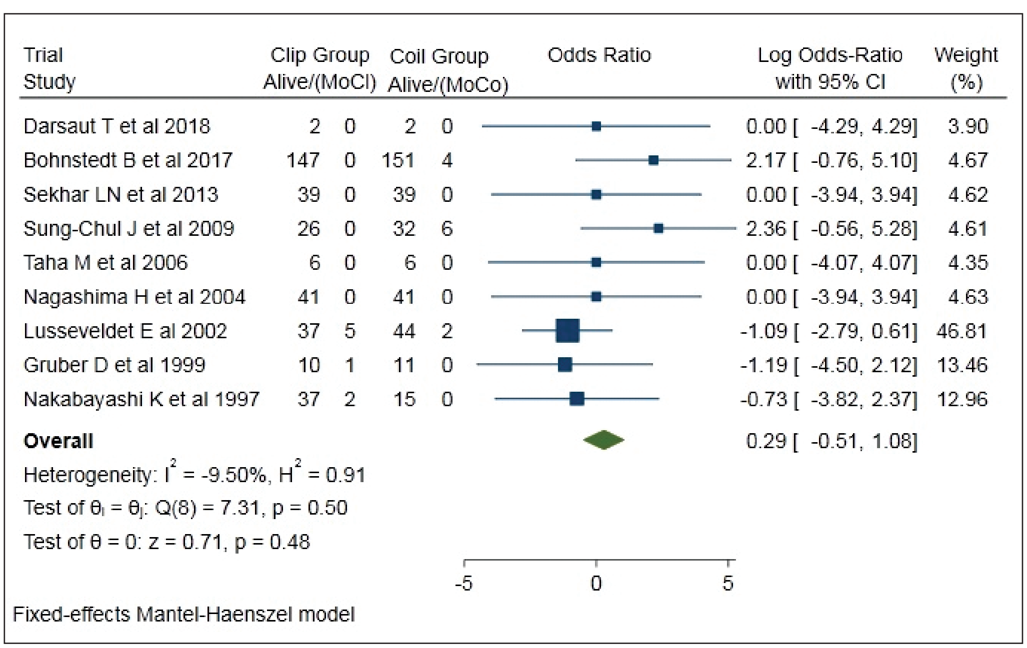

Figure 4: Late Mortality (LateMo): Results demonstrate no statistical significant difference between the two groups [Odd ratio-OR 0.29, CI 95%, (-0.51– 1.08), Chi^2=0.91 and p=0.48] with no heterogeneity (p=0.50 and I^2=-9.50%).

studies with alterable follow-up intervals, which reported no significant difference in the final outcome between both methods (3,25,33,35,37).

It is a fact, that microsurgical treatment is associated with high rates of temporary cranial nerve deficits due to direct manipulation, which improves by 6 months in up to 95% of patients (3,36). It is reasonable to accept the statement reported by a large randomized trial of ruptured aneurysms, where endovascular management of posterior circulation aneurysms was favored at 1-year, however, no statistically significant difference was reported in a long-term follow-up at 10-years (37).

Recurrence Rate and Reintervention

In line with other reports, our study demonstrated that recurrences and residuals were more common in the endovascular treatment (coiling) compared with the microsurgical (clipping) (Figure 5A, B) (3,13,37,38,42). Aneurysms treated in the rupture setting are more likely to have a remnant than when treated in an elective manner.

Coiling alone is the most ideal endovascular procedure in a ruptured situation since anticoagulants are not necessitated preoperatively. Therefore, coiling reduces the risk of associated complications while placing external ventricular drainages or shunts. However, it is assumed that among endovascular modalities, coiling alone has higher recanalization rates as compared to stent-assisted techniques (6). A recent meta-analysis and a long-term follow-up study confirmed the superiority of stent-assisted procedures over coiling alone among recanalization rates (12.7-15% vs 25-7.9%, respectively) (32,42). However, as mentioned previously this could be dangerous due to the possibility of hemorrhagic complications. On the other hand, clipping provides a higher rate of total obliteration (approximately 92% in larger surgical series) (9,29) as well as a lower rate of recurrences (< 1%) (37).

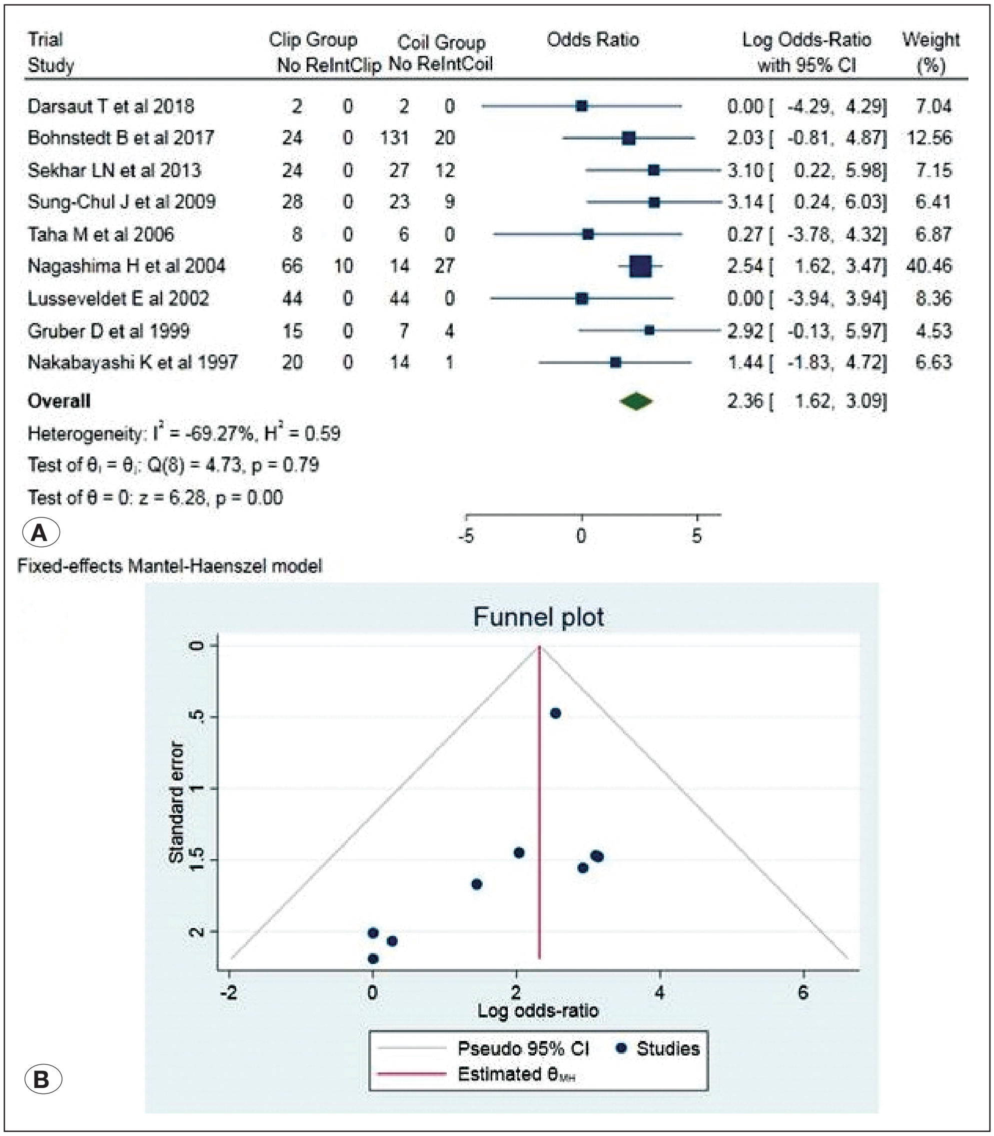

Figure 5: A) Re-intervention (ReInt.): Results demonstrate a statistically significant difference between the two groups [Odd ratio-OR 2.33, CI 95%, (1.62–3.09), Chi^2=0.59 and p=**0.001**] with no heterogeneity (p=0.79 and I^2=-69.27%); **B)** funnel plot of the same parameter, found that displayed better dispersion, with very low publication bias**.**

Based on the aforementioned, after successful clipping of a BX aneurysm, long-term follow-up angiographic and clinical controls are seldom necessary, however, this is considered necessary among patients undergoing endovascular treatment due to their higher recurrence rates and recanalization.

Hunt-Hess Grade as a Predictor of Poor Clinical Outcomes

Presenting Hunt-Hess (HH) grade has long been known to be an independent predictor of clinical outcome, where unruptured and low grade ruptured (HH grade I and II) result in significantly better outcomes than the higher grade. Moreover, given its vicinity to the vital brainstem and diencephalon structures, the ruptured basilar apex aneurysm potentially carries catastrophic consequences regardless of the treatment methods. The evidence from subgroup analysis on high grade HH documented on non-patient-selected studies showed the poor outcome rate [Glasgow Outcome Score (GOS) 1 - 3] varied around 14% - 64% for microsurgical arm (17,21,29,34,41) and 17 - 45% for endovascular procedure (2,12,31).

Treatment Options in Limited Resources Locations

During the last decades, endovascular treatment became rapidly the treatment of choice while dealing with BX aneurysms, mainly due to their easier access and lower procedure-related complications (11). In general terms when technically possible and available, endovascular treatment will be pursued when a multidisciplinary team believes that a coil could be maintained in the sac conveniently with or without balloon reconstruction in the rupture location, or with additional techniques during elective cases. Moreover, young patients (<50 years old), with large, complex shape, partially thrombosed aneurysms, and with long-life expectancy would undergo surgical treatment, since they benefit from a more durable treatment (3,13,37,42). However, these previous treatment-decision plans only apply to the developed world with both modalities available. Endovascular procedures are costly and require special training and equipment (43). Therefore, locations with limited resources or developing countries where endovascular treatment is not possible, surgical treatment should be offered to patients to secure ruptured BX aneurysms and to decrease the risk of rebleeding. However, this requires centralization among cerebrovascular centers and expertise in order to offer the best possible outcome for the patients (13).

CONCLUSION

Surgical clipping of BX aneurysms was related to an increased frequency of early postoperative complications rather than endovascular management. Regardless of this, the clinical outcome at 1-year follow-up was without any statistical difference between patient groups that underwent coil embolization versus clip ligation. However, recurrences, posttreatment residues, and reintervention of BX aneurysms are significantly more frequent among endovascularly treated aneurysms.

ACKNOWLEDGEMENTS

The authors thank Mrs. Alexandra Derek for proofreading, (Hons Bachelor's English literature and Psychology, Canadian citizen).

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