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REVIEW

Microsurgical clipping versus newer endovascular techniques in treatment of unruptured anterior communicating artery-complex aneurysms: a meta-analysis and systematic review

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Abstract
The aim of this study is to compare occlusion rate, complication rate, and clinical outcome of microsurgical clipping (MC) and advanced endovascular techniques (EVT) in unruptured anterior communicating artery-complex aneurysms (ACoCAs). We reviewed the scientific literature reporting occlusion rate, time of occlusion assessment, and clinical outcome of MC and EVT in patients with unruptured ACoCAs, from January 2009 to December 2019. We included in our analysis 25 studies and 872 patients with unruptured ACoCAs (434 treated with endovascular techniques and 438 with MC). Ninety-three (10.7%), 320 (36.7%), 21 (2.4%), and 438 (50.2%) were treated with flow diverter (FD), stent-assisted coiling (SAC), endosaccular devices (ES), and microsurgical clipping (MC) respectively. FD, SAC, ES, and MC subgroups presented minor complications in 11.8%, 3.8%, 14.3%, and 7.1% of cases (p=.016), and major complications in 3.2%, 4.4%, 0%, and 7.1% (p=.136) of patients. A total occlusion rate post-treatment has been achieved in 4.3%, 87.1%, 47.6%, and 98.2% of cases (p=.000), while at 12 months' follow-up in 50%, 66%, 83.3%, and 80% of patients (p=.001). FD, SAC, ES, and MC subgroups had a good clinical outcome at 12 months in 93.5%, 90.5%, 100%, and 67.8% of cases. MC is associated with higher post-treatment total occlusion rate, but higher complication and lower good clinical outcome rates. EVT are promising in treating unruptured anterior cerebral artery aneurysms with high margin of safety and good clinical outcome, despite the lower total occlusion rate.

Keywords Clipping · Endovascular treatment · Anterior cerebral artery · ACoCA · Unruptured brain aneurysms

Introduction

The anterior communicating artery-complex (ACoC) is one of the commonest sites of unruptured intracranial aneurysms [1]. Microsurgical clipping of ACoC aneurysms (ACoCAs) is more challenging than other locations [2], due to geometrical factors, frequent anatomical variations, and technical elements, as the need for deeper interhemispheric dissections with possible compromise of perforators. Endovascular treatment with standalone Guglielmi detachable coils (GDC) raised criticism due to the low complete occlusion rate, ranging from 10 to 72%, and the

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high recanalization rate over time [3–5]. However, since the introduction of new devices (intrasaccular and extra-saccular), the endovascular treatment of ACoCAs and small distal ACAs [6–11] increased. Due to this rapid paradigm shift in the treatment of unruptured ACoC aneurysms (ACoCAs), there are scanty data about the efficiency of these novel devices in achieving total occlusion with acceptable clinical outcomes. The aim of this meta-analysis is to compare the occlusion rate, complication rate, and clinical outcome of MC and EVT in ACoCAs.

Materials and methods

Literature search and eligibility criteria

We reviewed the English literature on PubMed, Scopus, and Cochrane databases until 2019, following the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) statement (Supplementary Fig 1). We used MeSH terms including "Anterior communicating aneurysms," "anterior cerebral artery aneurysms," "endovascular," "microsurgery," "clipping," "coiling," "flow diversion," "WEB device," "p-conus," and "stent assisted-coil," to identify all relevant studies evaluating the efficacy and safety of microsurgical clipping or endovascular treatment with new techniques in patients with unruptured saccular ACoCAs. We included studies that (a) reported clipping or endovascular treatment with aforementioned techniques, outcomes for adult patients (or a subgroup) with unruptured saccular ACoCAs; (b) reported occlusion rates, neurological morbidity, or both; (c) measured efficacy by complete occlusion of the aneurysm demonstrated by digital subtraction angiography, CT angiography, or MR angiography (primary outcome); (d) measured safety with the Modified Rankin Scale (mRS; 0–3) or the Glasgow Outcome Scale (GOS; 4–5) (secondary outcome); and (e) were published between 2009 and 2019. We considered modern endovascular techniques: flow diversion, stent-assisted coiling (SAC), treatment with intrasaccular flow disruptors (WEB, or Medina devices), and p-Conus. We excluded studies if they (a) were not English studies; (b) were conducted on animal models; (c) reported both procedures in a single patient; (d) reported ruptured ACoAAs; (e) reported treatment of distal ACA aneurysms; (f) reported dissecting or fusiform or blister aneurysms; (g) included simple coiling technique; (h) included <3 patients; and (i) 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 radiological results; follow-up at short (0–3 months), medium (6–12 months), and long (> 12 months) term; retreatment rate; year of treatment; and country. Two investigators (FD and GT) independently screened titles and abstracts and selected potentially relevant articles for full-text evaluation. We analyzed investigated outcomes with the random-effect meta-analysis, which incorporates heterogeneity among studies. The primary aim of this study was to determine the clinical and angiographic outcomes of patients treated with endovascular techniques or surgery. The secondary aim was to determine minor and major complication rates, mortality rate, and clinical outcomes in the endovascular and surgical groups. Major complications caused permanent neurological deficits or transient neurological deficits requiring more than 1 month to recovery and affecting patient's quality of life; all others were considered minor complications. Good clinical outcome was defined as Modified Rankin Scale (mRS; 0–3) or the Glasgow Outcomes Scale (GOS; 4–5).

Data extraction

Two investigators (FD, GT) independently conducted the data extraction, including study characteristics (publication year; country of origin; sample size; study design; number of aneurysms; study duration), intervention characteristics (surgery type), efficacy results (number of complete occlusions for coiling or clipping; time of occlusion assessment), and safety outcome (mRS and GOS, assessment time of mRS or GOS). Senior authors resolved potential discrepancies. One investigator (AP) has conducted the statistical analysis.

Statistical methods

We analyzed the sample with SPSS version 18. Data extraction concerning the clinical and angiographic outcomes produced dichotomous variable exclusively. We compared nominal and dichotomous variables with the chi-square test, using histogram plots for the graphical representation. We used the z-test, when appropriate, to compare the percentages of each group and to calculate the p values. Power of the study was calculated by means of GPower version 3.1; in regards to the comparison between endovascular and surgical techniques, $1\text{-}\beta = 0.997$ for α 0.05 and effect size 0.3 whereas in regards to the comparison between flow diverter and stent-assisted coiling approaches, $1\text{-}\beta = 0.995$ for α 0.05 and effect size 0.5, thus producing results of notable accuracy. Heterogeneity of the data was assessed by the Higgins index (I^2) and, subsequently, the DerSimonian and Laird random-effects model was applied. The graphical representation was performed using forest plot. 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). Threshold of statistical significance was considered if $p<.05$.

Table 1 Studies included in the meta-analysis

				Endovascular treatment				Surgical treatment					
N	Authors	Technique/devices	Study	*N* of patients	*N* of selected patients	*N* of aneurysms	Combined devices treatment	*N* of patients	*N* of selected patients	*N* of aneurysms	Combined devices treatment	Years	Country
1	Raslan et al., 2011 [[33]]	SAC	R	44	44	44	0	-	-	-	-	2003–2009	America
2	Akgul et al., 2011 [3]	SAC	R	9	3	3	0	-	-	-	-	-	Europe
3	Lai et al., 2013 [23]	Clipping	R	-	-	-	-	103	103	115	-	1992–2012	Asia
4	Galal et al., 2013 [15]	SAC	R	43	5	5	0	-	-	-	-	2005–2010	Europe
5	Bruneau et al., 2015 [8]	Clipping	R	-	-	-	-	183	183	228	-	2001–2012	Europe
6	Gherasim et al., 2015 [16]	ED	R	10	7	7	0	-	-	-	-	2013–2014	Europe
7	Bozzetto Ambrosi et al., 2015 [7]	ED	R	10	5	5	0	-	-	-	-	2013–2014	Europe
8	Lubicz et al., 2015 [24]	SAC	R	18	6	6	0	-	-	-	-	2013–2015	Europe
9	Puri et al., 2015 [32]	FD	R	7	4	4	0	-	-	-	-	2012–2014	Europe
10	Clarencon et al., 2015 [11]	FD	R	7	6	4	0	-	-	-	-	2010–2014	Europe
11	Nanda et al., 2016 [27]	Clipping	R	-	-	-	-	196	32	32	-	2000–2016	America
12	Kocur et al., 2016 [22]	SAC	R	34	28	28	0	-	-	-	-	2001–2012	Europe
13	Bhogal et al., 2016 [6]	FD	R	26	14	14	1	-	-	-	-	2009–2016	Europe
14	Colby et al., 2017 [12]	FD	R	41	41	41	6	-	-	-	-	2012–2016	America
15	Mori et al., 2018 [26]	Clipping	R	-	-	-	-	63	63	63	-	2005–2014	Asia
16	Khalid et al., 2018 [21]	ED	R	16	6	6	1	-	-	-	-	2012–2015	Europe
17	Haffaf et al., 2018 [17]	ED	R	19	3	3	0	-	-	-	-	2015–2016	Europe
18	Santillan et al., 2018 [36]	SAC	R	25	24	24	5	-	-	-	-	2015–2018	America

Table 1 (continued)

N	Authors	Technique/devices	Study	Endovascular treatment: N of patients	Endovascular treatment: N of selected patients	Endovascular treatment: N of aneurysms	Endovascular treatment: Combined devices treatment	Surgical treatment: N of patients	Surgical treatment: N of selected patients	Surgical treatment: N of aneurysms	Surgical treatment: Combined devices treatment	Years	Country
19	Samaniego et al., 2018 [35]	SAC	R	30	3	3	0	-	-	-	-	-	Europe
20	Santillan et al., 2018 [37]	SAC	R	35	17	17	9	-	-	-	-	2015–2017	America
21	Park et al., 2018 [30]	SAC	R	21	6	6	0	-	-	-	-	2015–2017	Asia
22	Choi et al., 2018 [10]	SAC	R	184	175	175	0	-	-	-	-	2008–2016	Asia
23	Lylyk et al., 2019 [25]	SAC	R	17	3	3	0	-	-	-	-	2015–2017	America
24	Park et al., 2019 [31]	SAC	R	16	6	6	0	-	-	-	-	2018–2019	Asia
25	Pagiola et al., 2019 [29]	FD	R	30	30	30	0	-	-	-	-	2014–2018	Europe

Results

A total of 872 patients extracted from 25 papers [11–35] composed the final study cohort (Table 1): 434 patients were treated with EVT (49.8%), 93 (10.7%) with flow diverter (FD), 320 (36.7%) with stent-assisted coiling (SAC), and 21 (2.4%) with endosaccular devices (ES) respectively, whereas 438 patients (50.2%) with MC. Relevant details are included in Table 2.

Major and minor complications

Data about major and minor complications were available in 866 cases (99.3%). A total of 103 patients presented complications, 56 minor (6.4%) and 48 major (5.6%). Minor complications of FD, SAC, ES, and MC subgroups were 11.8% (11/93; 95% CI, 6.0–20.2%; I^2 = 19.6%), 3.8% (12/314; 95% CI, 1.9–6.6%; I^2 = 33.3%), 14.3% (3/21; 95% CI, −3.0–36.4%; I^2 = 0%), and 7.1% (30/438; 95% CI, 4.8–9.9%; I^2 = 57.2%) respectively, whereas major complications of the same subgroups were 3.2% (3/93, CI 6.7–9.1%, I^2=0%), 4.4% (14/314, CI 2.4–7.3%, I^2=0%), 0% (0/48, CI −0–7.4%, I^2=0%), and 7.1% (31/438, CI 4.8–9.2%). Difference of minor complication rates was statistically significant (p=.016). However, single subgroup analyses demonstrated statistically significant values in SAC vs ES (3.8% vs 14.3%, p=.025) and FD vs SAC (11.8% vs 3.8%, p=.006). Other subgroup comparisons did not reach the threshold of statistical significance. The use of endovascular or surgical approach did not demonstrate significant statistical difference (p=.644) as in Fig. 1A. A forest plot summarizes the aforementioned findings disclosing an overall estimated minor complication rate of 0.070, with I^2 of 59.89% (p=.000) in Supplementary Fig 2.

Differences in terms of major complication rate were not statistically significant (p=.136), even in single subgroup comparisons, although the difference was statistically significant between endovascular and microsurgical treatment (p=.021), as seen in Fig. 1B. A subgroup analysis was performed with a stronger statistical power (1-β = 0.995 for α 0.05 and effect size 0.5) between FD and SAC. Figure 1C shows statistically significant difference with lower number of minor complications in the SAC subgroup (p=.006) and not statistically significant difference with respect to major complications (p=.624).

Intraoperative rupture, mortality, and rebleeding

Intraoperative rupture happened in 1.7% of cases (15/872). However, there was no case of intraoperative death and just one case of delayed mortality, after ≥ 1 month. No treated aneurysm rebled. Statistical analysis could not be performed because of inadequate events. Among the 15 patients with intraoperative rupture, 53.3% (8), 40% (6), and 6.7% (1) occurred in SAC, MC, and ES subgroups respectively.

Radiological outcome

Total, subtotal, and near total occlusion rates were reported in 64.0% (16/25), 64.0% (16/25), and 48.0% (12/25) of the reported studies as seen in Fig. 2. 67.6% (499/570; 95% CI, 58.7–76.6%; I^2 = 97.04%) of treated aneurysms were totally occluded after treatment. The FD, SAC, ES, and MC subgroups showed a total post-operative occlusion in 4.3% (1/18; 95% CI, 1.4–27.9%; I^2 = 0%), 87.1% (264/303; 95% CI, 82.0–90.7%; I^2 = 89.9%), 47.6% (10/21; 95% CI, 25.7–70.2%; I^2 =68.6%), and 98.2% (224/228; 95% CI, 95.6–99.5%) of cases, respectively (p=.000).

The FD, SAC, ES, and MC subgroups showed a total long-term complete occlusion in 47.9% (23/48, 95% CI 34.5–64.5%, I^2 = 80.8%), 66.3% (199/300, 95% CI 60.3–71.6%, I^2 = 94.2%), 66.7% (5/6, 95% CI 29.9–92.5%, I^2 = 61.1%), and 80.8% (144/178, 96% CI 74.6–86.4%, I^2 = 97.2%) of cases, respectively (p=.001).

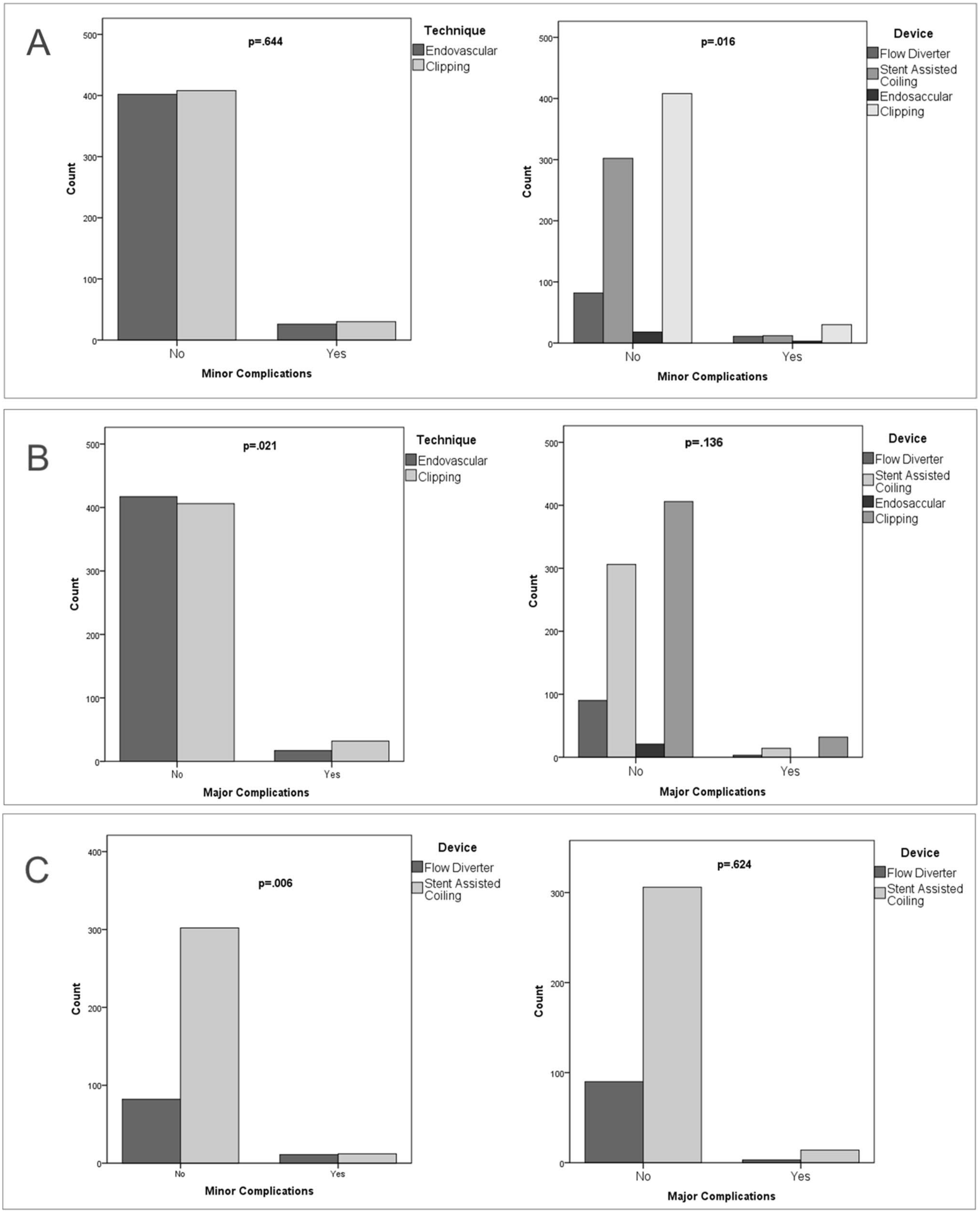
The MC group had a higher post-operative total occlusion than the EVT group with statistically significant difference (p=.001). Among the endovascular techniques, SAC was associated with the highest total occlusion rate (p=0.001). Endovascular technique showed a higher proportion of total occlusion in the FD subgroup at 6–12 months. At 12 months' follow-up, the SAC subgroup showed higher proportion of total occlusion than the other subgroups with statistically significant difference (p=0.001) as in Fig. 3. Direct comparison of FD and SAC subgroups showed higher proportion of total occlusion in SAC with statistically significant difference (p=.030). A forest plot summarizes the total occlusion rates at 0 and 12 months, with I^2 up to 97.04% and 73.09% (p>.0001 both; Supplementary Fig. 3). Data concerning retreatment were available in 855/872 patients (98.0% of the entire cohort). Second treatment was performed in 13 (1.5%) cases, with no statistically significant difference between the different techniques, and even between different approaches (Fig. 4).

Good clinical outcomes

75.9% (662/889) of patients had a preoperative good clinical status: it was higher in the EVT group than in the MC group with statistically significant difference (p=0.0001) (Fig. 5). Clinical outcomes were expressed as dichotomous variable as mentioned in the "Materials and methods" section. 89.7% (95.5%; CI, 85.1–94.3%; I^2 = 66.7%) of patients presented a post-operative good clinical outcome, with a higher rate in the EVT group than in the MC group (p=0.03). In a subgroup analysis, FD, SAC, ES, and MC subgroups were associated with good clinical outcome in 93.5% (87/93; 95% CI, 86.5–97.6%; I^2 = 6.8%), 90.5% (287/317; 95% CI,

Table 2 Procedure-related outcomes after endovascular and surgical treatments of unruptured saccular anterior cerebral artery-complex aneurysms

Variables	FD, *n*/*N* (%) (range), I^2 (%)	SAC, *n*/*N* (%) (range), I^2 (%)	ES, *n*/*N* (%) (range), I^2 (%)	Surgical group, *n*/*N* (%) (range), I^2 (%)	*p* value
Angiographic outcomes					
Long-term complete occlusion rate	50.0% (22/44, 95% CI 34.5–64.5%, I^2 = 80.8%)	66.0% (198/300, 95% CI 60.3–71.3%, I^2 = 94.2%)	83.3% (5/6, 95% CI 35.8–99.6%, I^2 = 61.1%)	80.8% (144/178, 96% CI 74.6–86.4%, I^2 = 97.2%)	.001
Immediate complete occlusion rate	4.3% (1/18, 95% CI, 1.4–27.9%, I^2 = 0%)	87.1% (264/303, 95% CI, 82.0–90.7%, I^2 = 89.9%)	47.6% (10/21, 95% CI, 25.7–70.2%, I^2 =68.6%)	98.2% (224/228, 95% CI, 95.6–99.5%)	0.000
Re-treatment rate	9/342			4/228	-
Clinical outcomes and procedure-related complications					
Good outcome rate	93.5% (87/93; 95% CI, 86.5–97.6%; I^2 = 6.8%)	90.5% (287/317; 95% CI, 86.7–93.5%; I^2 = 49.1%)	100% (21/21; 95% CI, 82–100.2%; I^2 = 0%)	67.8% (78/115; 95% CI, 58.7–76.2%)	0.03
Minor complication rate	11.8% (11/93; 95% CI, 6.0–20.2%; I^2 = 19.6%)	3.8% (12/314; 95% CI, 1.9–6.6%; I^2 = 33.3%)	14.3% (3/21; 95% CI, −3.0–36.4%; I^2 = 0%)	7.1% (30/438; 95% CI, 4.8–9.9%; I^2 = 57.2%)	0.016
Major complication rate	3.2% (3/93; CI 6.7–9.1%, I^2=0%)	4.4% (14/314, CI 2.4–7.3%, I^2=0%)	0% (0/48, CI −0–7.4%, I^2=0%)	7.1% (31/438, CI 4.8–9.2%)	0.136
Intraoperative rupture/perforation	0/93	2.5% (8/314)	2% (1/48)	1.4% (6/438)	-
Mortality	1/93	0/317	0/21	0/115	-
Re-bleed	0/93	0/317	0/21	0/115	-



86.7–93.5%; $I^2 = 49.1\%$), 100% (21/21; 95% CI, 82–100.2%; $I^2 = 0\%$), and 67.8% (78/115; 95% CI, 58.7–76.2%) respectively (Fig 5).

77.5% (629/793; 95% CI, 70.0–84.9%; I^2 = 94.3%) of patients presented a good clinical outcome 12 months after treatment (p=0.000). FD, SAC, ES, and MC subgroups were

◂**Fig. 1** Minor and major complications: comparison of techniques and devices. **A** The use of endovascular or surgical approach did not demonstrate significant statistical difference in terms of minor complications. **B** Major complication rates among various subgroups of endovascular techniques with statistically significant differences (p=.039), as well as between endovascular and microsurgical treatment (p=.021). **C** Sub-analysis of FD and SAC, showing statistically significant lower rate of minor complications in the FD subgroup (p=.006) and no statistically significant difference with respect to major complications (p=.624). FD, flow diverter; SAC, stent-assisted coiling

associated with a 12-month good clinical outcome in 91.9% (48/52; 95% CI, 80.7–103.1%; I^2 =33.3%, p=0.21), 68.1% (241/297; 95% CI, 43.7–92.4%; I^2 =95.3%, p=0.000), 83.3% (5/6; 95% CI, 53.5–113.2%), and 79.4% (335/448; 95% CI, 62.3–96.5%; I^2 =96.5%, p=0.000) of cases respectively (Fig. 5; Supplementary Fig. 4).

Discussion

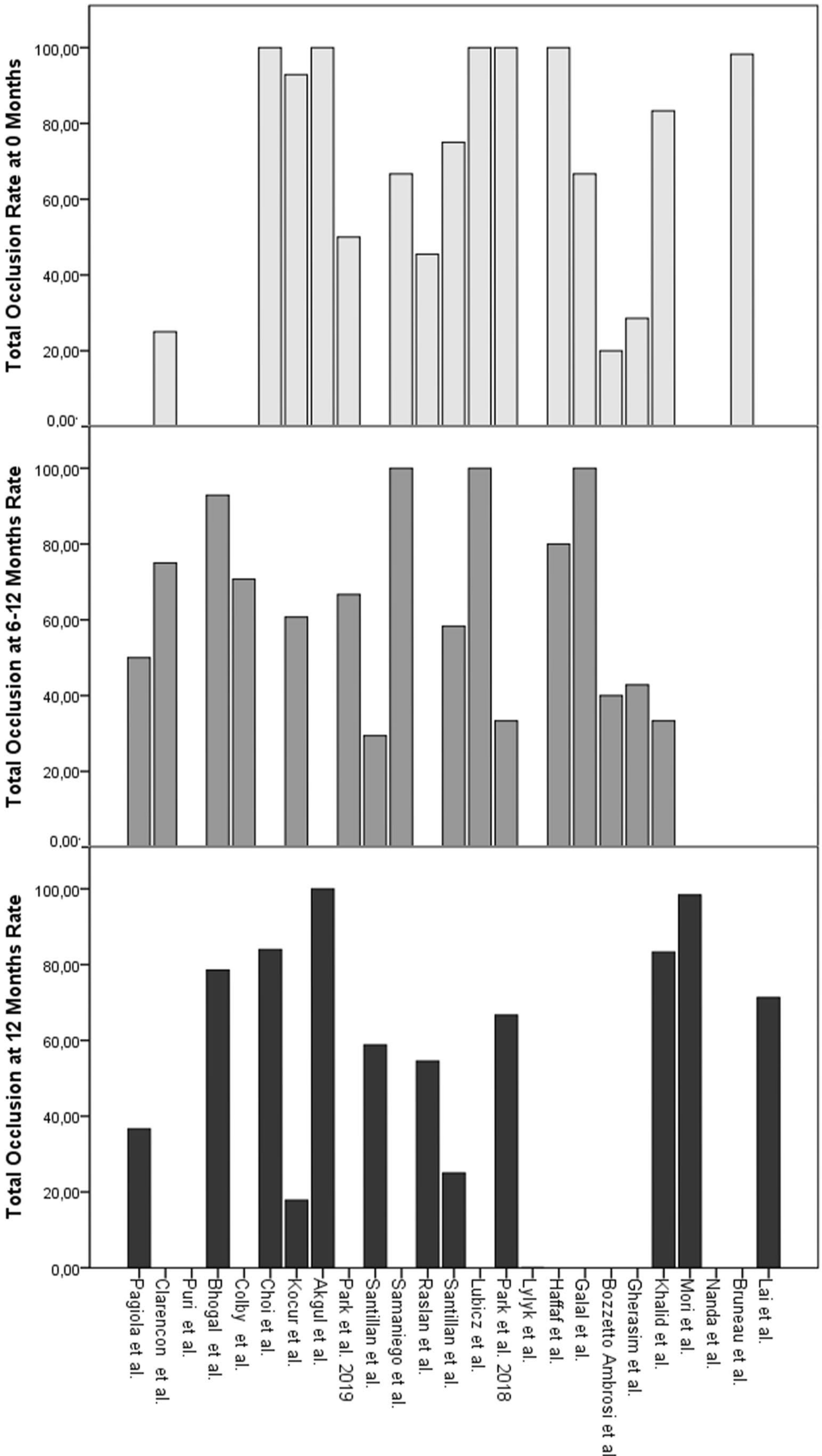
Management of unruptured ACoCAs includes microsurgical clipping and endovascular treatment with its own advantages and disadvantages. In the recent years, significant advances in the endovascular technique and devices expanded the armamentarium of the endovascular surgeons. This has created a major paradigm shift in treating ACoCAs. However, prophylactic treatment of these unruptured ACoCAs requires an acceptable procedure–related risk profile to justify intervention against that of the expected natural history. Understanding both the safety and effectiveness of treatment modalities becomes imperative to make pretreatment clinical decision-making and discussion with the patient. Until now, studies have compared surgical clipping with coil embolization without considering some of the most recent advances. Distal ACAAs have been excluded from our analysis, due to their anatomical localization requiring different approaches and therapeutic strategies. To our opinion, DACA aneurysms deserve a separate analysis.

In this meta-analysis, we have combined the data from 25 studies to analyze the radiological and clinical outcome of treating unruptured ACoCAs with advanced recent endovascular techniques (other than non-assisted coil embolization) and microsurgical clipping. We used a similar methodological approach in their meta-analysis about unruptured middle cerebral artery aneurysms [36]. Our results demonstrate that unruptured ACoCAs treated with new and advanced endovascular techniques seem to have superior safety than microsurgical clipping, although immediate total occlusion rate was higher with microsurgical clipping. Among the endovascular techniques, stent-assisted coiling has higher total occlusion rates at 12 months' follow-up. Good clinical outcome in the immediate post-procedure period and at 12 months' follow-up was observed more in patients treated with advanced endovascular technique than those treated by microsurgical clipping (FD 91.9%, SAC 68.1%, ES 83.3%, and MC 79.4%; p=0.0001). Those treated with flow diverters had good clinical outcomes in the immediate post-procedure period as well as at the end of 12 months than others. Microsurgical clipping was associated with higher number of major complications than other endovascular techniques (FD 6.3%, SAC 29.2%, ES 0%, and MC 64.6%; p=.021): that seems to demonstrate a lower risk and potential superior safety of the endovascular approaches in treating unruptured ACoCAs. This result could be affected by selection bias, as we included all the unruptured ACoCAs; however, the ACoC includes aneurysms with different locations and anatomical relations; hence, a subgroup analysis might be helpful to understand which ones have higher complication rates. Moreover, the MC subgroup patients had lesser proportion of good clinical preoperative status, probably because poor grade patients tent to be treated with MC. There was no significant difference in the retreatment rate and mortality between microsurgical clipping and advanced endovascular techniques.

Neill et al., in their systematic review, reported the superiority of microsurgical clipping in treating unruptured ACoA aneurysms and higher morbidity associated with stent-assisted coiling technique (MC 4.4% and SAC 7.9%) [37]. In the same review, simple endovascular coil embolization was found to be associated with better clinical outcomes than MC and SAC. However, the authors did not take into consideration the increase in the recent trends for use of novel endovascular devices like flow diverters and endosaccular devices, which is addressed in our meta-analysis.

In our review, we noticed the major complication in 64.6% of patients treated with MC. This drastic discrepancy could be due to variation in the cohort, as we have included all the unruptured saccular aneurysms in the ACoCA; moreover, the MC subgroup patients had lesser proportion of good clinical preoperative status.

Although, only 5 studies with ES treatment were included in our analysis, we observed total occlusion in 49% and 52.6% of patients in the immediate period and at 12 months' follow-up respectively. Despite our results are not statistically significant due to the unrepresentative sample, they are in line with the RISE trial, reporting successful results with intrasaccular flow disruptor device in 75–91% of cases [38]. Asnafi et al., in their systematic review and meta-analysis of WEB device in treating intracranial aneurysms, reported midterm complete occlusion rate of 39% but described a significant difference between ruptured and unruptured groups [39]. They reported midterm complete occlusion rate with ES in unruptured aneurysm as 22%. However, in our review 83.3% of patients treated with ES device had good


Total Occlusion Rate at 0 Months
Total Occlusion at 6-12 Months Rate
Total Occlusion at 12 Months Rate
0,00
20,00
40,00
60,00
80,00
100,00
Pagiola et al.
Clarencon et al.
Puri et al.
Bhogal et al.
Colby et al.
Choi et al.
Kocur et al.
Akgul et al.
Park et al. 2019
Santillan et al.
Samaniego et al.
Raslan et al.
Santillan et al.
Lubicz et al.
Park et al. 2018
Lylyk et al.
Haffaf et al.
Galal et al.
Bozzetto Ambrosi et al.
Gherasim et al.
Khalid et al.
Mori et al.
Nanda et al.
Bruneau et al.
Lai et al.

◂**Fig. 2** Occlusion rates at T0 16/25 (64.0%), 6–12 months 16/25 (64.0%), and 12 months 12/25 (48.0%) follow-up reported in selected papers

clinical outcome and total occlusion in 52.6% of patients at 12 months' follow-up.

In a systematic review, about the use of flow diverters in distal unruptured aneurysms in anterior circulation, Cagnazzo et al. reported long-term total/near total occlusion rate of 88% ACoAAs [40]. But in our review, we observed a contrasting result of about 66.1% total occlusion at 12 months' follow-up in patients treated with FD. The occlusion rates with intrasaccular devices and extra-saccular flow diverter generally increase with time. This interpretation may be an underestimation due to inconsistent long-term follow-up in the studies included for analysis. Thus, considering the natural history of these unruptured ACoCAs, novel advanced endovascular interventions have laid down promising results in terms of safety and good clinical outcomes although the microsurgical clipping provides a better immediate total occlusion rates with a compromise on safety and morbidity. Acceptance of optimal near total/subtotal occlusion of aneurysms with good clinical outcomes requires future studies of fluid dynamics in assessing the high risk of rupture. This would clarify the optimal targets for intervening on bleeding risks without necessarily achieving complete occlusion and good clinical outcome with these novel endovascular techniques.

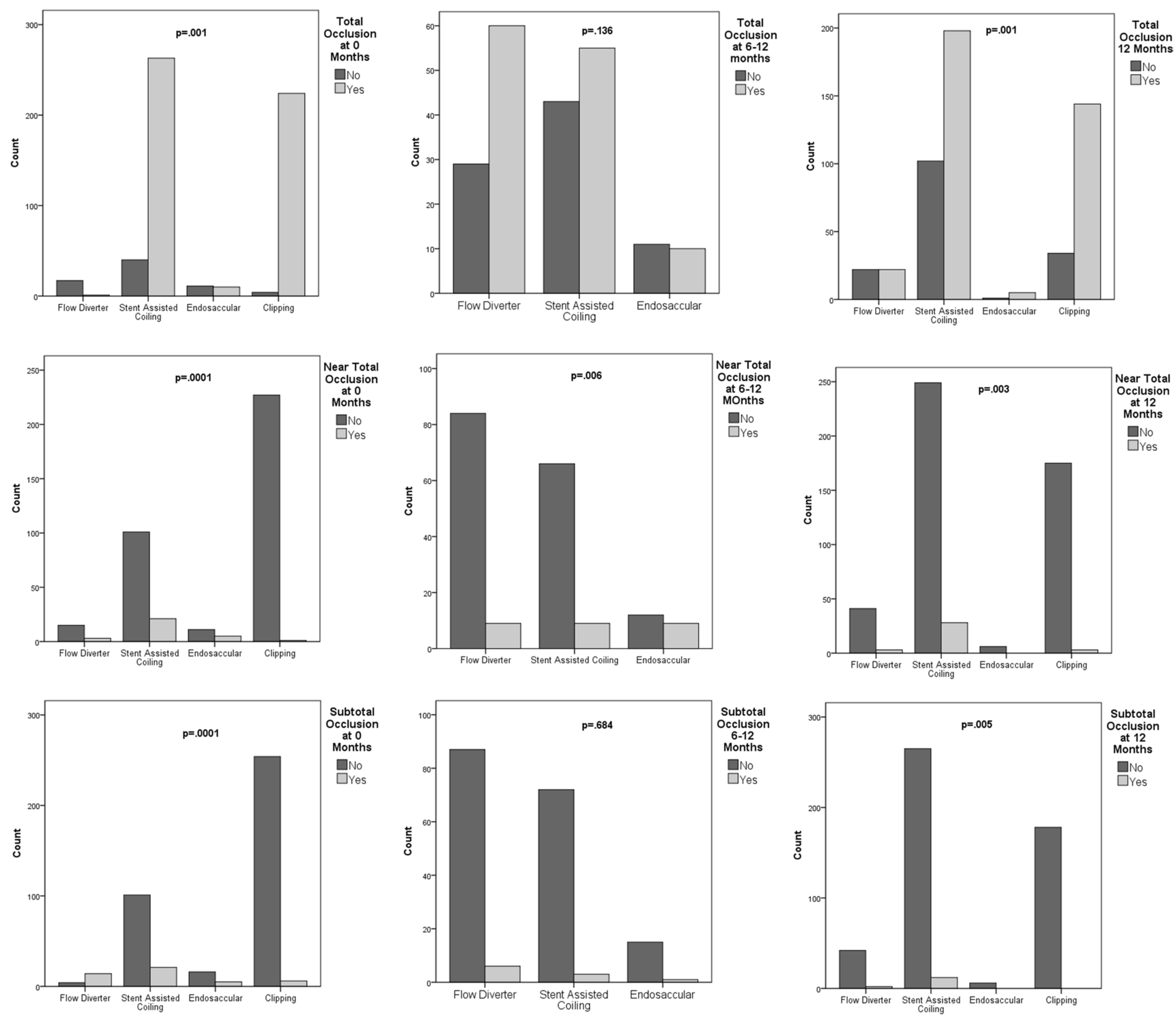


Fig. 3 Overall total, subtotal, and near total occlusion rate at T0, 6–12 months', and 12 months' follow-up reported in selected papers, showing a highest total occlusion rate in the clipping group than in the endovascular group (p=.001) and a higher total occlusion rate in the SAC subgroup among the endovascular techniques (p=0.001). SAC, stent-assisted coiling

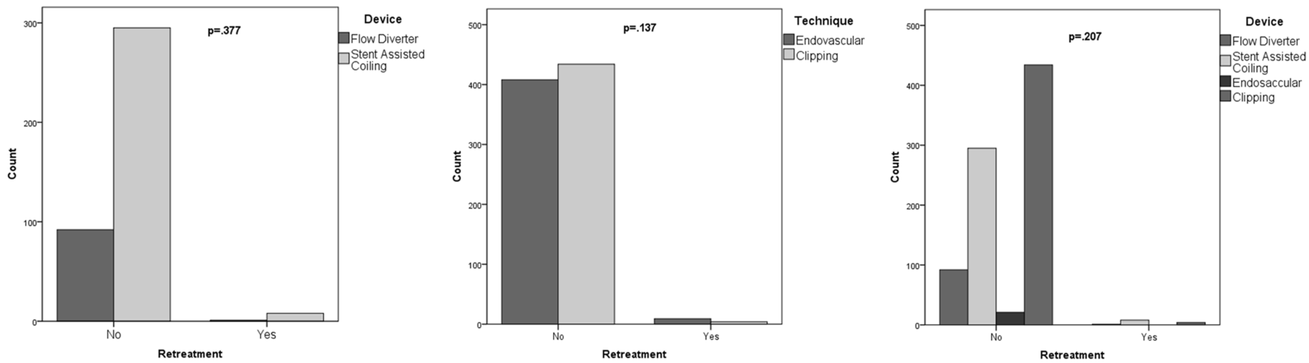


Fig. 4 Second treatment, with no statistically significant difference between the different approaches and techniques

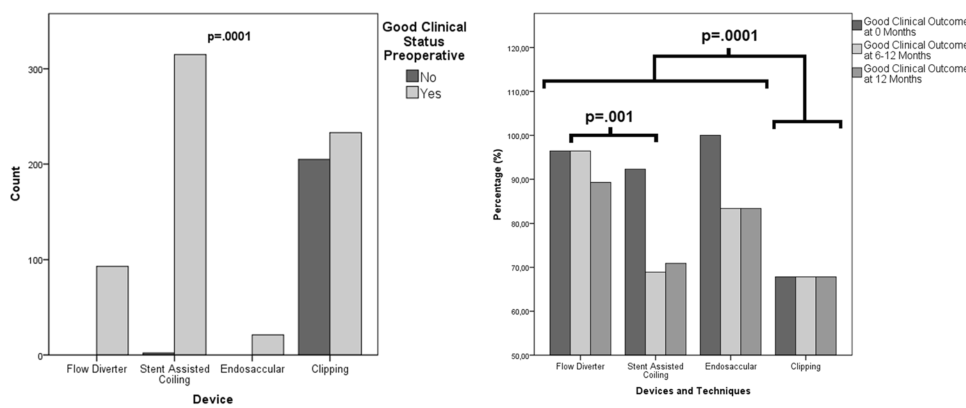


Fig. 5 Good clinical status in preoperative period and good clinical outcome at T0, 6–12 months, and 12 months. Patients of the endovascular groups had a higher good preoperative status and good clinical outcomes than those of the clipping group ($p = 0.0001$)

Limitations of the study

Our study has several limitations. The main limitation is the unavoidable bias produced by the statistical re-analysis of aggregated data from the previously published clinical records. We were not able to stratify the results, based on aneurysm geometry, dimension, and other relevant characteristics. Imaging follow-up was heterogenous regarding the timing and the technique used. The studies with long-term follow-up have extensive range.

Conclusions

Unruptured anterior communicating artery-complex aneurysms can be treated with both microsurgical clipping and advanced novel endovascular techniques. Microsurgical clipping is associated with higher immediate total occlusion rate with a compromise on good clinical outcome and major complication. Novel endovascular techniques are promising in treating unruptured anterior cerebral artery aneurysms with high margin of safety and good clinical outcome with a major compromise on total occlusion rate. Large-volume, long-term prospective trials are required to compare the efficacy of these novel endovascular techniques with microsurgical clipping.

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Data availability All data are available.

Declarations

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