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Microsurgical Clipping Compared with New and Most Advanced Endovascular Techniques in the Treatment of Unruptured Middle Cerebral Artery Aneurysms: A Meta-Analysis in the Modern Era

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Key words
- Aneurysms
- Endovascular
- Flow diverter
- Middle cerebral artery aneurysms
- Stent-assisted coiling
- Surgery
- WEB

Abbreviations and Acronyms
CI: Confidence interval
GOS: Glasgow Outcome Scale
MCA: Middle cerebral artery
MCAA: Middle cerebral artery aneurysm
mRS: Modified Rankin Scale
SAC: Stent-assisted coiling
WEB: Woven EndoBridge

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OBJECTIVE: **Analyzing occlusion, complications rate, and clinical results in unruptured saccular middle cerebral artery aneurysms (MCAAs) comparing clipping with the most advance and newer endovascular techniques.**

METHODS: **We conducted a literature research from January 2009 to December 2018 to evaluate the efficacy and safety of microsurgical clipping or endovascular treatment with new devices (such as Flow-diverter or Woven EndoBridge) in patients with unruptured MCAAs. We extracted data involved: study and intervention features, occlusion rate; time of occlusion assessment; and clinical outcome.**

RESULTS: **A total of 29 studies and 1552 patients with unruptured saccular MCAAs were included in our analysis (464 patients included in the endovascular group, 1088 patients in the surgical group). Overall, the rate of long-term complete/near-complete occlusion was 78.1% (311/405, 95% confidence interval [CI], 69%—87.1%) and 95.7% (113/118, 95% CI, 92%—99.3%) after endovascular and surgical treatments, respectively ($P = 0.001$). The long-term complete occlusion rate was 60% (153/405, 95% CI, 45%—74%) and 95% (112/118, 95% CI, 90%—98%) after endovascular and surgical treatments, respectively ($P = 0.001$). The overall rate of treatment-related complications was 5.6% (33/464, 95% CI, 3.6%—7.7%) and 2.9% (37/1088, 95% CI, 0.8%—5%) among the endovascular and surgical groups, respectively ($P = 0.001$). Endovascular treatments were associated with higher rates of good neurologic outcome (283/293 [97%], 95% CI, 95%—98% vs. 570/716 [84%], 95% CI, 67%—98%; $P = 0.001$). No difference was found for the mortality (3/464 [1.5%], 95% CI, 0.4%—2.6% vs. 1/1088, 95% CI, 0.1%—0.6%; $P = 0.5$).**

CONCLUSIONS: **Treatment-related complication and mortality are comparable among these techniques and the risk of aneurysm rupture seems very low for both strategies. The endovascular approach seems to increase the probability of good functional outcome after treatment, compared with surgery.**

INTRODUCTION

Rapid technological advances in endovascular neurosurgery have shaped treatment of intracranial aneurysms in the past 3 decades. The main limitation of endovascular surgery for complex and wide-neck aneurysms has been the risk of recurrence and risks associated with compromise of the parent artery and/or arterial branches incorporated in the neck of the aneurysm. With the availability of newer and more advanced devices used as stand-alone tools or in combination, aneurysms with complex geometry and a wide neck can be effectively treated with endovascular techniques.[1-3] These rapid changes are leading to a paradigm shift in the treatment of middle cerebral artery aneurysms (MCAAs), which for a long time have been considered to be better treated with open surgical clipping. Because of the rapidly changing field, there are scant data on the overall effectiveness of newer tools and techniques in the endovascular treatment of MCAAs compared with surgical clipping. The objective of this meta-analysis is to compare clipping of unruptured MCAAs with the most up-to-date endovascular techniques (i.e., stent-assisted coiling [SAC], flow diverter, and endosaccular devices) in terms of occlusion, complications rate, and clinical results.

Table 1. Quality Measure of Included Studies by the Modified Newcastle-Ottawa Quality Criteria Assessment Scale

	Selection				Comparability		Outcome/ Exposure			
Study Name	**1**	**2**	**3**	**4**	**a (Not Tested)**	**b**	**1**	**2**	**3**	**Total**
Endovascular retrospective design (score 0—8)										
Bhogal et al., 2017[4]	*	*				*	*		*	5
Möhlenbruch et al., 2017[5]	*	*				*	*		*	5
De Vries et al., 2013[6]	*	*					*		*	4
Iosif et al., 2017[7]	*	*				*	*		*	5
Gory et al., 2017[8]	*	*					*		*	4
Kim et al., 2011[9]	*	*				*	*		*	5
Mühl-Benninghaus et al., 2017[10]	*	*					*		*	4
Yang et al., 2010[11]	*	*				*	*		*	5
Topcuoglu et al., 2015[12]	*	*				*	*		*	5
Gory et al., 2015[13]										
Akgul et al., 2015[14]	*	*					*		*	4
Gawlitza et al., 2016[15]	*	*				*	*		*	5
Cekirge et al., 2011[16]	*	*					*		*	4
Fields et al., 2013[17]	*	*				*	*		*	5
Johnson et al., 2013[18]	*	*				*	*		*	5
Yavuz et al., 2014[19]	*	*				*	*		*	5
Endovascular prospective design (score 0—8)										
Möhlenbruch et al., 2017[5] (flow diverter)	*		*	*		*	*	*	*	7
Möhlenbruch et al., 2014[20] (stent-assisted coiling)	*		*	*		*	*	*	*	7
Aguilar Perez et al., 2017[21]	*		*	*		*	*	*	*	7
Briganti et al., 2016[22]	*		*	*		*	*	*	*	7
Pierot et al., 2013[23]	*		*	*		*	*	*	*	7
Surgical retrospective design (score 0—8)										
Yeon et al., 2011[24]	*	*				*	*		*	5
Morgan et al., 2010[25]	*	*					*		*	4
Nanda et al., 2017[26]	*	*					*		*	4
Chung et al., 2015[27]	*	*					*		*	4
Diaz et al., 2014[28]	*	*				*	*		*	5
Surgical prospective design (score 0—8)										
Haug et al., 2009[29]	*		*	*		*	*	*	*	7
Tenjin et al., 2016[30]	*		*	*		*	*	*	*	7
Bruneau et al., 2016[31]	*		*	*		*	*	*	*	7

METHODS

Literature Search

A systematic search was conducted using the PubMed, Scopus, and Cochrane databases from January 2009 to December 2018; to complete a comprehensive search of the English-speaking literature, a combination of MeSH (Medical Subject Heading) terms was used to identify all relevant studies evaluating the efficacy and safety of microsurgical clipping or endovascular treatment with new techniques in patients with unruptured saccular MCAAs, including: "MCA aneurysm," "middle

Table 2. Studies Included in the Meta-Analysis

	Authors	Technique/ Devices	Study	Endovascular Treatment				Surgical Treatment				Years	Country
				Number of Patients	Number of Selected Patients	Number of Aneurysms	Combined Devices Treatment	Number of Patients	Number of Selected Patients	Number of Aneurysms	Combined Devices Treatment		
1	Bhogal et al., 2017[4]	Flow diverter	R	13	9	9	0	—	—	—	—	2010—2016	Europe
2	Möhlenbruch et al., 2017[5]	Flow diverter	R	47	4	5	0	—	—	—	—	2015—2016	United States
3	De Vries et al., 2013[6]	Flow diverter	R		3	3	0	—	—	—	—	2010—2012	Asia
4	Iosif et al., 2017[7]	Flow diverter	R	58		63	8	—	—	—	—	2010—2014	SA
5	Gory et al., 2017[8]	pConus	R	40	38	38	0	—	—	—	—	2012—2014	Europe
6	Kim et al., 2011[9]	48 coils; 14 balloon —assisted13 SAC	R	103	70	75	—	—	—	—	—	2000—2009	Asia
7	Yeon et al., 2011[24]	Clipping	R	—	—	—	—	85	85	91	—	2005—2007	Asia
8	Morgan et al., 2010[25]	Clipping	R	—	—	—	—	263	263	280	—	1989—2009	Oceania
9	Nanda et al., 2017[26]	Clipping	R	—	—	—	—	221	—	67	0	2000—2016	United States
10	Mühl-Benninghaus et al., 2017[10]	SAC	R	17		9	1	—	—	—	—	2015—2016	Europe
11	Möhlenbruch et al., 2014[20]	SAC	P	22	5	5	0	—	—	—	—	2012—2013	Europe
12	Haug et al., 2009[29]	Clipping	P	—	—	—	—	37	15	15	—	2005—2006	Europe
13	Yang et al., 2010[11]	SAC	R	16	5	5	1	—	—	—	—	2003—2009	Asia
14	Aguilar Perez et al., 2017[21]	Flow disruptor	P	15	3	3	0	—	—	—	—	2015—2016	Europe
15	Tenjin et al., 2016[30]	Clipping	P	—	—	—	—	—	14	14	—	2013—2015	Asia
16	Topcuoglu et al., 2015[12]	Flow diverter	R	29	14	14	3				—	2010—2015	Europe

SAC, stent-assisted coiling; R, retrospective; P, prospective.

Continues

Table 2. Continued

	Authors	Technique/ Devices	Study	Endovascular Treatment: Number of Patients	Endovascular Treatment: Number of Selected Patients	Endovascular Treatment: Number of Aneurysms	Endovascular Treatment: Combined Devices Treatment	Surgical Treatment: Number of Patients	Surgical Treatment: Number of Selected Patients	Surgical Treatment: Number of Aneurysms	Surgical Treatment: Combined Devices Treatment	Years	Country
17	Bruneau et al., 2016[31]	Clipping	P		—	—	—	183	75	75	0	2001–2012	Europe
18	Gory et al., 2015[13]	pConus	P	40	38	38	2	—	—	—	—	2012–2014	Europe
19	Akgul et al., 2015[14]	SAC	R	20	7	7	7	—	—	—	—		Europe
20	Gawlitza m et al., 2016[15]	Flow diverter	R	17	6	7	0	—	—	—	—	2010–2014	Europe
21	Feng et al., 2015[32]	SAC	R	37	18	13	0	—	—	—	—	2013–2014	Asia
22	Chung et al., 2015[27]	Clipping	R	—	—	—	—	416	416	416		2003–2014	Asia
23	Cekirge et al., 2011[16]	SAC	R	8	4	4	4	—	—	—	—	—	Africa
24	Diaz et al., 2014[28]	Clipping	R	—	—	—	—	34	24	29	—	2005–2010	United States
25	Briganti et al., 2016[22]	Flow diverter	P	15	15	15	1	—	—	—	—	2010–2013	Europe
26	Fields et al., 2013[17]	SAC	R	22	22	22	0	—	—	—	—	2004–2009	United States
27	Johnson et al., 2013[18]	SAC	R	91	91	100	16	—	—	—	—	2002–2012	United States
28	Pierot et al., 2013[23]	Flow disruptors	P	33	28	29	5	—	—	—	—	2010–2012	Europe
29	Yavuz et al., 2014[19]	Flow diverter	R	21	21	25	2	—	—	—	—	—	Europe

SAC, stent-assisted coiling; R, retrospective; P, prospective.

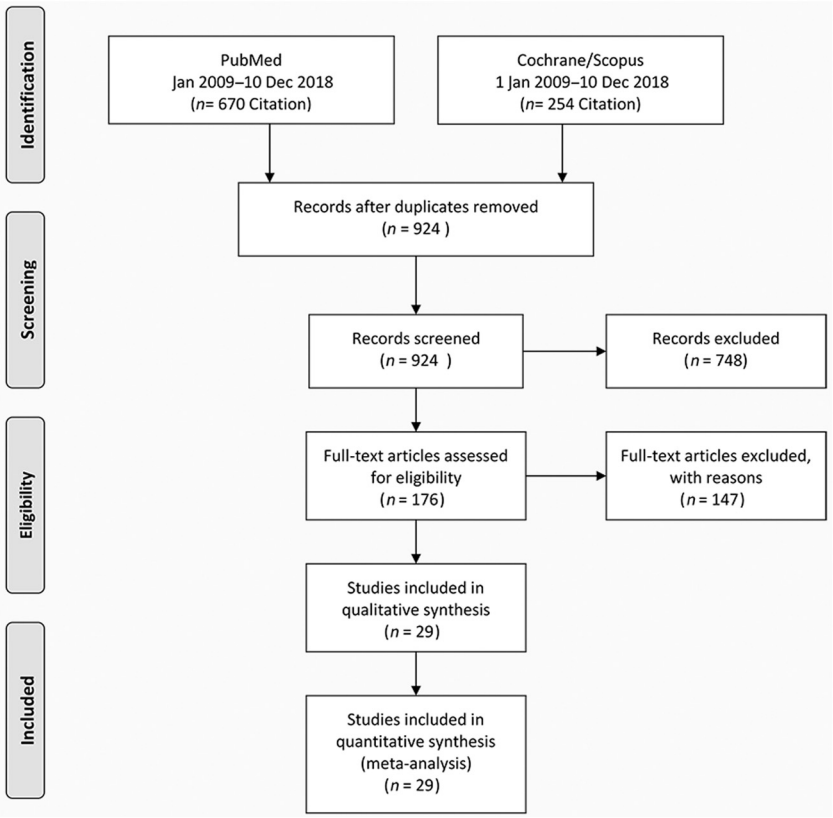

Figure 1. PRISMA diagram detailing the specifics of the systematic literature review.

cerebral artery aneurysms," "endovascular," "microsurgery," "clipping," "coiling," "flow diversion," "WEB device," "p-conus," and "stent assisted-coil." Studies were included if they 1) reported clipping or endovascular treatment with aforementioned techniques, outcomes for adult patients (or a subgroup) with unruptured saccular MCAAs; 2) reported occlusion rates, neurologic morbidity, or both; 3) measured efficacy by complete occlusion of the aneurysm shown by digital subtraction angiography, computed tomography angiography, or magnetic resonance angiography (primary outcome); 4) measured safety with the modified Rankin Scale (mRSo (score 0–3) or the Glasgow Outcome Scale (GOS) (score 4–5) (secondary outcome); and 5) were published between 2009 and 2018. Modern endovascular techniques were considered flow diversion, SAC, treatment with intrasaccular flow disruptors (Woven EndoBridge [WEB; Sequent Medical, Aliso Viejo, California, USA], or Medina devices [Medtronic, Dublin, Ireland]), and pConus (Phenox, Bochum, Germany). Studies were excluded if they: 1) were not English studies; 2) were studies conducted on animal models; 3) were articles that reported both procedures in a single patient; 4) reported ruptured MCAAs; 5) reported dissecting or fusiform aneurysms; 6) included simple coiling technique; 7) included <3 patients; or 8) were systematic reviews, review articles, or meta-analyses. We collected data about treatment technique; number of patients and number of selected patients; number of aneurysms; number of combined device treatments; minor and major complications; intraoperative rupture; intraoperative and late mortality; rebleeding rate; clinical and radiologic results and follow-up at short (0–3 months), medium (6–12 months), and long (>12 months) term; retreatment rate; year of treatment; and country.

Titles and abstracts were screened and potentially relevant articles were selected for full-text evaluation, which was performed independently by 2 investigators. Discrepancies were resolved by the senior authors. Moreover, study quality was evaluated using the modified Newcastle-Ottawa Scale (**Table 1**; **Supplementary Material**). The investigated outcomes were analyzed with the random-effect meta-analysis because this model incorporates heterogeneity among studies.

The primary objective of this study was to determine the clinical and angiographic outcomes of patients treated with endovascular procedures or surgery. The secondary objective was to determine minor and major complications and mortality in the endovascular and surgical groups and the clinical outcome in relation to the technique used.

Data Extraction

Extracted data included study characteristics (publication year; country of origin; sample size; study design; number of aneurysms; and study duration), intervention characteristics (surgery type), efficacy results (number of complete occlusions for coiling or clipping and time of occlusion assessment), and safety outcome (mRS score and GOS score and assessment time of mRS or GOS). Data extraction was conducted independently by 2 investigators. Discrepancies were resolved by the senior authors.

Statistical Analysis

We estimated, from each cohort, the cumulative prevalence (percentage) and 95% confidence interval (CI) for each outcome. Heterogeneity of the data was assessed by the Higgins index (I^2) and, subsequently, the DerSimonian and Laird random-effects model was applied. The graphic representation was performed by forest plot. To evaluate the source of heterogeneity, a subgroup analysis was performed. To assess the risk of bias, the funnel plot followed by the Egger linear regression test was evaluated. To verify the consistency of outcome meta-analysis results, the influence of each individual study on the summary effect estimate was assessed by the sensitivity analysis ("leave-one-out" approach). To compare the percentages of each groups and to calculate the *P* values, the z test was used when appropriate.

Table 3. Procedure-Related Outcomes After Endovascular and Surgical Treatments of Unruptured Saccular Middle Cerebral Artery

Variables	Endovascular Group, n/N (%) (Range), I^2 (%)	Number of Articles	Surgical Group, n/N (%) (Range), I^2	Number of Articles	*P* Value*
Angiographic outcomes					
Long-term complete/near-complete occlusion rate	311/405 (78.1) (69—87.1), 88.5	19	113/118 (95.7) (92—99.3), 0	3	0.001
Long-term complete occlusion rate	153/405 (60) (45—74), 92	19	112/118 (95) (90—98), 0	3	0.001
Immediate complete/near-complete occlusion rate	298/457 (65) (45—84), 97	19	157/185 (88.5) (77—99), 87	4	0.001
Immediate complete occlusion rate	152/457 (31.5) (19—43), 91	19	151/185 (86.3) (72—99), 89	4	0.001
Retreatment rate	24/439 (6) (2.4—9.7), 70	17	2/133 (1) (0.1—2.6), 0	4	0.01
Endovascular occlusion					
Flow diverters	116/132 (84.3) (72—96), 85 (7 studies)				NA
pConus	38/76 (50) (87—91), 90 (2 studies)				
SAC	132/165 (82) (76—88), 0 (7 studies)				
Flow disruptor	25/32 (8) (64—92), 0 (2 studies)				
Clinical outcomes and procedure-related complications					
Overall rate of procedure-related complications	33/464 (5.6) (3.6—7.7), 0	21	37/1088 (2.9) (0.8—5), 0	8	0.001
Minor complications rate	20/464 (2.9) (1.4—4.3), 0	21	0/672 $I^2 = 0$	7	0.001
Major complications rate	13/464 (1.8) (0.6—3), 0	21	22/672 (2.9) (0.5—5.4), 0	7	0.6
Intraoperative rupture/perforation	3/489 (1.1) (0.2—2), 0	21	6/987 (0.2) (0.1—0.5), 0	8	0.9
Mortality	3/464 (1.5) (0.4—2.6), 0	21	1/1088 (0.3) (0.1—0.6), 0	8	0.5
Good outcome rate	283/293 (97) (95—98), 0	15	570/716 (84) (67—98), 0	5	0.001
Endovascular complications					
Flow diverters	11/131 (7.3) (3—11.7), 0 (8 studies)				NA
p-Conus	3/76 (3.5) (0.6—7.7), 0 (2 studies)				
SAC	15/226 (5.4) (2.5—8.3), 0 (9 studies)				
Flow disruptor	4/31 (14) (2—26), 0 (2 studies)				

SAC, stent-assisted coiling.
*The 2-proportions *z* test has been used.

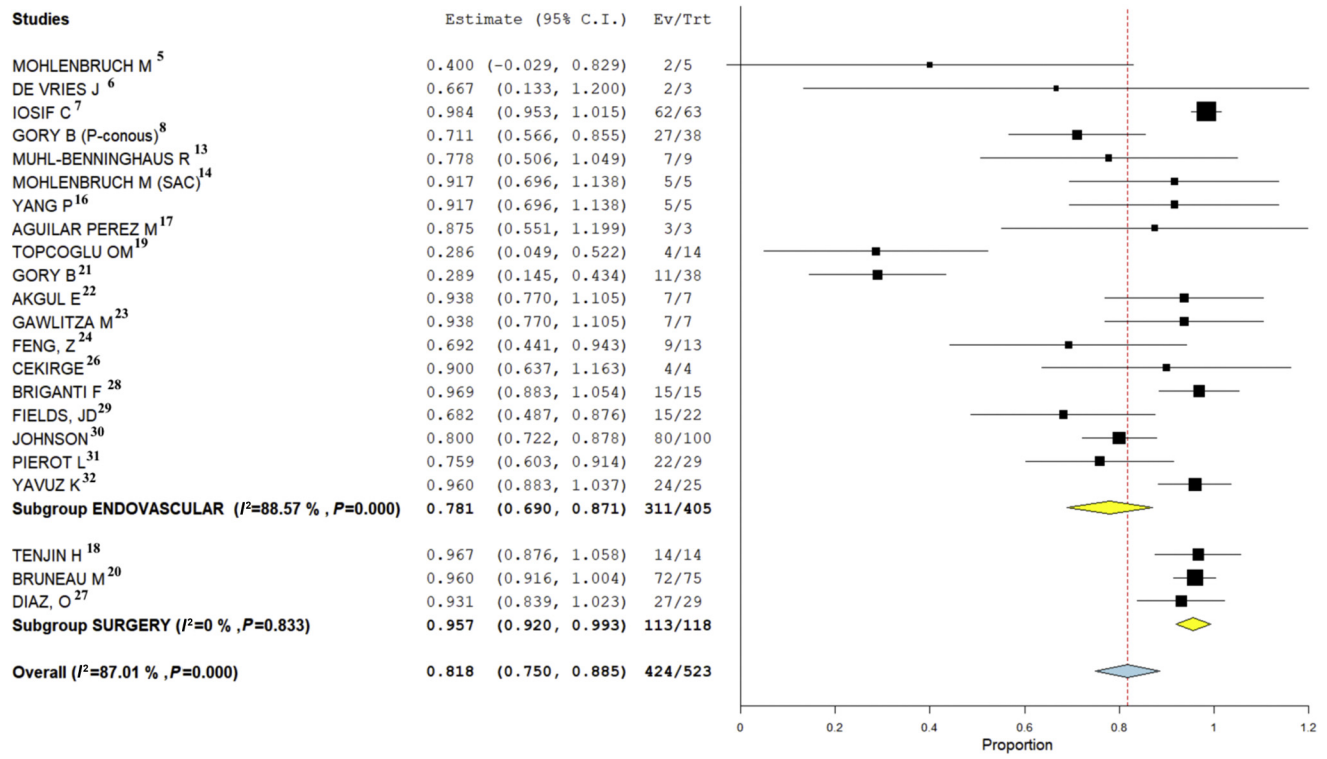

Figure 2. Forest plot with random-effect model showing the overall rate of complete/near-complete occlusion after endovascular and surgical group. C.I., confidence interval; Ev/Trt, endovascular and surgical treatments.

Statistical significance was set at $P < 0.05$. Meta-analysis was performed with ProMeta-2 (Internovi, Cesena, Italy) and OpenMeta-Analyst (MetaMorph Inc., Nashville, Tennessee).

RESULTS

Literature Review

Studies included in our meta-analysis are summarized in Table 2. The search flow diagram is shown in Figure 1. A total of 29 studies and 1552 patients with unruptured saccular middle cerebral artery (MCA) were included in our review.[4-32] Overall, 464 patients were treated with endovascular strategies (endovascular group), whereas 1088 patients (surgical group) were treated with surgical clipping. Twenty-one studies reported endovascular techniques (8 flow diversion series, 2 studies of flow disruption with WEB and Medina devices, 2 series of PConus, and 9 studies reporting SAC strategy); 8 studies reported surgically treated patients with clipping technique.

Quality of Studies

There were 8 studies presenting a prospective design, and 21 retrospective series. Among the 21 endovascular series, 24% (5 studies) were prospective, whereas among the 8 surgical series, 62% (5 studies) were prospective. Overall, 20 studies were rated "high quality" based on the Newcastle-Ottawa quality assessment criteria (Table 1). Among the endovascular group, 71% of the studies were rated high quality (15 series), whereas among the surgical literature 62% (5 studies) were rated high quality. In general, the endovascular literature included in our review presented a higher number of small and retrospective series, compared with the surgical studies.

Angiographic Outcomes

Overall, the rate of long-term complete/near-complete occlusion was 78.1% (311/405; 95% CI, 69%–87.1%; $I^2 = 88.4\%$) and 95.7% (113/118; 95% CI, 92%–99.3%; $I^2 = 0\%$) after endovascular and surgical treatments, respectively ($P = 0.001$) (Table 3 and Figure 2). The funnel plot, followed by the Egger linear regression test, excluded publication bias although the test showed a tendency toward publication bias ($P = 0.06$) likely related to the presence of small series (Figure 3A). Meta-regression showed a nonsignificant variation of the effect size ($P = 0.4$) over the investigated period (Figure 3B). The sensitivity analysis showed the influence of individual studies on the occlusion rate (Figure 3C). Because of the low numbers in the studies (3 series), funnel plot, sensitivity, and meta-regression were not performed for the occlusion rate among the surgical group. Long-term complete occlusion rate was 60% (153/405; 95% CI, 45%–74%; $I^2 = 92\%$) and 95% (112/118; 95% CI, 90%–98%; $I^2 = 0\%$) after endovascular and surgical treatments, respectively ($P = 0.001$). Endovascular immediate complete/near-complete occlusion rate

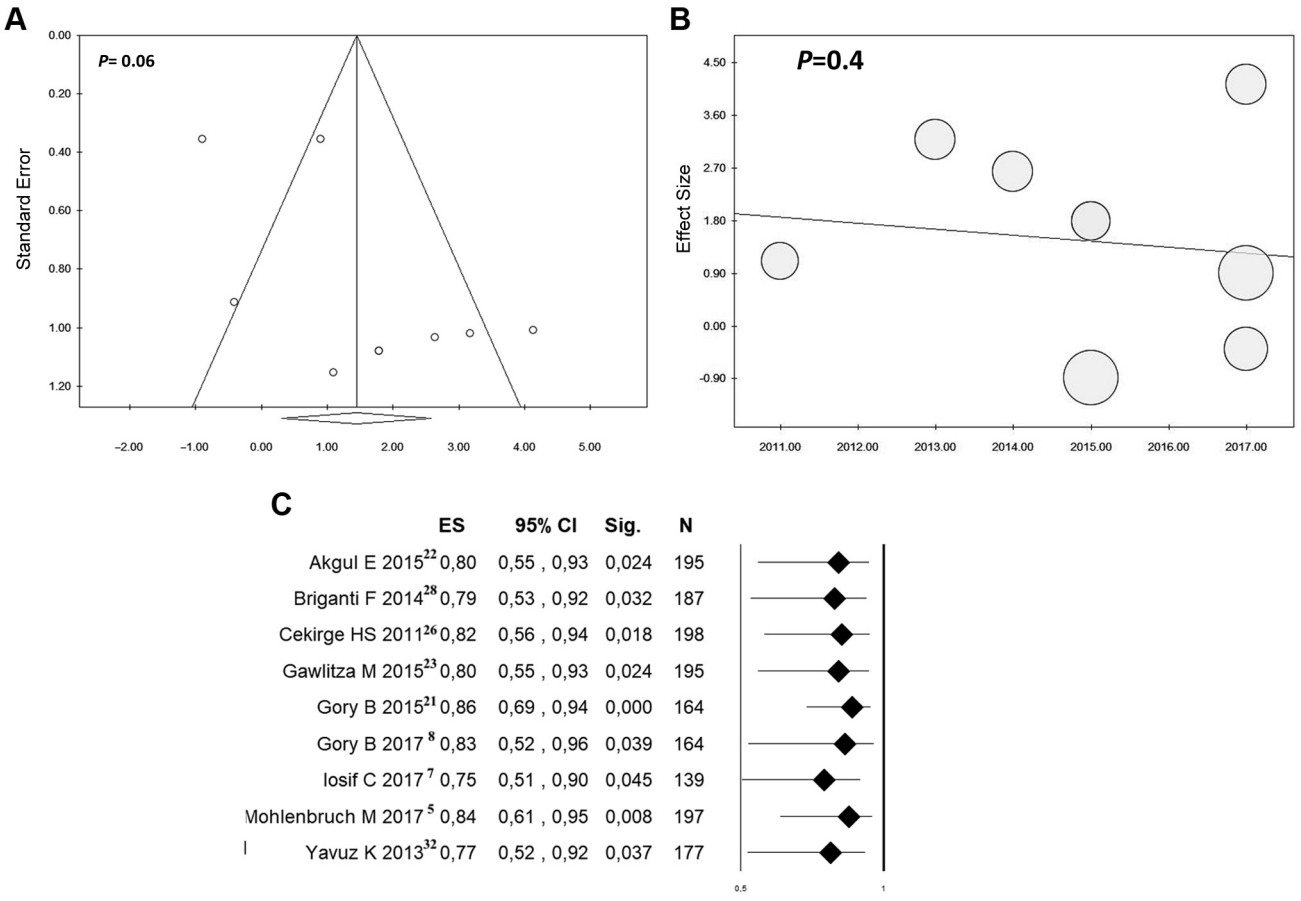

Figure 3. Angiographic long-term adequate occlusion among the endovascular group. The funnel plot followed by Egger linear regression test reasonably excludes publication bias although a trend toward a risk of bias was detected ($P = 0.06$) (**A**). Meta-regression showed an insignificant variation of the effect size (**B**) over the investigated years. The sensitivity analysis showing the influence of each individual study on the explored outcome (**C**). ES, effect size; CI, confidence interval; Sig, significance.

was 65% (298/457; 95% CI, 48%–84%; $I^2 = 97\%$), whereas surgical immediate adequate occlusion rate was 88.5% (157/185; 95% CI, 77%–99%; $I^2 = 87\%$) ($P = 0.001$). Immediate complete occlusion after treatment was achieved among 31.5% (152/457; 95% CI, 19%–43%; $I^2 = 91\%$) and 86.3% (151/185; 95% CI, 72%– 99%; $I^2 = 89\%$) of patients undergoing endovascular and surgical procedures, respectively ($P = 0.001$). Retreatment rate was 6% (24/439; 95% CI, 2.4%–9.7%; $I^2 = 70\%$) and 1% (2/133; 95% CI, 0.1%–2.6%; $I^2 = 88.4\%$) after endovascular and surgical treatment, respectively ($P = 0.01$). The highest adequate occlusion rates were achieved after flow diversion (157/185 [84.3%]; 95% CI, 72%–96%; $I^2 = 85\%$), and SAC (132/165 [82%]; 95% CI, 76%–88%; $I^2 = 0\%$), followed by flow disruptors (25/32 [78%]; 95% CI, 64%–92%; $I^2 = 0\%$), and treatment with pConus (38/76; 95% CI, 87%–91%; $I^2 = 90\%$) (Table 3 and Figure 4).

Clinical Outcomes and Procedure-Related Complications

The overall rate of treatment-related complications was 5.6% (33/464; 95% CI, 3.6%–7.7%; $I^2 = 0\%$) and 2.9% (37/1088; 95% CI, 0.8%–5%; $I^2 = 0\%$) among the endovascular and surgical groups, respectively ($P = 0.001$) (Figure 5). Funnel plot, sensitivity analysis, and meta-regression are reported in Figures 6 and 7 for the endovascular and surgical outcomes, respectively. The Egger linear regression test excluded publication bias, whereas meta-regression, investigating the rate of complication over the studied period, showed a significant decrease of the adverse events among the surgical group (Figure 6B). Minor complications were 2.9% (20/464; 95% CI, 1.4%–4.3%; $I^2 = 0\%$) after endovascular procedures, whereas no minor events were reported among the surgical group. Major complications were comparable among the 2 groups (13/464 [1.8%]; 95% CI, 0.6%–3%; $I^2 = 0\%$ vs. 22/672; 95% CI, 0.5%–5.4%; $I^2 = 0\%$; $P = 0.6$), as well as the rate of intraoperative rupture/perforation (3/489 [1.1%]; 95% CI, 0.2%–2%; $I^2 = 0\%$ vs. 6/987; 95% CI, 0.1%–0.5%; $I^2 = 0\%$; $P = 0.9$) (endovascular vs. surgery). In addition,

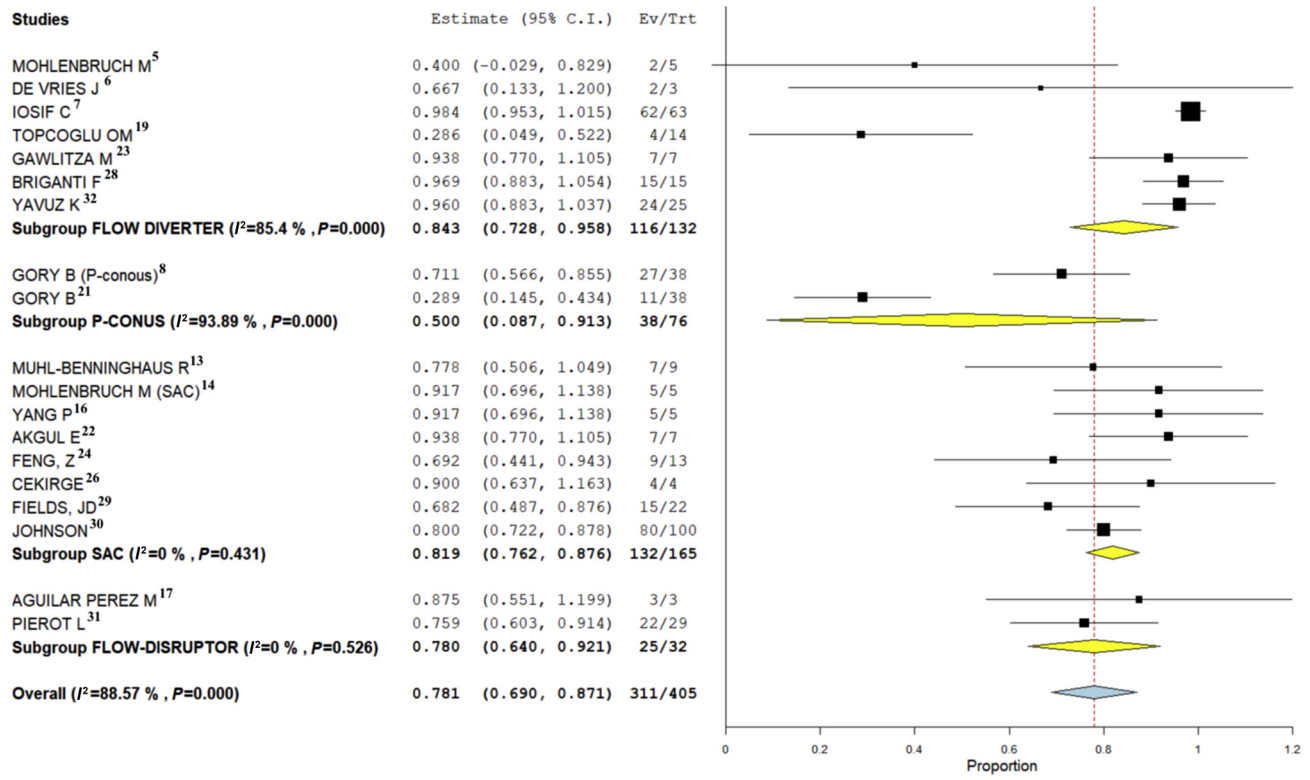

Figure 4. Forest plot with random-effect model showing the subgroup analysis of the occlusion rates after treatment with flow diversion, pConus, stent-assisted coiling, and flow disruptor. C.I., confidence interval; Ev/Trt, endovascular and surgical treatments.

no difference was found for mortality (3/464 [1.5%]; 95% CI, 0.4%– 2.6%; I^2 = 0% vs. 1/1088; 95% CI, 0.1%–0.6%; I^2 = 0%; P = 0.5). Endovascular treatments were associated with higher rates of good neurologic outcome (283/293 [97%]; 95% CI, 95%–98%; I^2 = 0% vs. 570/716 = 84%; 95% CI, 67%–98%; I^2 = 0%; P = 0.001). Procedure-related complications were comparable in relation to the different devices, although flow disruptors were associated with 14% (4/31; 95% CI, 2%–26%; I^2 = 0%) of adverse events, compared with 7.3% (11/131; 95% CI, 3%–11.7%; I^2 = 0%), 5.4% (15/226; 95% CI, 2.5%–8.3%; I^2 = 0%), and 3.5% (3/76; 95% CI, 0.6%–7.7%; I^2 = 0%) for flow diversion, SAC, and pConus, respectively (Table 3 and Figure 8).

Study Heterogeneity

Substantial heterogeneity (>50%) was noted for the angiographic outcomes after endovascular treatments. When the subgroup analysis was performed, heterogeneity was low (0%) among the SAC and flow disruptor groups, whereas it seemed still high among the flow diversion and pConus groups. Surgical outcomes presented low rates of heterogeneity. Heterogeneity was low also among the investigated clinical outcomes, after both endovascular and surgical treatments.

DISCUSSION

The state of knowledge regarding the natural history of unruptured intracranial aneurysms does not satisfy the increasing demand; the incidence of intracranial aneurysm in the population is higher than that of subarachnoid hemorrhage, so in the management of intracranial aneurysms, it is essential to offer patients the best treatment option. Although there is still a place for microsurgical clipping, the role of endovascular treatment, even in the management of MCA aneurysms, has changed.

In this meta-analysis comparing surgical treatment of unruptured saccular MCA aneurysms with newer endovascular devices, we found that, despite recent innovation, surgical treatment continues to be associated with higher rates of immediate and long-term complete occlusion. However, the gap between the 2 techniques in affording durable occlusion of the aneurysm is narrowing as newer tools are introduced in clinical practice. Major complication rates and mortality are similar between the 2 methods. Modern management of unruptured MCAAs includes surgical and endovascular options, each of which provide significant advantages and disadvantages. Over the last few years, there has been a remarkable evolution in terms of technique and endovascular devices (Figure 9). The introduction of flow diverters first and intrasaccular devices afterward has potentially expanded the

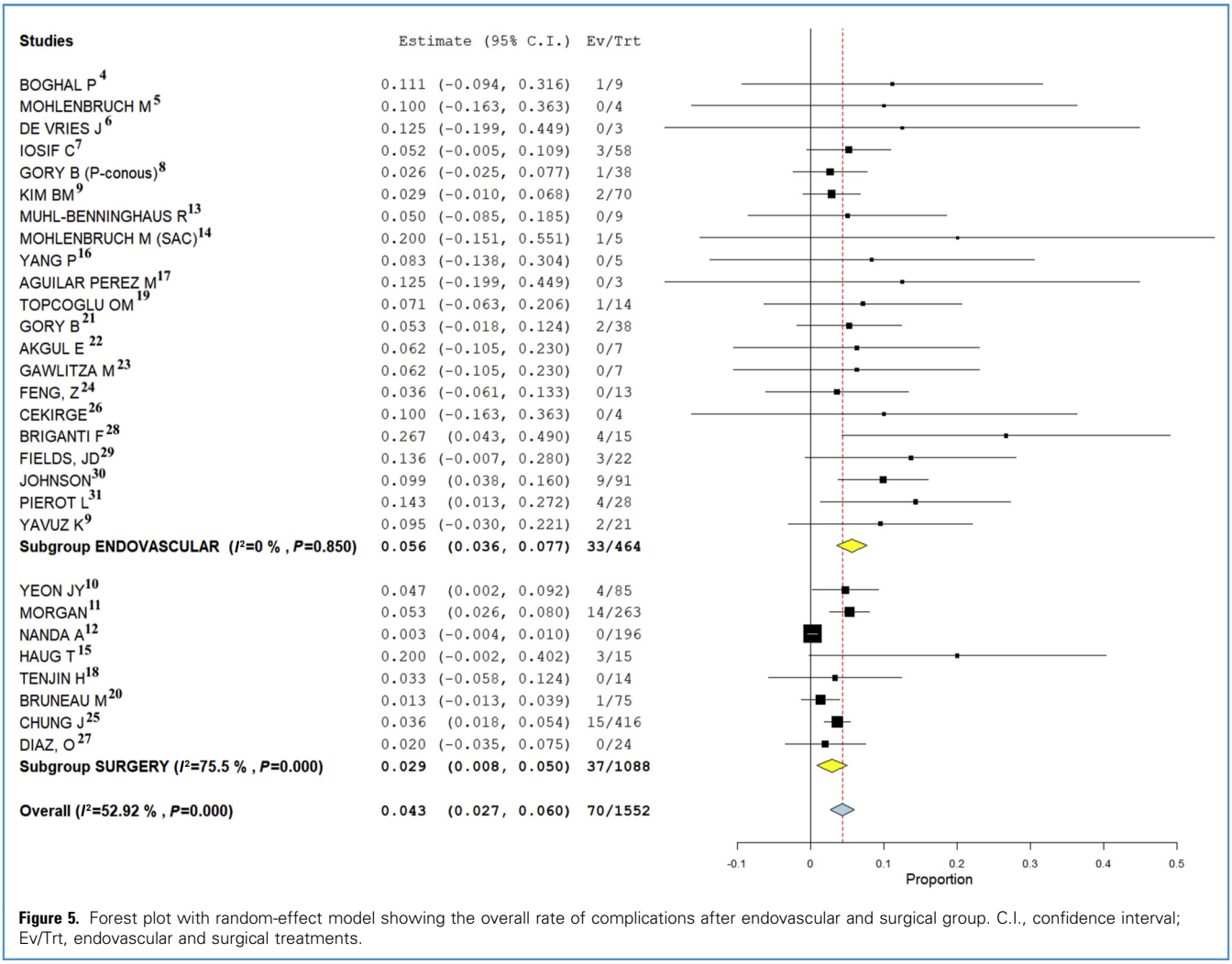

Figure 5. Forest plot with random-effect model showing the overall rate of complications after endovascular and surgical group. C.I., confidence interval; Ev/Trt, endovascular and surgical treatments.

armamentarium of tools available to endovascular neurosurgeons. Until now, studies have compared surgical clipping with coil embolization without considering some of the most recent advances. Although our analysis confirms previous similar studies confirming a lower rate of recanalization after surgical therapy, it seems that newer endovascular tools have represented a step in the correct direction. In a meta-analysis, comparing surgical clipping with simple coiling for MCA aneurysms, Smith et al.[33] reported recanalization rates of 51.8% (vs. 97% for surgery) after simple coiling. More recently, Alreshidi et al.[34] reported only a 53% rate of complete exclusion after coiling, in contrast to 94.2% for surgery. As endovascular techniques other than simple coiling have been applied to treatment of MCAAs, occlusion rates have improved. In a study that compared microsurgical clipping and endovascular treatment (coiling with or without stenting) of 92 ruptured and unruptured MCA aneurysms, Schwartz et al.[35] reported a 78.9% occlusion rate for the endovascular cohort. Johnson et al.[18] in 2013 reported a 95.2% occlusion rate when analyzing stent-assisted coil embolization of 100 MCAAs. Our meta-analysis confirms an improvement in the rate of complete occlusion with newer endovascular tools; these rates are still lower than those seen with surgical treatment, suggesting that these newer tools should be used with caution when treating unruptured MCA aneurysms and should be preferably used only in those cases in which comorbidities, technical challenges, and patient preference may make surgery a less preferable choice. Among newer endovascular techniques, flow diversion and SAC provided the highest occlusion rates, which were close to 85% and 82%, respectively. However, these techniques require the use of dual antiplatelet treatments, to minimize the risk of ischemic events. A recent meta-analysis of MCA aneurysms treated with flow diversion[36] reported a 16% rate of ischemic complications, with about 8% related to the discontinuation of the antiplatelet therapy. On the other hand, flow disruption with WEB is a

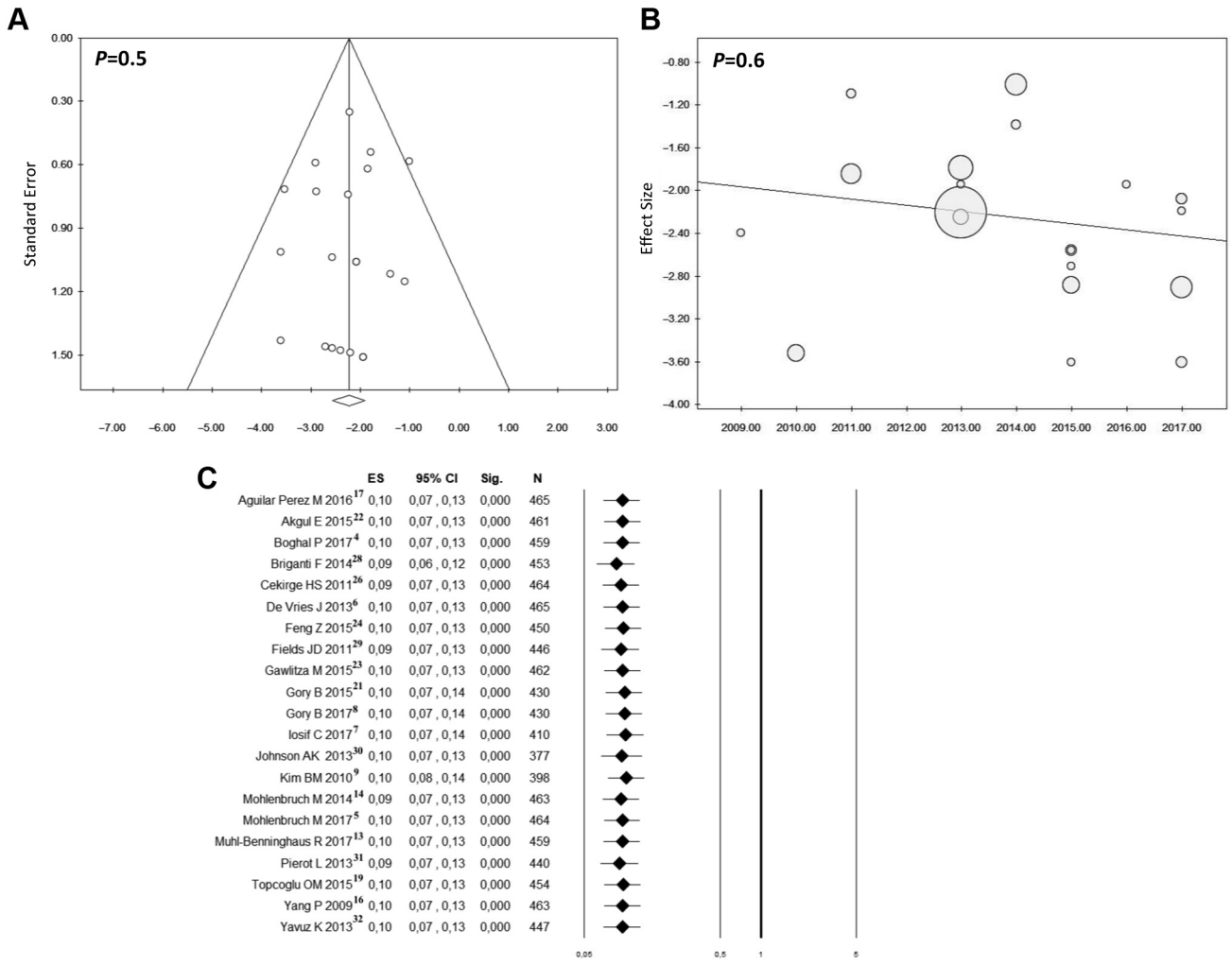

Figure 6. Treatment-related complications among the endovascular group. The funnel plot followed by Egger linear regression test excludes publication bias (**A**). Meta-regression showed an insignificant variation of the effect size (**B**) over the investigated years. The sensitivity analysis showing the influence of each individual study on the explored outcome (**C**). ES, effect size; CI, confidence interval; Sig, significance.

promising strategy not requiring dual antiplatelet therapy, although aneurysm shape and size are important factors determining the possibility of the use of this device.

In a recent meta-analysis, Lv et al. underlined the new role of WEB endosaccular flow disruptors in the endovascular treatment of aneurysms: they reported 6%–8% for thromboembolic rate, 5%–10% for hemorrhagic complications, and 1%–5% for morbidity. The complete occlusion rate is 55% at short-term and mid-term follow-up (95% CI, 50%–60%) and the adequate occlusion rate is 81% (95% CI, 76%–85%).[37] However, although only 2 studies were analyzed in this meta-analysis, both Pierot[23] and Aguilar Perez[21] showed good results in terms of safety and exclusion of the aneurysm; in particular, for the Pierot study, clinical outcome at 1 month was satisfactory, with a mortality of 0.0% and a morbidity of 3.1%, recommending the use of WEB for aneurysm with neck >4 mm. No aneurysm rupture after treatment was reported in both groups. In our analysis, endovascular treatments were associated with higher rates of good neurologic outcome (97%; $P = 0.001$) compared with the surgical group (84%). These results contrast with the meta-analysis mentioned earlier, which considers surgery more secure than coiling or similar in terms of unfavorable neurologic outcome; Smith et al.[33] attribute fewer neurologic complications at surgery, assessed as safer in the long-term perspective (2.1% unfavorable neurologic outcome for surgical procedures vs. 6.5%–4.9% for coiling), but Alreshidi et al.[34] considered both clipping and coiling as equivalent in terms of security and clinical outcome. Despite a higher percentage of complete/near-complete occlusion in the surgical group, this does not seem to have influenced the risk of bleeding. Both treatments seem

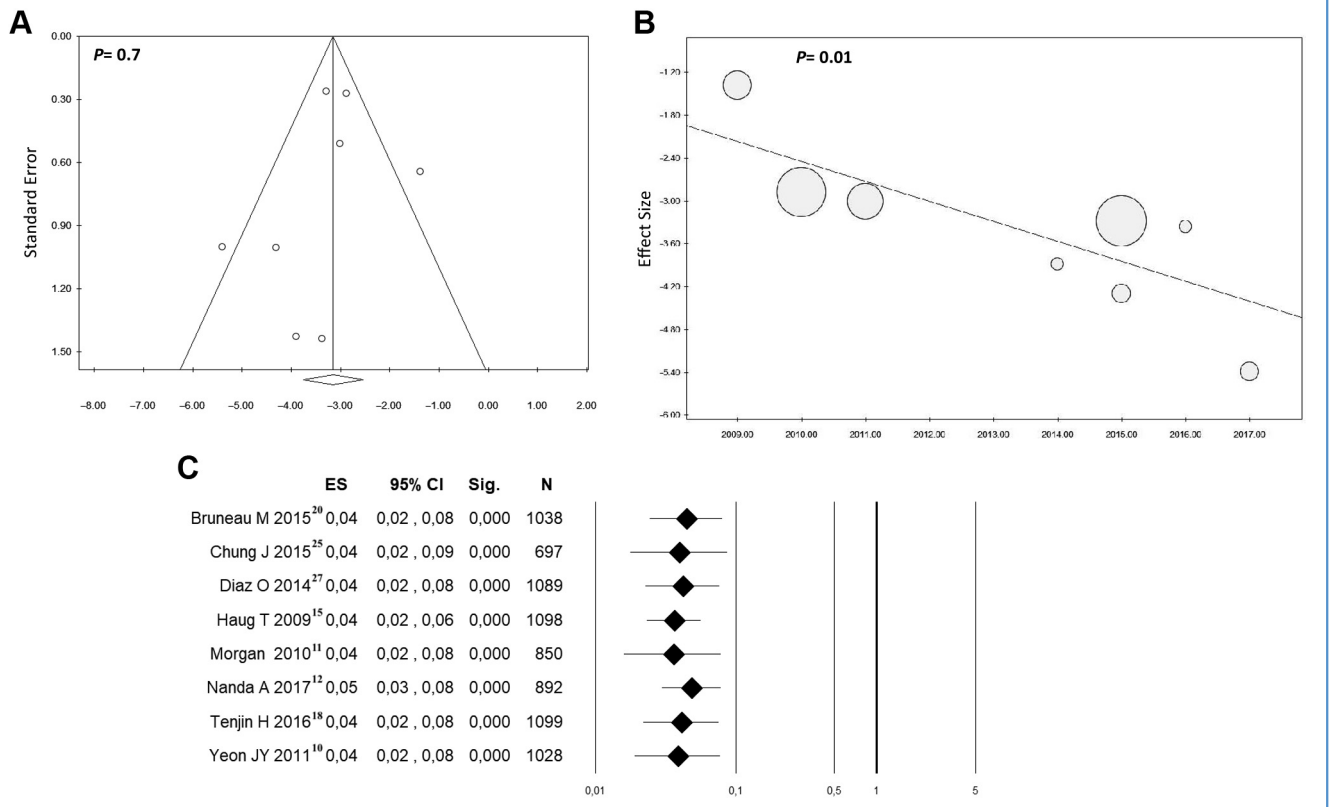

Figure 7. Treatment-related complications among the surgical group. The funnel plot followed by Egger linear regression test excludes publication bias (**A**). Meta-regression showed a significant decrease of the effect size (**B**) over the investigated years. The sensitivity analysis showing the influence of each individual study on the explored outcome (**C**). ES, effect size; CI, confidence interval; Sig, significance.

safe and effective, which could be explained by the fact that surgical and endovascular procedures are performed by operators with increasingly high competence and knowledge of both procedures in terms of indications and treatment modalities. For these reasons, selection of patients with MCA aneurysms is always careful to achieve the most correct approach. This careful selection allows a better result in terms of rate occlusion and clinical outcome. In addition, different endovascular devices are available, which allows selection of the most appropriate technique and tailored treatment based on the patient characteristics (age and comorbidities) and aneurysm morphology (neck size, shape, and dimension). Considering all these factors and despite the limitations of this study, we can cautiously affirm that MCAAs are no longer the exclusive competence of surgery because the introduction of new devices and the refinement of endovascular techniques introduce new perspectives for treating these types of aneurysms. As mentioned earlier, the incomplete occlusion of aneurysms is not correlated to rebleeding, and future studies of fluid-dynamic factors related to high risk of rupture may clarify how to set targets for intervening on bleeding risks without necessarily achieving complete occlusion.

Limitations

Our study has several limitations. Most series, especially among the endovascular group, were retrospective single-center studies. There was a trend toward a significant risk of bias for angiographic occlusion after endovascular treatment, which can be overrated. This trend is related to the presence of small series, as well as small subgroups of endovascular treatment. Imaging follow-up was heterogeneous regarding the timing and the technique used (magnetic resonance imaging, computed tomography angiography, or digital subtraction angiography). The studies analyzed present a long-term radiologic follow-up varying from 12 to 62 months, but only 10/29 studies had a long-term follow-up and, in most of these, data about final occlusion are incomplete. The influence of antiplatelet therapy in endovascular treatment (especially for flow diversion and SAC) was not evaluated. Regarding retreatment rates and complications, all the available data were collected.

Furthermore, in many centers, MCA aneurysms are still considered more appropriate candidates for surgical clipping. Probably, the patients selected for endovascular treatment are those with aneurysms with favorable anatomy for such modalities and those with unfavorable anatomy would be considered surgical candidates, requiring sometimes complex clipping or bypass. This situation would potentially change the outcome in favor of endovascular treatment.

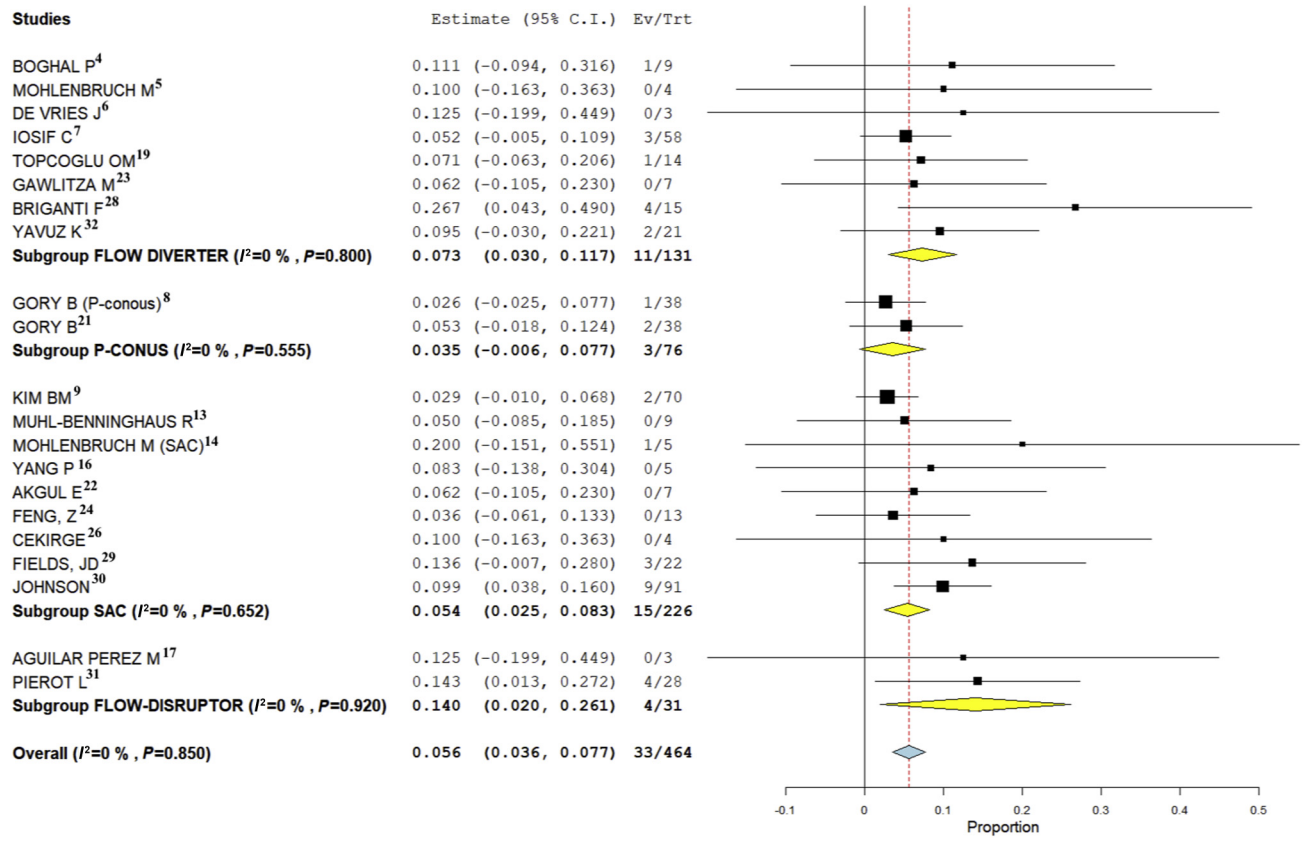

Figure 8. Forest plot with random-effect model showing the subgroups analysis of the complication rates after treatment with flow diversion, pConus, stent-assisted coiling, and flow disruptor. C.I., confidence interval; Ev/Trt, endovascular and surgical treatments.

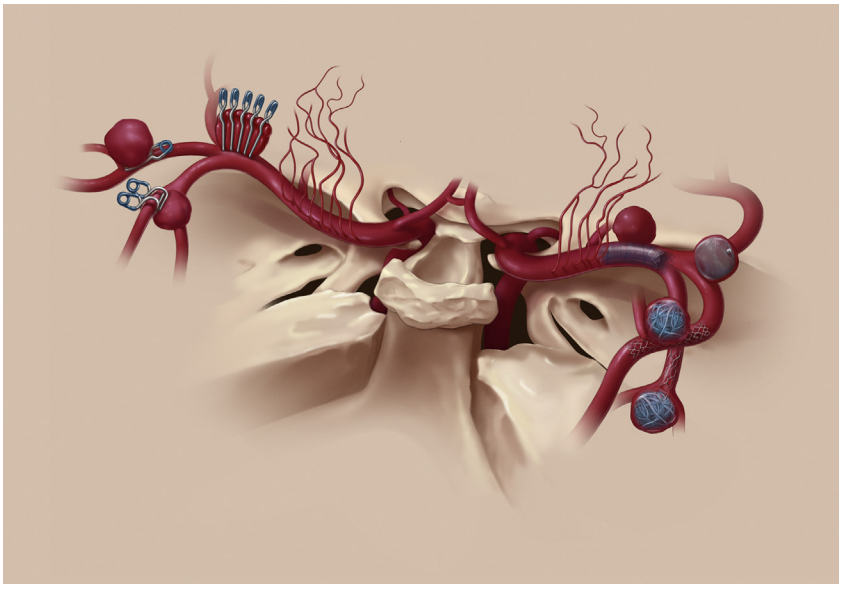

Figure 9. Comparison between some clipping techniques (on the left) and endovascular devices (on the right) in middle cerebral artery aneurysms.

CONCLUSIONS

Unruptured saccular MCA aneurysms can be effectively treated with both surgical and modern endovascular techniques, although clipping is still associated with higher occlusion rates. Morbidity and mortality are comparable, and the risk of aneurysm rupture seems low for both strategies. The endovascular approach with new available devices seems to increase the probability of good functional outcome after treatment, compared with surgery, and would be a reasonable option for selected MCA aneurysm. Large prospective studies are needed to compare surgical outcomes and modern endovascular strategies.

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SUPPLEMENTARY MATERIAL

MODIFIED NEWCASTLE-OTTAWA QUALITY ASSESSMENT SCALE FOR RETROSPECTIVE STUDIES

(Score 0–8; studies with ≥5 stars were considered high quality)

Selection

1) Is the case definition adequate?
   a) yes, with independent validation*
   b) yes, e.g., record linkage or based on self-reports
   c) no description
2) Representativeness of the cases
   a) consecutive or obviously representative series of cases*
   b) potential for selection biases or not stated
3) Selection of Controls
   a) community controls*
   b) hospital controls
   c) no description
4) Definition of Controls
   a) no history of disease (end point)*
   b) no description of source

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
   a) study controls for (Select the most important factor)*
   b) study controls for any additional factor* This criterion could be modified to indicate specific

control for a second important factor)

Note=

Comparability (point A) was NOT tested because of the design of the reported studies.

Comparability (point B) was tested comparing subgroups of analysis: one point was attributed if the study reported the analysis of the subgroups.

Exposure

1) Ascertainment of exposure
   a) secure record (e.g., surgical records) with adequate length of follow-up*
   b) structured interview where blind to case/control status*
   c) interview not blinded to case/control status
   d) written self-report or medical record only
   e) no description
2) Same method of ascertainment for cases and controls
   a) yes*
   b) no
3) Nonresponse rate
   a) <20%*
   b) nonrespondents described
   c) rate different and no designation

MODIFIED NEWCASTLE-OTTAWA QUALITY ASSESSMENT SCALE FOR PROSPECTIVE STUDIES

(Score 0–8; studies with ≥5 stars were considered high quality)

Selection

1) Representativeness of the exposed cohort
   a) truly representative of the average (patients treated with flow diverter in the acute phase) in the community*
   b) somewhat representative of the average (patients treated with flow diverter in the acute phase) in the community*
   c) selected group of users (e.g., nurses, volunteers)
   d) no description of the derivation of the cohort
2) Selection of the nonexposed cohort
   a) drawn from the same community as the exposed cohort*
   b) drawn from a different source
   c) no description of the derivation of the nonexposed cohort
3) Ascertainment of exposure
   a) secure record (e.g., surgical records) with adequate length of follow-up*
   b) structured interview*
   c) written self-report
   d) no description
4) Demonstration that outcome of interest was not present at start of study
   a) yes*
   b) no

Comparability

1) Comparability of cohorts on the basis of the design or analysis
   a) study controls for _____ (select the most important factor)*
   b) study controls for any additional factor* (This criterion could be modified to indicate specific control for a second important factor.)

Note=

Comparability (point A) was NOT tested because of the design of the reported studies.

Comparability (point B) was tested comparing subgroups of analysis: 1 point was attributed if the study reported the analysis of the subgroups.

Outcome

1) Assessment of outcome
   a) independent blind assessment*
   b) record linkage*
   c) self-report
   d) no description
2) Was follow-up long enough for outcomes to occur (Adequate follow-up was considered a follow-up longer than the median follow-up time of the reported studies)
   a) yes (select an adequate follow-up period for outcome of interest)*
   b) no
3) Adequacy of follow-up of cohorts
   a) complete follow-up—all subjects accounted for*
   b) subjects lost to follow-up unlikely to introduce bias—small number lost—(<20% of the original population) follow-up, or description provided of those lost)*
   c) follow-up rate (<80% of the original population) and no description of those lost
   d) no statement